VOLUME ONE

Second Edition

Handbook of Pharmaceutical Manufacturing Formulations

Compressed Solid Products

SARFARAZ K. NIAZI

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SARFARAZ K. NIAZI

Pharmaceutical Scientist, Inc.
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Handbook of Pharmaceutical Manufacturing Formulations: Liquid Products

Volume 4
Handbook of Pharmaceutical Manufacturing Formulations: Semisolid Products

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to the memory of Sidney Riegelman

Preface to the Series—Second Edition

The science and the art of pharmaceutical formulation keeps evolving as new materials, methods, and machines become readily available to produce more reliable, stable, and release-controlled formulations. At the same time, globalization of sourcing of raw and finished pharmaceuticals brings challenges to regulatory authorities and results in more frequent revisions to the current good manufacturing practices, regulatory approval dossier requirements, and the growing need for cost optimization. Since the publication of the first edition of this book, a lot has changed in all of these areas of importance to pharmaceutical manufacturers. The second edition builds on the dynamic nature of the science and art of formulations and provides an evermore useful handbook that should be highly welcomed by the industry, the regulatory authorities, as well as the teaching institutions.

The first edition of this book was a great success as it brought under one umbrella the myriad of choices available to formulators. The readers were very responsive and communicated with me frequently pointing out to the weaknesses as well as the strengths of the book. The second edition totally revised attempts to achieve these by making major changes to the text, some of which include:

1. Complete, revised errors corrected and subject matter reorganized for easy reference. Whereas this series has six volumes differentiated on the basis of the type of dosage form and a separate inclusion of the U.S. OTC products, ideally the entire collection is needed to benefit from the myriad of topics relating to formulations, regulatory compliance, and dossier preparation.
2. Total number of pages is increased from 1684 to 2726.
3. Total number of formulations is expanded by about 30% with many newly approved formulations.
4. Novel formulations are now provided for a variety of drugs; these data are collected from the massive intellectual property data and suggest toward the future trend of formulations. While some of these formulations may not have been approved in the United States or Europe, these do provide additional choices, particularly for the NDA preparation. As always, it is the responsibility of the manufacturer to assure that the intellectual property rights are not violated.
5. A significant change in this edition is the inclusion of commercial products; while most of this information is culled out from the open source such as the FOIA (http://www.fda.gov/foi/default.htm), I have made attempts to reconstruct the critical portions of it based on what I call the generally acceptable standards. The drug companies are advised to assure that any intellectual property rights are not violated and this applies to all information contained in this book. The freedom of information act (FOIA) is an extremely useful conduit for reliable information and manufacturers are strongly urged to make use of this information. Whereas this information is provided free of charge, the process of obtaining the information may be cumbersome, in which case, commercial sources of these databases can prove useful, particularly for the non-U.S. companies.
6. Also included are the new Good Manufacturing Guidelines (2007) with amendments (2008) for the United States and similar updates for European Union and WHO; it is strongly urged that the companies discontinue using all old documents as there are significant changes in the revised form, and many of them are likely to reduce the cost of GMP compliance.
7. Details on design of clean rooms is a new entry that will be of great use to sterile product manufacturers; whereas the design and flow of personnel and material flow is of critical nature, regulatory agencies view these differently and the manufacturer is advised always to comply with most stringent requirements.
8. Addition of a self-auditing template in each volume of the series. While the cGMP compliance is a complex issue and the requirements diversified across the globe, the basic compliance remains universal. I have chosen the European Union guidelines (as these are more in tune with the ICH) to prepare a self-audit module that I recommend that every manufacturer adopt as a routine to assure GMP compliance. In most instances reading the template by those responsible for compliance with keep them sensitive to the needs of GMP.
9. OTC products cross-referenced in other volumes where appropriate. This was necessary since the regulatory authorities worldwide define this class of drug differently. It is important to iterate that regardless of the prescription or the OTC status of a product, the requirements for compliance with the cGMP apply equally.
10. OTC monograph status is a new section added to the OTC volume and this should allow manufacturers to chose appropriate formulations that may not require a filing with the regulatory agencies; it is important to iterate that an approved OTC monograph includes details of formulation including the types and quantities of active drug and excipients, labeling, and presentation. To qualify the exemption, the manufacturer must comply with the monograph in its entirety. However, subtle modifications that are merely cosmetic in nature and where there is an evidence that the modification will not affect the safety and efficacy of the products can be made but require prior approval of the regulatory agencies and generally these approvals are granted.
11. Expanded discussion on critical factors in the manufacturing of formulations provided; from basic shortcuts to smart modifications now extend to all dosage forms. Pharmaceutical compounding is one of the oldest professions and whereas the art of formulations has been

relegated to more objective parameters, the art nevertheless remains. An experienced formulator, like an artist, would know what goes with what and why; he avoids the pitfalls and stays with conservative choices. These sections of the book present advice that is time tested, although it may appear random at times; this is intended for experienced formulators.

12. Expanded details on critical steps in the manufacturing processes provided but to keep the size of the book manageable, and these are included for prototype formulations. The reader is advised to browse through similar formulations to gain more insight. Where multiple formulations are provided for the same drug, it intended to show the variety of possibilities in formulating a drug and whereas it pertains to a single drug, the basic formulation practices can be extended to many drugs of same class or even of diversified classes. Readers have often requested that more details be provided in the Manufacturing Direction sections. Whereas sufficient details are provided, this is restricted to prototype formulations to keep the size of the book manageable and to reduce redundancy.
13. Addition of a listing of approved excipients and the level allowed by regulatory authorities. This new section allows formulators a clear choice on which excipients to choose; the excipients are reported in each volume pertaining to the formulation type covered. The listing is drawn from the FDA-approved entities. For the developers of an ANDA, it is critical that the level of excipients be kept within the range generally approved to avoid large expense in justifying any unapproved level. The only category for which the listing is not provided separately is the OTC volume since it contains many dosage forms and the reader is referred to dosage form–specific title of the series. The choice of excipients forms keeps increasing with many new choices that can provide many special release characteristics to the dosage forms. Choosing correct excipients is thus a tedious exercise and requires sophisticated multivariate statistical analysis. Whereas the formulator may choose any number of novel or classical components, it is important to know the levels of excipients that are generally allowed in various formulations to reduce the cost of redundant exercises; I have therefore included, as an appendix to each volume, a list of all excipients that are currently approved by the U.S. FDA along their appropriate levels. I suggest that a formulator consult this table before deciding on which level of excipient to use; it does not mean that the excipient cannot be used outside this range but it obviates the need for a validation and lengthy justification studies in the submission of NDAs.
14. Expanded section on bioequivalence submission was required to highlight the recent changes in these requirements. New entries include a comprehensive listing of bioequivalence protocols in abbreviated form as approved by the U.S. FDA; these descriptions are provided in each volume where pertinent. To receive approval for an ANDA, an applicant must generally demonstrate, among other things, equivalence of the active ingredient, dosage form, strength, route of administration and conditions of use as the listed drug, and that the proposed drug product is bioequivalent to the reference listed drug [21 USC 355(j)(2)(A); 21 CFR 314.94(a)]. Bioequivalent drug products show no significant difference in the rate and extent of absorption of the therapeutic ingredient [21 U.S.C. 355(j)(8); 21 CFR 320.1(e)]. BE studies are undertaken in support of ANDA submissions with the goal of demonstrating BE between a proposed generic drug product and its reference listed drug. The regulations governing BE are provided at 21 CFR in part 320. The U.S. FDA has recently begun to promulgate individual bioequivalence requirements. To streamline the process for making guidance available to the public on how to design product-specific BE studies, the U.S. FDA will be issuing product-specific BE recommendations (www.fda.gov/cder/ogd/index.htm). To make this vital information available, an appendix to each volume includes a summary of all currently approved products by the U.S. FDA where a recommendation on conducting bioequivalence studies is made available by the U.S. FDA. When filing an NDA or an ANDA, the filer is faced with the choice of defending the methods used to justify the bioavailability or bioequivalence data. The U.S. FDA now allows application for waiver of bioequivalence requirement; a new chapter on this topic has been added along with details of the dissolution tests, where applicable, approved for various dosage forms.
15. Dissolution testing requirements are included for all dosage forms where this testing is required by the FDA. Surrogate testing to prove efficacy and compliance is getting more acceptance at regulatory agencies; in my experience, a well-designed dissolution test is the best measure of continuous compliance. Coupled with chapters on waivers of bioequivalence testing, this information on dissolution testing should be great value to all manufacturers; it is recommended that manufacturers develop their own in-house specifications, more stringent than those allowed in these listings and the USP.
16. Best-selling products (top 200 prescription products) are identified with an asterisk and a brand name where applicable; in all instances, composition of these products is provided and formulation of generic equivalents. Despite the vast expansion of pharmaceutical sales and shifting of categories of blockbuster drugs, basic drugs affecting gastrointestinal tract, vascular system, and brain remain most widely prescribed.
17. Updated list of approved coloring agents in the United States, Canada, European Union, and Japan is included to allow manufactures to design products for worldwide distribution.
18. Tablet-coating formulations that meet worldwide requirements of color selection are included in the Volume 1 (compressed solids) and Volume 5 (OTC) because these represent the products often coated.
19. Guidelines on preparing regulatory filings are now dispersed throughout the series depending on where these guidelines are more crucial. However, the reader would, as before, need access to all volumes to benefit from the advice and guidelines provided.

As always, comments and criticism from the readers are welcomed and these can be sent to me at Niazi@pharmsci.com or Niazi@niazi.com. I would try to respond to any inquiries requiring clarification of the information enclosed in these volumes.

I would like to express deep gratitude to Sherri R. Niziolek and Michelle Schmitt-DeBonis at Informa, the publisher of

this work, for seeing an immediate value to the readers in publishing the second edition of this book and allowing me enough time to prepare this work. The diligent editing and composing staff at Informa, particularly Joseph Stubenrauch, Baljinder Kaur and others are highly appreciated. Regardless, all errors and omissions remain altogether mine.

In the first edition, I had dedicated each volume to one of my mentors; the second edition continues the dedication to these great teachers.

Sarfaraz K. Niazi, Ph.D.
Deerfield, Illinois, U.S.A.

Preface to the Series—First Edition

No industry in the world is more highly regulated than the pharmaceutical industry because of potential threat to a patient's life from the use of pharmaceutical products. The cost of taking a new chemical entity (amortized over the cost of all molecules racing) to final regulatory approval is a staggering $800 million, making the pharmaceutical industry one of the most research-intensive industries in the world. In the year 2004, it is anticipated that the industry will spend about $20 billion on research and development. The generic market of drugs as the new entities come off patent is one of the fastest growing segments of the pharmaceutical industry, with every major multinational company having a significant presence in this field.

Whereas many stages of new drug development are inherently constrained with time, the formulation of drugs into desirable dosage forms remains an area where expediency can be practiced with appropriate knowledge by those who have mastered the skills of pharmaceutical formulations. The *Handbook of Pharmaceutical Manufacturing Formulations* is the first major attempt to consolidate the available knowledge about formulations in a comprehensive, and by nature a rather voluminous, presentation.

The book is divided into six volumes, based strictly on the type of formulation science involved in the development of these dosage forms: sterile products, compressed solids, uncompressed solids, liquid products, semisolid products, and OTC products. The separation of OTC products even though they may easily fall into one of the other five categories is made to comply with the industry norms of separate research divisions for OTC products. Sterile products require skills related to sterilization of product, and of less importance is the bioavailability issue, which is an inherent problem of compressed dosage forms. These types of considerations have led to the classification of products into these six categories.

Each volume includes a description of regulatory filing techniques for the formulations described. Also included are the current regulatory guidelines on cGMP compliance specific to the dosage form. Advice is offered on how to scale up the production batches.

It is expected that formulation scientists will use this information to benchmark their internal development protocols and cut the race to file short by adopting formulae that have survived the test of time. Many of us who have worked in the pharmaceutical industry suffer from a close paradigm when it comes to selecting formulations—"not invented here" perhaps reigns in the mind of many seasoned formulations scientists subconsciously when they prefer to choose only a certain platform for development. It is expected that with the quick review of possibilities available to formulate made available in this book, scientists will benefit from the experience of others.

For the teachers of formulation sciences, this series offers a wealth of information. Whether it is a selection of a preservative system or the choice of a disintegrant, the series offers a wide choice to study and rationalize.

Many have assisted me in the development of this work that has taken years to compile, and I thank scores of my graduate students and colleagues for their help. A work of this size cannot be produced without errors, although I hope that these errors do not distract the reader from the utility of the book. I would sincerely appreciate if readers point out these mistakes for corrections in future editions.

Sarfaraz K. Niazi, Ph.D.
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Preface to the Volume—First Edition

Compressed solids present one of the greatest challenges to formulation scientists, as they offer remarkable marketing opportunities to marketers. A solid oral dosage form is easy to ingest, is relatively more stable than other dosage forms (longer shelf life), and with it, opportunities to design delivery profiles to meet specific therapeutic requirements are offered. As a result, almost two-thirds of all dosage forms fall into this category. The challenge in formulating these products includes finding an optimum medium of compromises that will ensure releases of an active drug at the most desired and consistent rate. The formulation components and process of manufacturing thus take pivotal importance. As a result, the formulations provided in this volume offer a rare opportunity for formulators to start with an optimal composition. Described in this volume are formulations for over 200 of the most widely used drugs for all types of release profiles.

The most significant issues in the formulation of compressed solids are related to bioequivalence. Over the past quarter of a century, the science of evaluating equivalence of products has taken a greater emphasis on testing in human subjects. Although they are expensive to conduct, such trials are now routine, requiring frequent evaluation during the development phases and before marketing new entities. Most frequently, trials are required when establishing generic equivalences. The U.S. FDA may require additional biostudies if there is a change in the manufacturing site or even a change in the specification of a raw material. This aspect of formulation development clearly differentiates the compressed solids category; as a result, chapter 1 in the book deals with the guidelines for bioavailability and bioequivalence testing of pharmaceutical products. Noteworthy are the changes proposed in this guideline from what is the currently accepted methodology; for example, what was long considered necessary, the multiple-dose studies of modified release products, will yield to single-dose studies, which are considered more discriminating. The manufacturers are particularly reminded to understand the changes in the requirements of bioavailability and bioequivalence studies that are on the horizon.

The formulation of compressed solids involves a highly intricate series of events, from the characterization of the active pharmaceutical ingredient, to the choice of excipients, to the selection of processing, compression, and coating equipment and packaging systems appropriate for the specific drug and the dosage form. In chapter 2 of this volume, we highlight what the manufacturers need to be aware of in establishing a manufacturing process based on the formulations presented.

In other volumes of this series, details are provided on various other issues that pertain to the manufacturing of compressed solids, including validation issues, compliance with cGMP, laboratory guidelines, etc. The reader is referred to the other volumes for further understanding of the subject matter.

Compressed solids or tablets are usually applied with coatings, mainly aqueous film coatings, for many reasons, from aesthetics to imparting higher physical–chemical stability. Coating technology is a separate science. Fortunately, the major suppliers of equipment, such as Accela-Cota® and Glatt® and coating materials such as Colorcon® and Röhm®, are very helpful in establishing coating parameters and choosing the right coating materials and formulations. A large number of coating formulations are listed in a separate section in this book, including sugar coating, film coating, and enteric coatings. With such a wide variety available, coating steps are omitted from all formulations where coating is recommended. Instead, the reader is referred to the appropriate section of the book to make an appropriate choice.

The formulations are presented with a scale for each unit, per tablet; and quantities are expressed for 1000 tablets. It is customary for manufacturers to scale formulas for a specific weight, such as 100 or 1000 kg, to match mixing vessel requirements. This can be done roughly by multiplying the weight of each tablet by the quantity desired to calculate the size of the batch. Remember that the actual yield may be different because of differences in the scale and quantity, due to differences in the chemical forms of the drugs used, excesses added, and losses of moisture during manufacturing. Further, the adjustment of quantity based on the potency of the raw material, where pertinent, changes the quantity requirements.

A distinctive feature of this volume is the identification and inclusion of the most popular prescription products. The 200 most widely prescribed drugs (by brand name) are marked with a bracketed number to indicate their rankings. These data are derived from over 3 billion prescriptions filled during 2002 in the United States, comprising the majority of the U.S. prescription market. Because in some instances more than one brand name is prescribed, only the top brand is listed; therefore, the total number of chemical equivalents is less than 200. The compressed solids represent more than an 80% share of this list, therefore expounding the need to elaborate this list in this particular volume. Obviously, for a generic manufacturer, it would be advantageous to enter the market with products that have a wide market, not necessarily the largest margin, and this list will further help in the selection of products. It is noteworthy that in the preparation of an ANDA (Abbreviated New Drug Application), it is important for both regulatory and scientific reasons to keep the selection of excipients as close as possible to the innovator's product. The listing provided here includes every excipient used in the innovator listing. Whereas, in most instances, sufficient details are provided to assist in the formulation of a generic equivalent with exact quantities of excipients and conditions appropriate for processing, the examples provided for other drugs of similar types should be sufficient for an astute formulator to quickly develop these formulations. However, should there be a need for assistance in finalizing

the formulation, the reader is invited, without any obligation, to write to the author at niazi@pharmsci.com.

I am grateful to CRC Press for taking this lead in publishing what is possibility the largest such work in the field of pharmaceutical products. It has been a distinct privilege to have known Mr. Stephen Zollo, the senior editor at CRC Press, for many years. Stephen has done more than any editor can to encourage me to complete this work on a timely basis. The editorial assistance provided by the CRC Press staff was exemplary, particularly the help given by Erika Dery, Joette Lynch, and others at CRC Press. Although much care has gone into correcting errors, any errors remaining are altogether mine. I would appreciate it if the readers bring these errors to my attention so that they can be corrected in future editions of this volume (niazi@pharmsic.com).

This book is dedicated to Sidney Riegelman, who was born July 19, 1921, in Milwaukee, Wisconsin. He attended the University of Wisconsin, graduating with a Bachelor of Science degree in pharmacy in 1944 and a Ph.D. in pharmacy in 1948. Following his graduate work, Sid joined the faculty of the School of Pharmacy at the University of California at San Francisco. In 1958, Sid published a series of papers with graduate student Wilfred Crowell, which appeared in the scientific edition of the *Journal of the American Pharmaceutical Association* under the major heading of "The Kinetics of Rectal Absorption." For these studies, Sid was awarded the Ebert Prize in 1959, which recognized Sid's publications as the best work published in the journals of the American Pharmaceutical Association during the year 1958. Sid's contributions to pharmaceutical sciences, particularly in the field of pharmacokinetics, earned him a revered place in the profession. On April 4, 1981, Sid drowned while scuba diving with his wife at Salt Point, California, a coastal area just north of San Francisco. At the University of California, a plaque is dedicated to Sid "by his graduate students, who honor his scientific achievements and excellence, his inspirations and contagious enthusiasm in research and teaching. We shall always remember Sid as our mentor, scientific father and most importantly, as our beloved friend and confidant."

I had the distinct privilege, both during my graduate studies and later as a faculty member teaching biopharmaceutics and pharmacokinetics, to interact with Sid. When my book, *Textbook of Biopharmaceutics and Clinical Pharmcokinetics*, was published, Sid called to congratulate me. It was like receiving a call from God—that is how he was revered in the profession. I remember vividly how he would argue in seminars while appearing to be dozing off during the presentation. Sid was a giant: a scientist, a scholar, and, above all, a loving human being. When a professional crisis arose, I called Sid for advice. Instead of telling me what I should do, Sid told me a story about his childhood: "Sarf, my brother was much stronger than I and every time he would run into me, he would take a jab at me, and when I would return his jab, he would knock me down. I complained about this to my father, and my father advised me not to return the jabs. My brother became so frustrated, he started jabbing others." I have never forgotten his advice.

Sarfaraz K. Niazi, Ph.D.
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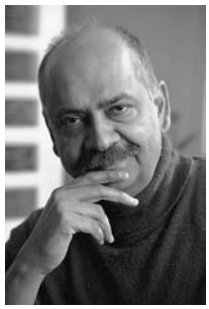
About the Author



Sarfaraz K. Niazi has been teaching and conducting research in the pharmaceutical industry for over 35 years. He has authored hundreds of scientific papers, textbooks, and presentations on the topics of pharmaceutical formulation, biopharmaceutics, and pharmacokinetics of drugs. He is also an inventor with scores of patents in the field of drug and dosage form delivery systems; he is also licensed to practice law before the U.S. Patent and Trademark Office. Having formulated hundreds of products from the most popular consumer entries to complex biotechnology-derived products, he has accumulated a wealth of knowledge in the science and art of formulating and regulatory filings of investigational new drugs (INDs) and new drug applications (NDAs). Dr. Niazi advises the pharmaceutical industry internationally on issues related to formulations, cGMP compliance, pharmacokinetics and bioequivalence evaluation, and intellectual property issues (http://www.pharmsci.com). He can be contacted at Niazi@pharmsci.com

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Part I

Regulatory and Manufacturing Considerations

1

Bioequivalence Testing Rationale and Principles

I. BACKGROUND

The bioavailability of a drug is controlled by three factors, namely:

- the rate and extent of release of the drug from the dosage form,
- its subsequent absorption from the solution state, and
- the biotransformation during the process of absorption.

In all quantitative determinations of bioavailability, concentration is measured in blood, plasma, and urine. Plasma concentrations following the oral administration of a drug assume four sequential phases depending on the magnitude of absorption and elimination:

1. Absorption > elimination
2. Absorption = elimination
3. Absorption < elimination
4. Absorption = elimination = 0

The shape of the plasma concentration profile depends on the relative rates of absorption and elimination and thus, the plasma concentration profiles may be quite different with different routes of administration. Intravenous and sometimes intramuscular routes yield an early peak due to fast or almost instantaneous absorption, whereas oral, subcutaneous, rectal, and other routes may show delayed peaks due to slower rates of absorption. It should be noted that the rate of elimination is considered constant since it depends primarily in the specific nature of the active drug ingredient.

The purpose of bioavailability studies is to demonstrate therapeutic equivalence. However, depending on the mechanism of action, more meaningful comparisons can be made from such parameters as peak plasma concentration or the time to reach peak plasma concentration. For example, in the case of antibiotics, it is important to know how soon the minimum inhibitory concentration is reached and maintained. The choice of single-dose versus multiple-dose study depends on the mechanism of drug action. For example, antidepressants like imipramine show delayed action, a characteristic of many psychotropic and antihypertensive agents. In these instances, a new product should be judged for its quality from repeated administration because in these examples the peak concentration or time for peak concentration is relatively unimportant. It is therefore important to isolate the clinically important parameter, but in all instances, the AUC must be monitored since it represents the proportionality to the total amount of drug eliminated from the body and hence absorbed.

The estimation of bioavailability from plasma concentration profiles requires a thorough understanding of the nature of plasma level profiles. For example, a higher or earlier peak does not necessarily mean greater overall absorption than from a product giving a smaller or delayed peak. The total absorption of drugs is, therefore, proportional not only to the plasma concentrations achieved but also to the length of time these concentrations persist in the blood. One parameter that characterizes this aspect is the area under the plasma concentration versus time profile.

The major contribution to the area under the curve (AUC) for a fast-absorbed formulation is due to the high, peak concentration; whereas for a slowly absorbed formulation, the area is mainly because of sustained or prolonged plasma concentration. It should be noted that the area under the plasma concentration versus time profile is only proportional to the total amount of drug absorbed and cannot be used to determine the actual amount of drug administered unless it is compared with a known standard, whereby the extent of absorption is either measured by other methods or assumed to be 100%, as in the case of intravenous administration.

The in vivo bioavailability of a drug product is measured if the product's rate and extent of absorption, as determined by comparison of measured parameters, for example, concentration of the active drug ingredient in the blood, urinary excretion rates, or pharmacological effects, do not indicate a significant difference from the reference material's rate and extent of absorption. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action.

Statistical techniques used in establishing bioequivalence shall be of sufficient sensitivity to detect differences in rate and extent of absorption that are not attributable to subject variability.

A drug product that differs from the reference material in its rate of absorption, but not in its extent of absorption, may be considered to be bioavailable if the difference in the rate of absorption is intentional, is appropriately reflected in the labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug product.

Two drug products will be considered bioequivalent drug products if they are pharmaceutical equivalents or pharmaceutical alternatives whose rate and extent of absorption do not show a significant difference when administered at the same molar dose of the active moiety under similar experimental conditions, either single dose or multiple dose. Some pharmaceutical equivalents or pharmaceutical alternatives may be equivalent in the extent of their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the rate of absorption are intentional and are reflected in the labeling, are not essential to the attainment of effective body drug concentrations on chronic use, and are considered medically insignificant for the particular drug product studied.

II. EVIDENCE TO MEASURE BIOEQUIVALENCE

In vivo bioequivalence may be determined by one of several direct or indirect methods. Selection of the method depends

upon the purpose of the study, the analytical method available, and the nature of the drug product. Bioequivalence testing should be conducted using the most appropriate method available for the specific use of the product.

The preferred hierarchy of bioequivalence studies (in descending order of sensitivity) is the blood-level study, pharmacologic end-point study, and clinical end-point study. When absorption of the drug is sufficient to measure drug concentration directly in the blood (or other appropriate biological fluids or tissues) and systemic absorption is relevant to the drug action, then a blood (or other biological fluid or tissue) level bioequivalence study should be conducted. The blood-level study is generally preferred above all others as the most sensitive measure of bioequivalence. The sponsor should provide justification for choosing either a pharmacologic or clinical end-point study over a blood-level (or other biological fluids or tissues) study.

When the measurement of the rate and extent of absorption of the drug in biological fluids cannot be achieved or is unrelated to drug action, a pharmacologic end-point (i.e., drug-induced physiologic change which is related to the approved indications for use) study may be conducted. Lastly, in order of preference, if drug concentrations in blood (or fluids or tissues) are not measurable or are inappropriate, and there are no appropriate pharmacologic effects that can be monitored, then a clinical end-point study may be conducted, comparing the test (generic) product to the reference (pioneer) product and a placebo (or negative) control.

Bioavailability may be measured or bioequivalence may be demonstrated by several in vivo and in vitro methods. FDA may require in vivo or in vitro testing, or both, to measure the bioavailability of a drug product or establish the bioequivalence of specific drug products. Information on bioequivalence requirements for specific products is included in the current edition of FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" and any current supplement to the publication. The selection of the method used to meet an in vivo or in vitro testing requirement depends upon the purpose of the study, the analytical methods available, and the nature of the drug product. The following in vivo and in vitro approaches, in descending order of accuracy, sensitivity, and reproducibility, are acceptable for determining the bioavailability or bioequivalence of a drug product:

- An in vivo test in humans in which the concentration of the active ingredient or active moiety, and when appropriate, its active metabolite(s), in whole blood, plasma, serum, or other appropriate biological fluid is measured as a function of time. This approach is particularly applicable to dosage forms intended to deliver the active moiety to the bloodstream for systemic distribution within the body.
- An in vitro test that has been correlated with and is predictive of human in vivo bioavailability data.
- An in vivo test in humans in which the urinary excretion of the active moiety, and when appropriate, its active metabolite(s), is measured as a function of time. The intervals at which measurements are taken should ordinarily be as short as possible so that the measure of the rate of elimination is as accurate as possible. Depending on the nature of the drug product, this approach may be applicable to highly metabolized drugs. This method is not appropriate where urinary excretion is not a significant mechanism of elimination.
- An in vivo test in humans in which an appropriate acute pharmacological effect of the active moiety, and when appropriate, its active metabolite(s), is measured as a function of time if such effect can be measured with sufficient accuracy, sensitivity, and reproducibility. This approach is applicable only when appropriate methods are not available for measurement of the concentration of the moiety, and when appropriate, its active metabolite(s), in biological fluids or excretory products but a method is available for the measurement of an appropriate acute pharmacological effect. This approach may be particularly applicable to dosage forms that are not intended to deliver the active moiety to the bloodstream for systemic distribution.
- Well-controlled clinical trials that establish the safety and effectiveness of the drug product, for purposes of measuring bioavailability, or appropriately designed comparative clinical trials, for purposes of demonstrating bioequivalence. This approach is the least accurate, sensitive, and reproducible of the general approaches for measuring bioavailability or demonstrating bioequivalence. For dosage forms intended to deliver the active moiety to the bloodstream for systemic distribution, this approach may be considered acceptable only when analytical methods cannot be developed to permit use of one of the approaches outlined above are not available. This approach may also be considered sufficiently accurate for measuring bioavailability or demonstrating bioequivalence of dosage forms intended to deliver the active moiety locally, for example, topical preparations for the skin, eye, and mucous membranes; oral dosage forms not intended to be absorbed, for example, an antacid or radiopaque medium; and bronchodilators administered by inhalation if the onset and duration of pharmacological activity are defined.
- A currently available in vitro test acceptable to FDA (usually a dissolution rate test) that ensures human in vivo bioavailability.
- Any other approach deemed adequate by FDA to measure bioavailability or establish bioequivalence.

FDA may require in vivo testing in humans of a product at any time if the agency has evidence that the product

- may not produce therapeutic effects comparable to a pharmaceutical equivalent or alternative with which it is intended to be used interchangeably,
- may not be bioequivalent to a pharmaceutical equivalent or alternative with which it is intended to be used interchangeably, or
- has greater than anticipated potential toxicity related to pharmacokinetic or other characteristics.

A list of therapeutic, pharmacokinetic, and physicochemical factors has been compiled to classify which product needs demonstration of bioequivalence by in vivo testing (Table 1.1). A large number of drugs have been classified in this category (Table 1.2). All enteric-coated and -controlled release dosage forms of any solid oral dosage form require in vivo bioavailability testing. It is generally suggested that if there is more than 25% intrabatch or batch-to-batch variability in bioavailability is observed, in vivo tests will be required for batch certification. Any changes in the manufacturing process, including product formulation or dosage strength change, beyond that suggested in the NDA or ANDA and changes in labeling for a new indication or new dosage regimen also require in vivo bioavailability testing.

The pharmacotherapeutic nature of the drug plays an important role in the regulations regarding its bioavailability.

Table 1.1 Factors Determining the Establishment of Biequivalence Requirement by the FDA

1. Therapeutic factors evidence from
   a. clinical trials,
   b. controlled observations on patients, and
   c. well-controlled bioequivalence studies that
      i. the drug exhibits a low therapeutic ratio,
      ii. the drug requires careful dosage titration, and
      iii. bioinequivalence would produce adverse prophylacitc or therapeutic effects.
2. Pharmacokinetic factors evidence that the drug entity
   a. is absorbed from localized sites in the gastrointestinal tract,
   b. is subject to poor absorption,
   c. is subject to first-pass metabolism,
   d. requires rapid dissolution and absorption for effectiveness,
   e. is unstable in specific portions of the gastrointestinal tract, and
   f. is subject to dose-dependent kinetics in or near the therapeutic range.
3. Physiochemical factors evidence that the drug
   a. possesses low solubility in water or gastric fluids,
   b. is dissolved slowly from one or more of its dosage forms,
   c. particle size and/or surface area affects bioavailability,
   d. exhibits certain physical-structural characteristics e.g., polymorphism, solvates, etc. which modify its bioavailability,
   e. has a high ratio of excipients to active ingredients as formulated, and
   f. has a bioavailability which may be affected by the presence or absence of hydrophilic or hydrophobic excipients and lubricant.

Drugs which exhibit narrow therapeutic index, that is, less than a twofold difference in median lethal dose and median effective dose values (or less than a twofold difference in the minimum effective concentration and minimum toxic concentration in the blood), require careful demonstration of bioavailability and the consistency with which this requirement is met. Further consideration is needed in the type of side effects occurring if a toxic level is reached. For example, the therapeutic index (the U.S. FDA prefers to call this therapeutic range) for salicylates is smaller than cardiac glycosides; it does not mean that cardiac glycosides are less toxic. It merely signifies that the concentration of salicylates for therapeutic response is closer to the concentration where undesirable side effects start to appear. Another consideration along the same line is the potency of drug in question. Generally, highly potent drugs will require greater control of bioavailability than the one with lesser potency. Because of the logarithmic nature of the response, the curves flatten out at low and high doses. Thus a highly potent drug used in large doses will show lesser variability in response due to bioavailability factor than a low-potency drug used at a dose level where the response is log-linear. Any such comparison, however, should take into account the relative nature of the slope of the response to dose.

Table 1.2 Drugs with Potential Bioequivalency Problems

Acetazolamide	Hydrofluemthiazide	Propylthiouracil
Acetyldigitoxin	Imipramine	Pyrimethamine
Alseroxylon	Isoproterenol	Quinethiazide
Aminophyllin	Liothyronine	Quinidine
Aminosalicylic acid	Menadione	Rauwolfia serpentina
Bendrolflumethiazide	Mephenytoin	Rescinnamine
Benzthiazide	Methazolamide	Reserpine
Betamethasone	Methyclothizaide	Salicylazosulfapyridine
Bishydroxycoumarin	Methylprednisolone	Sodium sulfoxone
Chlorambucil	Methyltestosterone	Spironolactone
Chlorodiazepoxide	Nitrofurantoin	Sulfadiazine
Chloropromazine	Oxtriphylline	Sulfadimethoxine
Chlorothiazide	Para-aminosalicylic acid	Sulfamerazine
Cortisone acetate	Para-methadione	Sulfaphenazole
Deserpidine	Perphenazine	Sulfasomidine
Dexamethasone	Phenacemide	Sulfasoxazole
Dichlorphenamide	Phensuximide	Theophylline
Dienestrol	Phenylaminosalicylate	Thioridazine
Diethylstilbestrol	Phenytoin	Tolbutamide
Dyphylline	Pheytonadione	Triamcinolone
Ethinyl estradiol	Polythiazide	Trichlormethiazide
Ethosuxmide	Prednisolone	Triethyl melamine
Ethotoin	Primidone	Trifluoperazine
Ethoxzolamide	Probenecid	Triflupromazine
Fludrocortisone	Procainamide	Trimeprazine
Fluphenazine	Prochlorperazine	Trimethadione
Fluprednisolone	Promazine	Uracil mustand
Hydralazine	Promethazine	Warfarin
Hydrochlorothiazide		

The physicochemical evidence needed to establish a bioequivalence includes low water solubility, for example, less than 5 mg/mL, or if dissolution in the stomach is critical to absorption, the volume of gastric fluids required to dissolve the recommended dose (gastric fluid content is assumed to be 100 mL for adults and is prorated for infants and children). The dissolution rates are also taken into consideration if less than 50% of the drug dissolves in 30 minutes using official methods. Also included under physicochemical evidence are particle size and surface area of the active drug ingredient. Certain physical structural characteristics of the active drug ingredient, for example, polymorphism, solvation, etc., are also considered. Drug products which have a high ratio of excipients to active ingredients (e.g., greater than 5:1) may also be subjected to bioequivalency demonstration. Other evidence includes specific absorption sites or where the available dose is less than 50% of an administered dose. Drugs which are rapidly biotransformed in the intestinal wall or liver during absorption, and drugs which are unstable in specific portions of the gastrointestinal tract requiring special coating or formulations, are also subjected to bioequivalency requirements, as are drugs which show dose-dependent absorption, distribution, biotransformation, or elimination.

For some dosage forms, bioequivalency requirements can be waived such as with topical products, oral dosage forms not intended for absorption, inhalations, and solutions if there is sufficient evidence that the inactive ingredients do not affect the release and delivery of drugs from the dosage form.

III. PIVOTAL PARAMETERS FOR BLOOD-LEVEL BIOEQUIVALENCE

The sponsor is encouraged to calculate parameters using formulas which involve only the raw data (i.e., so-called model-independent methods).

A. Area Under the Curve Estimates

The extent of product bioavailability is estimated by the area under the blood concentration versus time curve (AUC). AUC is most frequently estimated using the linear trapezoidal rule. Other methods for AUC estimation may be proposed by the sponsor and should be accompanied by appropriate literature references during protocol development. For a single-dose bioequivalence study, AUC should be calculated from

time 0 (predose) to the last sampling time associated with quantifiable drug concentration AUC (0–LOQ). The comparison of the test and reference product value for this noninfinity estimate provides the closest approximation of the measure of uncertainty (variance) and the relative bioavailability estimate associated with AUC (0–INF), the full extent of product bioavailability. The relative AUC values generally change very little once the absorption of both products has been completed. However, because of the possibility of multifunctional absorption kinetics, it cannot always be determined when the available drug has been completely absorbed. Therefore, FDA recommends extending the duration of sampling until such time that AUC (0–LOQ)/AUC (0–INF) = 0.80. Generally, the sampling times should extend to at least 3 multiples of the drug's apparent terminal elimination half-life, beyond the time when maximum blood concentrations are achieved.

AUC (0–INF) should be used to demonstrate that the concentration time curve can be quantitated such that AUC (0–LOQ)/AUC (0–INF) $>=$ 0.80. The method for estimating the terminal elimination phase should be described in the protocol and the final study report. The AUC (0–LOQ)/AUC (0–INF) is calculated to determine whether AUC (0–LOQ) adequately reflects the extent of absorption.

The sponsor should consult with FDA if AUC (0–LOQ)/AUC (0–INF) is determined to be <0.80. If AUC (0–LOQ)/AUC (0–INF) is <<0.80, then a multiple-dose study to steady state may be needed to allow an accurate assessment of AUC (0–INF) (where AUC (0–INF) = AUC (0–t) at steady state and t is the dosing interval).

In a multiple-dose study, the AUC should be calculated over one complete dosing interval AUC (0–t). Under steady-state conditions, AUC (0–t) equals the full extent of bioavailability of the individual dose AUC (0–INF) assuming linear kinetics. For drugs which are known to follow nonlinear kinetics, the sponsor should consult with FDA to determine the appropriate parameters for the bioequivalence determination.

IV. RATE OF ABSORPTION

The rate of absorption will be estimated by the maximum observed drug concentration (C_{max}) and the corresponding time to reach this maximum concentration (T_{max}). When conducting a steady-state investigation, data on the minimum drug concentrations (trough values) observed during a single dosing interval (C_{min}) should also be collected. Generally, three successive C_{min} values should be provided to verify that steady-state conditions have been achieved. Although C_{min} most frequently occurs immediately prior to the next successive dose, situations do occur with C_{min} observed subsequent to dosing. To determine a steady-state concentration, the C_{min} values should be regressed over time and the resultant slope should be tested for its difference from zero.

V. DETERMINATION OF PRODUCT BIOEQUIVALENCE

Unless otherwise indicated by FDA during the protocol development for a given application, the pivotal bioequivalence parameters will be C_{max} and AUC (0–LOQ) (for a single-dose study) or AUC (0–t) (for a multiple-dose study). To be indicative of product bioequivalence, the pivotal metrics should be associated with confidence intervals which fall within a set of acceptability limits.

The sponsor and FDA should agree to the acceptable bounds for the confidence limits for the particular drug and formulation during protocol development. If studies or literature demonstrate that the pioneer drug product exhibits highly variable kinetics, then the generic drug sponsor may propose alternatives to the generally acceptable bounds for the confidence limits. T_{max} in single-dose studies and C_{min} in multiple-dose studies will be assessed by clinical judgment.

VI. ERRORS IN BE STUDIES

Erroneous conclusions can easily be made if the logic behind bioavailability studies is not clearly understood. The following are the important highlights of the most common errors:

1. When concentrations are monitored in the biologic fluids, the specificity of the assay methods is of utmost importance. This is especially applicable to single-dose studies in which small concentrations should be monitored in order to allow study of the complete elimination of the drug from the body.
2. It is generally assumed that the absorption rates of drugs are higher than the rates of elimination, but there can be exceptions, in which case the terminal plasma concentration profiles would represent both the absorption and elimination processes and the mathematical/statistical models used should take this into account.
3. The extrapolation of plasma or urinary concentration data to compensate for missing experimental points always introduces some error in the calculations; it is desirable to extend the study to at least three elimination half-lives when plasma concentration is monitored, and for at least seven half-lives when monitoring urinary excretion of drugs to estimate their bioavailability.
4. There is often lack of sufficient data points to characterize the plasma concentration profiles. Significant area can be lost if sufficient points are not collected during the peaking of the concentration. In general, there should be at least three data points before the peak occurs and at least four or five values after the peak, if possible.
5. The variation among individuals in the elimination rates of a drug should be considered. The proportionality between AUC and bioavailability is based on the assumption that the elimination rates are invariant; any deviation from the norm will result in significant error. Correction of this error can be made if the elimination rate constants are calculated for each subject and the AUC is corrected. If a drug is eliminated fast, K will be large, accounting for possible underestimation of the AUC.
6. Comparison of data for different studies which may not be well matched in terms of the characteristics of the subject population, study conditions, or routes of drug administration should be made with due consideration to these factors. It is ironic that such cross-study comparisons are both very common and very misleading.
7. When identical drug concentrations are obtained in the plasma following administration of equimolar doses from different formulations, these formulations are considered bioequivalent and the principle is referred to as the superimposition principle. In using this principle, one must choose a number of subjects in accordance with the statistical criteria which will demonstrate at least 20% differences in the means of values in order to make them clinically significant. This criterion can be applied to the concentration

at each sampling time, to the peak concentration, and to the time of the peak concentrations and the AUCs.

8. It should be noted that just because a drug product meets compendial standards of purity and other criteria, its bioavailability is not assured. In fact, compendial requirements fall far short of assuring the efficiency of dosage forms in releasing drugs. The latest edition of USP and NF requires demonstration of sufficient dissolution for many drugs where evidence of dissolution affecting bioavailability has been suggested. A large number of drugs remain to be included in this list and it is hoped that eventually demonstration of bioavailability will become a compendial requirement. The costs of performing bioavailability studies make such requirements impractical for some drugs. However, without such requirements it is difficult to justify the rejection of a product on the grounds that its chemical equivalence varies by more than 10%, when its biologic equivalent is allowed to vary to any degree.

VII. ABSORPTION PROFILING

The following are factors and oral drugs/drug products that should be considered when requesting a waiver of evidence of in vivo bioavailability or bioequivalence documentation. Generally, both in vivo and in vitro testing are necessary for orally administered drug products. In vivo testing is required for all generic drug products with certain exceptions. Based on scientific information, regulatory authorities may waive the requirement for bioavailability or bioequivalence.

1. For certain formulations and under certain circumstances, equivalence between two pharmaceutical products may be considered self-evident and no further documentation is required. For example:
   a. When multisource pharmaceutical or generic products are to be administered parenterally (e.g., intravenous, intramuscular, subcutaneous, intrathecal administration) as aqueous solutions and contain the same active substance(s) in the same concentration and the same excipients in comparable concentrations.
   b. When multisource pharmaceutical or generic products are solutions for oral use, contain the active substance in the same concentration, and do not contain an excipient that is known or suspected to affect gastrointestinal transit or absorption of the active substance.
   c. Gas-based multisource pharmaceutical or generic products.
   d. When the multisource pharmaceutical or generic products are powders for reconstitution as a solution and the solution meets either criterion (a) or criterion (b) above.
   e. *When multisource pharmaceutical or generic products are otic or ophthalmic products prepared as aqueous solutions, containing the same active substance(s) in the same concentration and essentially the same excipients in comparable concentrations.
   f. *When multisource pharmaceutical or generic products are topical products prepared as aqueous solutions, containing the same active substance(s) in the same concentration and essentially the same excipients in comparable concentrations.
   g. *When multisource pharmaceutical or generic products are inhalation or nasal spray products, tested to be administered with or without essentially the same device, prepared as aqueous solutions, and containing the same active substance(s) in the same concentration and essentially the same excipients in comparable concentrations. Special in vitro testing should be required to document comparable device performance of the multisource inhalation product.
2. In the event the applicant cannot provide this information about the reference product and the drug regulatory authority does not have access to these data or the data is protected under data exclusivity rights according to local regulations, in vivo studies should be performed.
3. For certain drug products, bioavailability or bioequivalence may be demonstrated by evidence obtained in vitro in lieu of in vivo data. Regulatory authorities should waive the requirement for the submission of evidence obtained in vivo demonstrating the bioavailability of the drug product if the drug product meets one of the following criteria:
   a. The drug product is in the same dosage form, but in a different strength, and is proportionally similar in its active and inactive ingredients to another drug product manufactured at the same site for which the same manufacturer has obtained approval and the following conditions are met:
   b. The bioavailability of this other drug product has been demonstrated;
   c. Both drug products meet an appropriate in vitro test approved by a drug regulatory authority and/or accepted reference pharmacopeias, or has demonstrated in vivo–in vitro correlation (e.g., correlation level A, etc.).
   d. The applicant submits evidence showing that both drug products are proportionally similar in their active and inactive ingredients. That is, the ratio of active ingredients and excipients between strengths is essentially the same.
   e. The drug product is a reformulated product that is identical, except for a different color, flavor, or preservative that could not affect the bioavailability of the reformulated product, to another drug product for which the same manufacturer has obtained approval and the following conditions are met:
   f. The bioavailability of the other product has been demonstrated;
   g. Both drug products meet an appropriate in vitro test approved by the regulatory authority.
   h. Regulatory authorities, for good cause, may require evidence of in vivo bioavailability or bioequivalence for any drug product if the agency determines that any difference between the drug product and a listed drug may affect the bioavailability or bioequivalence of the drug product. The Bioavailability and Bioequivalence Working Group strongly recommends that in the case of antiretroviral drug products proof of pharmaceutical equivalence and bioequivalence be required to infer therapeutic equivalence.

VIII. PHARMACOKINETIC MEASURES OF SYSTEMIC EXPOSURE

Direct (e.g., rate constant, rate profile) and indirect (e.g., C_{max}, T_{max}, mean absorption time, mean residence time, C_{max}

*For elements (e), (f), and (g) above, it is incumbent upon the applicant to demonstrate that the excipients in the multisource product are essentially the same and in comparable concentrations as those in the reference product.

normalized to AUC) pharmacokinetic measures are limited in their abilities to assess rate of absorption. This guideline, therefore, recommends a change in focus from these direct or indirect measures of absorption rate to measures of systemic exposure. The C_{max} and AUC values can continue to be used as measures for product quality BA and BE, but more in terms of their capacity to assess exposure than their capacity to reflect the rate and extent of absorption. Reliance on systemic exposure measures should reflect comparable rates and extents of absorption, which, in turn, should achieve the underlying statutory and regulatory objective of ensuring comparable therapeutic effects. Exposure measures are defined relative to early, peak, and total portions of the plasma, serum, or blood concentration–time profile.

A. Early Exposure

For orally administered immediate-release drug products, BE may generally be demonstrated by measurements of peak and total exposure. An early exposure measure may be informative on the basis of appropriate clinical efficacy and safety trials or pharmacokinetic and pharmacodynamic studies that call for better control of drug absorption into the systemic circulation (e.g., to ensure rapid onset of an analgesic effect or to avoid an excessive hypotensive action of an antihypertensive). In this setting, the guidance recommends use of partial AUC as an early exposure measure. The partial area should be truncated at the population median of T_{max} values for the reference formulation. At least two quantifiable samples should be collected before the expected peak time to allow adequate estimation of the partial area.

B. Peak Exposure

Peak exposure should be assessed by measuring the peak drug concentration (C_{max}) obtained directly from the data without interpolation.

C. Total Exposure

For single-dose studies, the measurement of total exposure should be as follows:

- Area under the plasma/serum/blood concentration–time curve from time 0 to time t (AUC_{0-t}), where t is the last time point with measurable concentration for individual formulation.
- Area under the plasma/serum/blood concentration–time curve from time 0 to time infinity ($AUC_{0-\infty}$), where $AUC_{0-\infty} = AUC_{0-t} + C_t/l_z$, C_t is the last measurable drug concentration, and l_z is the terminal or elimination rate constant calculated according to an appropriate method; the terminal half-life ($t_{1/2}$) of the drug should also be reported.

For steady-state studies, the measurement of total exposure should be the area under the plasma, serum, or blood concentration–time curve from time 0 to time t over a dosing interval at steady state (AUC_{0-t}), where t is the length of the dosing interval.

IX. STATISTICAL ANALYSIS

The statistical models used in the evaluation of BE data have been evolving over the past few decades. The standard statistical method of null hypothesis were the first to be used where no difference is proved and rejection of null indicates statistically significant different ($p < 0.05$). A problem arises since small differences with $p < 0.05$ may be unimportant and large differences with $p > 0.05$ may be important. This prompted FDA to solve the problem by requesting power analysis confidence interval test of Schuirman where two one-sided comparisons are made; this also evolved in the use of the famous 75 to 125 rule to deal with individual effects.

FDA advocates the use of 90% confidence intervals, as the best available method for evaluating bioequivalence study data. The confidence interval approach should be applied to the individual parameters of interest (e.g., AUC and C_{max}). The sponsor may use untransformed or log-transformed data. However, the choice of untransformed or log-transformed data should be made by the sponsor with concurrence by FDA prior to conducting the study.

X. UNTRANSFORMED DATA

If we let T_1 be the mean for the test drug in period 1, T_2 the mean for the test drug in period 2, and R_1 and R_2 the respective means for the reference drug, then the estimates for the drugs averaged over both periods are $T = (1/2)(T_1 + T_2)$ for the test drug and $R = (1/2)(R_1 + R_2)$ for the reference drug. Although both sequence groups usually start with the same number of animals, the number of animals in each sequence group (n_A and n_B) that successfully finish the study may not be equal. The formulas above utilize the marginal or least squares estimates of μT and μR, the corresponding means in the target population. These means are not a function of the sample size in each sequence.

An analysis of variance is needed to obtain the estimate of σ^2, the error variance. The estimator, s^2, which will be used in the calculation of the 90% confidence interval should be obtained from the "error" mean square term found in the following ANOVA table.

Source	Degrees of freedom
Sequence	1
Animal (sequence)	$n_A + n_B - 2$
Period	1
Formulation	1
Error	$n_A + n_B - 2$
Total	$2n_A + 2n_B - 1$

Lower and upper 90% confidence intervals are then found by formulas based on Student's t-distribution.

$$L = (T - R) - t_{(n_A+n_B-2);0.05^s}\sqrt{\frac{1}{2}\left(\frac{1}{n_A} + \frac{1}{n_B}\right)} \quad (1)$$

$$U = (T - R) + t_{(n_A+n_B-2);0.05^s}\sqrt{\frac{1}{2}\left(\frac{1}{n_A} + \frac{1}{n_B}\right)} \quad (2)$$

The procedure of declaring two formulations bioequivalent, if the 90% confidence interval is completely contained in some fixed interval, is statistically equivalent to performing two one-sided statistical tests ($\alpha = 0.05$) at the end points of the interval.

Consider the following example with $L = 3$, $U = 17$, $T = 110$ and $R = 100$. By the traditional hypothesis testing approach, the result would be considered statistically significant since the confidence interval does not include 0. Using the confidence interval approach, the entire confidence interval lies within 17% of R. (The lower end of the confidence interval lies within $L/R = 3/100 = 3\%$ of R, while the upper end of the confidence interval lies within $U/R = 17/100 = 17\%$ of R.) If it were determined by FDA that only differences larger than 20% were biomedically important,

then using the confidence interval approach the results of this study would be considered adequate to demonstrate bioequivalence.

Now consider an example with $L = -4$, $U = 24$, $T = 110$, and $R = 100$. In this case, by the traditional hypothesis testing approach the result would not be considered statistically significant since the confidence interval includes 0. However, the confidence interval extends as far as 24% from R. (The lower end of the confidence interval lies within $L/R = -4/100 = -4\%$ of R, while the upper end of the confidence interval extends to $U/R = 24/100 = 24\%$ of R.) If it were determined by FDA that only differences larger than 20% were biomedically important, then the results of this study would be considered inadequate to demonstrate bioequivalence, since the entire confidence interval is not within 20% of R.

XI. LOGARITHMICALLY TRANSFORMED DATA

This section discusses how the 90% confidence interval approach should be applied to log-transformed data. In this situation the individual animal AUC and C_{max} values are log-transformed and the analysis is done on the transformed data. For a two-period crossover study, the ANOVA model used to calculate estimates of the error variance and the least square means are identical for both transformed and untransformed data. The procedural difference comes after the lower and upper 90% confidence intervals are found by formulas based on Student's t-distribution.

The lower and upper confidence bounds of the log-transformed data will then need to be back-transformed in order to be expressed on the original scale of the measurement. One thing to keep in mind when moving between the logarithm scale and the original scale is that the back-transformed mean of a set of data that has been transformed to the logarithm scale is not strictly equivalent to the mean that would be calculated from the data on the original scale of measurement. This back-transformed mean is known instead as the geometric mean.

It may help to see the calculations involved. If the AUC from each animal has been transformed to the logarithm scale, we can express the transformed AUC as lnAUC. Then the mean on the logarithm scale is as follows:

$$\bar{L}\bar{n}AUC_t = \sum_{i=1}^{N} LnAUC_t/n \tag{3}$$

where the subscript t represents the AUC determinations for the test article, i is the AUC of the ith animal, and n is the total number of animals receiving the test article. When this mean is back-transformed, it becomes the geometric mean: $e^{(\ln AUC_t)}$. This geometric mean will be on the original scale of the measurement. It will be close to but not exactly equal to the mean obtained on the original scale of the measurement. The back-transformation of the confidence bounds is accomplished in the following way:

Lower bound (expressed as a percentage) $= (e^{L} - 1) \times 100$
Upper bound (expressed as a percentage) $= (e^{U} - 1) \times 100$

Where L is the lower 90% confidence interval and calculated on the log-transformed data; U is the upper 90% confidence interval and calculated on the log-transformed data.

As an example, consider the data for AUC from a hypothetical crossover study in the following table:

		Reference article		Test article	
Animal	Crossover sequence	AUC	LogAUC	AUC	LogAUC
1	1	518.0	6.25	317.8	5.76
2	1	454.9	6.12	465.0	6.14
3	1	232.8	5.45	548.4	6.31
4	1	311.1	5.74	334.8	5.81
5	2	340.4	5.83	224.7	5.41
6	2	497.7	6.21	249.2	5.52
7	2	652.0	6.48	625.4	6.44
8	2	464.1	6.14	848.7	6.74
	MEAN	433.8	6.03	451.7	8602
	Standard Deviation	133.3	0.33	214.3	0.47
	Geometric Mean		414.7		

The statistics for AUC will be calculated from the log-transformed data. In this example, L, the lower 90% confidence interval calculated on the log scale is -0.395. U, the upper 90% confidence interval calculated on the log scale is 0.372. To back-transform these intervals and express them as percentages, we do the following:

Back-transformed lower bound:
$(e^{-0.395} - 1) \times 100 = (0.674 - 1) \times 100 = (-0.326) \times 100 = -32.6\%$
Back-transformed upper bound:
$(e^{0.372} - 1) \times 100 = (1.451 - 1) \times 100 = (0.451) \times 100 = 45.1\%$

Therefore, the lower end of the confidence bound lies within -32.6% of the geometric mean of the reference article, while the upper end of the confidence interval lies within 45.1% of the geometric mean of the reference article. If it were determined by FDA that the acceptable confidence bound was 80% to 125% of the geometric mean of the reference article in order to demonstrate bioequivalence, then the back-transformed lower bound can be as low as -20% and the back-transformed upper bound can be as high as 25%. In this example, we would determine that the study had not demonstrated an acceptable level of bioequivalence between the test article and the reference article.

The width of the confidence interval is determined by the within subject variance (between subject variance for parallel group studies) and the number of subjects in the study. In general, the confidence interval for untransformed data should be 80% to 120% (the confidence interval should lie within $\pm 20\%$ of the mean of the reference product). For logarithmically transformed data, the confidence interval is generally 80% to 125% (the confidence interval should lie within -20% to $+25\%$ of the mean of the reference product). The sponsor and FDA should determine the acceptable bounds for confidence limits for the particular drug and formulation during protocol development.

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2

Bioequivalence Testing Protocols-FDA-Compressed Dosage Forms

To receive approval for an ANDA, an applicant generally must demonstrate, among other things, that its product has the same active ingredient, dosage form, strength, route of administration, and conditions of use as the listed drug, and that the proposed drug product is bioequivalent to the reference listed drug [21 USC 355(j)(2)(A); 21 CFR 314.94(a)]. Bioequivalent drug products show no significant difference in the rate and extent of absorption of the therapeutic ingredient [21 USC 355(j)(8); 21 CFR 320.1(e)]. BE studies are undertaken in support of ANDA submissions with the goal of demonstrating BE between a proposed generic drug product and its reference listed drug. The regulations governing BE are provided at 21 CFR in part 320. The U.S. FDA has recently begun to promulgate individual bioequivalence requirements. To streamline the process for making guidance available to the public on how to design product-specific BE studies, the U.S. FDA will be issuing product-specific BE recommendations (www.fda.gov/cder/ogd/index.htm). Given below are the current recommendations for the products of relevance to this specific volume of the book:

- Abacavir Sulfate; Lamivudine; Zidovudine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 300 mg/150 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 300 mg/150 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Abacavir, Lamivudine, and Zidovudine in plasma. Bioequivalence based on (90% CI): Abacavir, Lamivudine, and Zidovudine. Waiver request of in vivo testing: Not applicable.
- Abacavir Sulfate and Lamivudine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Abacavir and lamivudine in plasma. Bioequivalence based on (90% CI): Abacavir and lamivudine. Waiver request of in vivo testing: Not applicable.
- Abacavir Sulfate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Abacavir in plasma. Bioequivalence based on (90% CI): Abacavir. Waiver request of in vivo testing: Not applicable.
- Acamprosate Calcium Delayed Release Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 333 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 333 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Analytes to measure: Acamprosate in plasma Acamprosate exists completely dissociated in plasma. Therefore, BE measures may be reported in terms of acetylhomotaurine. Bioequivalence based on (90% CI): Acamprosate. Waiver request of in vivo testing: Not applicable.
- Acyclovir Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Acyclovir in plasma. Bioequivalence based on (90% CI): Acyclovir. Waiver request of in vivo testing: 400 mg based on (i) acceptable bioequivalence studies on the 800-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Alendronate Sodium Tablets/Oral. Recommended studies: 1 study. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 70 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Alendronate in urine. Bioequivalence based on (90% CI): Alendronate. The bioequivalence study should be based on urinary excretion data. The following pharmacokinetic parameters should be calculated: A_e (amount of drug excreted during each collection interval). Total A_e (0–48) (total amount of drug excreted over the entire period of sample collection), R_e (rate of drug excretion), R_{max} (maximum excretion rate), and T_{max} (time of the maximum excretion rate). All parameters should be calculated using a noncompartmental model. The statistical analysis using ANOVA should be performed on Total A_e (0–48) and R_{max}. The 90% confidence interval criteria should be applied to these parameters and should be within the limits of 80% to 125%. Waiver request of in vivo testing: 5 mg, 10 mg,

35 mg, and 40 mg based on (i) acceptable bioequivalence study on the 70-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Alfuzosin Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Alfuzosin. Bioequivalence based on (90% CI): Alfuzosin. Waiver request of in vivo testing: Not applicable. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Almotriptan Malate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Almotriptan in plasma. Bioequivalence based on (90% CI): Almotriptan. Waiver request of in vivo testing: 6.25 mg based on (i) acceptable bioequivalence studies of the 12.5-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Alosetron Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1 mg (base); Subjects: Normal, healthy females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 1 mg (base); Subjects: Normal, healthy females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Alosetron in plasma. Bioequivalence based on (90% CI): Alosetron. Waiver request of in vivo testing: 0.5 mg (base) based on (i) acceptable bioequivalence studies on the 1-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Alprazolam Tablet/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Alprazolam in plasma. Bioequivalence based on (90% CI): Alprazolam. Waiver request of in vivo testing: 0.25 mg, 0.5 mg, and 2 mg based on (i) acceptable bioequivalence studies on the 1-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Alprazolam Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 3 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 3 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Alprazolam in plasma. Bioequivalence based on (90% CI): Alprazolam. Waiver request of in vivo testing: 0.5 mg, 1 mg, and 2 mg based on (i) acceptable bioequivalence studies on the 3-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Amlodipine Besylate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Amlodipine in plasma. Bioequivalence based on (90% CI): Amlodipine. Waiver request of in vivo testing: 2.5 mg and 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Amoxicillin; Clavulanate Potassium Chewable Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg/62.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg/62.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Amoxicillin and clavulanic acid in plasma. Bioequivalence based on (90% CI): Amoxicillin and clavulanic acid. Waiver request of in vivo testing: 125 mg/31.25 mg, based on (i) acceptable bioequivalence studies on the 250-mg/62.5-mg strength, (ii) formulation proportionality across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Amoxicillin; Clavulanate Potassium Chewable Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 400 mg/57 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength:

400 mg/57 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Amoxicillin and clavulanic acid in plasma. Bioequivalence based on (90% CI): Amoxicillin and clavulanic acid. Waiver request of in vivo testing: 200 mg/28.5 mg, based on acceptable (i) bioequivalence studies on the 400-mg/57-mg strength, (ii) proportional similarity of the formulations, and (iii) acceptable in vitro dissolution testing of all strengths.

- Anastrozole Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Please conduct the studies in postmenopausal subjects or surgically sterile females. Additional comments: Please do not include subjects who are using female hormone replacement therapies, thyroid hormone replacement therapies, or antihypertensive therapies in the study population. Anastrozole has a long terminal elimination half-life. Please ensure adequate washout periods between treatments in the crossover studies. You may also consider using a parallel study design due to anastrozole's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC0–t or AUC0–8. Please collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (T_{max}). 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Please see comments above. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Anastrozole in plasma. Bioequivalence based on (90% CI): Anastrozole. Waiver request of in vivo testing: Not applicable.
- Aripiprazole Tablets/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Dose and Tablet Strength: 10 mg; Subject: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Dose and Tablet Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 3. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Dose and Tablet Strength: 5 mg, if adequate exposure is not possible with a 5 mg dose, you may consider using a 10 mg dose (2 × 5 mg). Subjects: Normal, healthy males and females, general population. Additional comments: Notes: Life-threatening adverse events attributed to acute laryngeal dystonia have been reported following administration of a single dose of 30 mg aripiprazole to healthy volunteers in bioequivalence studies. Although such events have not been reported at doses lower than 30 mg, because of the life-threatening nature of these events, and because the dose response relationship is not known for this event, the following safety precautions are recommended for healthy volunteer studies of aripiprazole at all doses: Study protocols should specify standard procedures to diagnose and treat dystonic reactions should they occur. Subjects younger than 45 years should be excluded. There appears to be an inverse linear relationship between age and the incidence of acute dystonic reactions. Adults younger than 35 years were reported to have a 15-fold higher rate of neuroleptic-induced dystonia compared to a group of patients 60 to 80 years of age. The occurrence of dystonias appears to be rare at ages of approximately 45 years and higher. Protocols should include stringent drug screening procedures to ensure that subjects are free of illicit drugs at the time of administration of each study drug dose. The screening interview should include specific questions to exclude subjects with a prior personal or family history of dystonic reactions to medications. Prospective study subjects should also be specifically questioned about prior neuroleptic drug exposures. Aripiprazole has been poorly tolerated by healthy volunteers in some bioequivalence studies, particularly at the 15 and 30 mg dose levels. In several cases, adverse events have resulted in a high incidence of dropouts. Adverse events in aripiprazole studies have included nausea, vomiting, dizziness, syncope, insomnia, headache, fatigue, hypotension, hot flashes, weakness, diaphoresis, and confusion. To minimize the occurrence of adverse events, and to ensure the safety of healthy volunteer subjects in clinical trials of aripiprazole, the following is recommended: Subjects should be monitored in-house for at least 3 days after dosing and until adverse events have resolved. Subjects should be kept supine for at least 8 hours starting no longer than 15 minutes after each dose. Subjects should be asked to use the bathroom soon before dosing. Subjects should be encouraged to use urinals or bedpans during the first 8 hours after dosing and at any time after dosing if the subject is experiencing adverse events such as nausea, dizziness, or hypotension. If subjects do use the bathroom during the first 8 hours after dosing or while experiencing adverse events such as nausea, dizziness, or hypotension, they should be assisted to and from the bathroom by study personnel. At a minimum, routine 12-lead EKGs should be performed at 3 to 5 hours after dosing and at 8 to 12 hours after dosing. Continuous EKG monitoring during those time periods may be considered as an alternative. Vital signs monitoring should continue postdosing throughout the period that subjects are housed, commencing no later than 30 minutes following dosing. Vital signs should be monitored frequently (at least every 0.5–1 hour) for at least the first 8 hours after dosing and the first hour after subjects are allowed to rise from the supine position. Prespecified limits should be defined for reporting adverse events related to vital signs (e.g., hypotension, bradycardia, etc.). Vital sign readings that meet these predefined limits should be reported as adverse events, even if they are not performed during a scheduled assessment (e.g., vital signs performed as part of an assessment of an adverse event). The protocol should include standard procedures for the assessment and management of potential adverse events, including vital signs and EKG monitoring as appropriate for adverse events possibly associated with hypotension. Women of childbearing potential should be enrolled only if they are using effective contraceptives. A negative pregnancy test is needed within 24 hours prior to each dose. These subjects should also be informed of the potential teratogenicity of the study drug as part of the informed consent process. Nursing women should also be excluded. The protocol should include measures to prevent relative dehydration at the time of dosing, such as encouragement of water intake whenever possible prior to dosing. Consideration should be made to providing a standard meal just prior to the standard fasting period before dosing. During the informed consent process, subjects should be advised of the high incidence of adverse events that have occurred in some healthy volunteer studies of aripiprazole. Aripiprazole has a long terminal elimination half-life. Please ensure adequate washout periods between treatments in the crossover studies. You may also consider using a

parallel study design due to aripiprazole's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC0–t or AUC0–inf. Please collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (T_{max}). Analytes to measure (in appropriate biological fluid): Aripiprazole in plasma. Bioequivalence based on (90% CI): Aripiprazole. Waiver request of in vivo testing (assuming conduct of the three in vivo studies above): 2 mg, 15 mg, 20 mg, and 30 mg, based on (i) acceptable bioequivalence studies on the 5 mg, and 10-mg strengths (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Armodafinil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Armodafinil in plasma. Bioequivalence based on (90% CI): Armodafinil. Waiver request of in vivo testing: 50 mg and 150 mg, based on acceptable (i) bioequivalence studies on the 250-mg strength, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.
- Atorvastatin Calcium Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Atorvastatin, ortho-, and parahydroxylated metabolites of atorvastatin. The ortho- and parahydroxylated metabolites of atorvastatin are formed by presystemic metabolism and contribute meaningfully to efficacy. For the metabolites, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Atorvastatin. Waiver request of in vivo testing: 10 mg, 20 mg, and 40 mg based on (i) acceptable bioequivalence studies on the 80-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Atovaquone Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: You may also consider using a parallel study design due to atovaquone's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC0–t or AUC0–8. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Atovaquone in plasma. Bioequivalence based on (90% CI): Atovaquone. Waiver request of in vivo testing: Not applicable. Atovaquone is known to be practically insoluble in both water and 0.1 M HCl (<0.0002 mg/mL at 25°C). Use of conventional aqueous dissolution media with and without surfactant has been found unsuccessful and not reproducible in some laboratories working with atovaquone tablet products. If encountering the same difficulty, you may consider developing a dissolution method similar to the method available in the Dissolution Database. Although the use of the high alcoholic medium is not considered conventional, it has been found justifiable by the FDA for this drug substance. You may develop an alternate dissolution testing method for the drug product and submit the dissolution testing results when the application is filed.
- Azithromycin Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Azithromycin. Bioequivalence based on (90% CI): Azithromycin. Waiver request of in vivo testing: 250 mg and 500 mg based on (i) acceptable bioequivalence studies on the 600-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Since Azithromycin tablets, 250 mg, 500 mg, and 600 mg, are the subject of three separate new drug applications (NDAs), three separate abbreviated new drug applications (ANDAs) must be submitted. You may request (a) Waiver of in vivo bioequivalence testing of the 250-mg and the 500-mg strengths if you meet the criteria. In addition, please cross-reference the in vivo bioequivalence studies conducted on the higher strength along with your Waiver request.
- Benzphetamine Hydrochloride Tablet/Oral. Recommended studies: Benzphetamine Hydrochloride Tablet is a DESI-effective drug product without known bioequivalence problems. Therefore, in vivo bioequivalence testing is not requested. Comparative dissolution testing on 12 dosage units of all strengths of the test and reference products is requested. You may request (a) Waiver of in vivo bioequivalence study requirements on this product under 21 CFR 320.22(c). Analytes to measure: Not applicable. Bioequivalence based on (90% CI): Not applicable. Waiver request of in vivo testing: 50 mg.
- Bicalutamide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the bioequivalence studies if they are pregnant. Bicalutamide has a long terminal elimination half-life. Please ensure adequate washout periods between treatments in the crossover studies. You may also consider using a parallel study design due to bicalutamide's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC0–t or AUC0–8. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure: Bicalutamide, using an achiral assay. Bioequivalence based on (90% CI): Bicalutamide. Waiver request of in vivo testing: Not applicable.
- Bisoprolol Fumarate; Hydrochlorothiazide Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength:

10 mg/6.25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg/6.25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Bisoprolol and Hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Bisoprolol and Hydrochlorothiazide. Waiver request of in vivo testing: 2.5 mg/6.25 mg and 5 mg/6.25 mg based on (i) acceptable bioequivalence studies on the 10-mg/6.25-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Bisoprolol Fumarate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Bisoprolol in plasma. Bioequivalence based on (90% CI): Bisoprolol. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Bupropion Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 150 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 150 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Bupropion and Hydroxybupropion (active metabolite of bupropion) in plasma. Bioequivalence based on (90% CI): Bupropion. Waiver request of in vivo testing: 300 mg based on (i) acceptable bioequivalence studies on the 150-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation. Because of concerns of dose dumping from this drug product when taken with alcohol, please conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium, as follows: Testing Conditions: 900 mL, 0.1 N HCl, Apparatus I (basket) at 75 rpm, with and without the alcohol (see below): Test 1: 12 units tested according to the proposed method (with 0.1 N HCl), with data collected every 15 minutes for a total of 2 hours. Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range, and %CV on both strengths.
- Candesartan Cilexetil; Hydrochlorothiazide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 32 mg/12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the bioequivalence studies if they are pregnant. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 32 mg/12.5 mg; Subjects: Normal, healthy males and females, general population Additional comments: Female subjects should be excluded from the bioequivalence studies if they are pregnant. Analytes to measure (in appropriate biological fluid): Candesartan and hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Candesartan and hydrochlorothiazide requests of Waivers of in vivo testing: 16 mg/12.5 mg, based on (i) acceptable bioequivalence studies on the 32-mg/12.5-mg strength, (ii) formulation proportionality across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Candesartan Cilexetil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 32 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 32 mg; Subjects: Normal, healthy males and females, general population Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Candesartan in plasma. Bioequivalence based on (90% CI): Candesartan requests for Waivers of in vivo testing: 4 mg, 8 mg, and 16 mg based on (i) acceptable bioequivalence studies on the 32-mg strength, (ii) acceptable dissolution testing of all strengths, and (iii) proportional similarity in the formulations of all strengths.
- Carbamazepine Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Carbamazepine in plasma. Bioequivalence based on (90% CI): Carbamazepine. Waiver request of in vivo testing: 100 mg and 200 mg, based on acceptable (i) bioequivalence studies on the 400 mg tablet, (ii) proportional similarity of the formulations, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at

50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.

- Carbidopa; Entacapone; Levodopa Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo. Strength: (37.5 mg, 200 mg, and 150 mg) Carbidopa; Entacapone; Levodopa. Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional Comments: 2. Type of study: Fasting Design: single-dose, two-way crossover in vivo. Strength: (12.5 mg, 200 mg, and 50 mg) Carbidopa; Entacapone; Levodopa. Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Analytes to measure (in appropriate biological fluid): Carbidopa, Entacapone, and Levodopa in plasma. Bioequivalence based on (90% CI): Carbidopa, Entacapone, and Levodopa. Waiver request of in vivo testing: (25 mg, 200 mg, and 100 mg) Carbidopa, Entacapone and Levodopa tablets, based on (i) acceptable bioequivalence study on the 37.5 mg; 200 mg; 150 mg tablet, (ii) formulation proportionality across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Carvedilol Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, the OGD recommends that you conduct the bioequivalence studies using Carvedilol Tablets, 12.5 mg, instead of the 25-mg strength. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Carvedilol and 4-hydroxyphenyl-carvedilol metabolite of Carvedilol in plasma. Bioequivalence based on (90% CI): Carvedilol. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 3.125 mg, 6.25 mg, and 25 mg based on (i) acceptable bioequivalence studies on the 12.5-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Cefditoren Pivoxil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Cefditoren (not the prodrug cefditoren pivoxil) in plasma. Bioequivalence based on (90% CI): Cefditoren. Waiver request of in vivo testing: Not applicable.
- Cetirizine Hydrochloride; Pseudoephedrine Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 5 mg/120 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 5 mg/120 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Cetirizine and Pseudoephrine in plasma. Bioequivalence based on (90% CI): Cetirizine and Pseudoephrine. Waiver request of in vivo testing: Not applicable. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Cetirizine Hydrochloride Chewable Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Cetirizine in plasma. Bioequivalence based on (90% CI): Cetirizine. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Cilostazol Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Patients should be advised to take Cilostazol at least one-half hour before or 2 hours after food. Therefore, a fed study is not recommended. 2. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure: Cilostazol in plasma. Bioequivalence based on (90% CI): Cilostazol. Waiver request of in vivo testing: Not applicable.
- Cinacalcet Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 90 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 90 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Analytes to measure (in appropriate biological fluid): Cinacalcet in plasma. Bioequivalence based on (90% CI): Cinacalcet. Waiver request of in vivo testing:

60 mg and 30 mg based on (i) acceptable bioequivalence studies on the 90-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Ciprofloxacin; Ciprofloxacin Hydrochloride Extended Release Tablets/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1000 mg (425.2 mg; EQ 574.9 mg base); Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 1000 mg (425.2 mg; EQ 574.9 mg base); Subjects: Normal, healthy males and females, general population. 3. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 500 mg (212.6 mg; EQ 287.5 mg base); Subjects: Normal, healthy males and females, general population. Analytes to measure: Ciprofloxacin. Bioequivalence based on (90% CI): Ciprofloxacin. Waiver request of in vivo testing: The 500-mg strength of ciprofloxacin extended-release tablets is NOT eligible for (a) Waiver of in vivo testing based on an acceptable in vivo bioequivalence study of the 1000-mg strength. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Ciprofloxacin Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Ciprofloxacin in plasma. Bioequivalence based on (90% CI): Ciprofloxacin. Waiver request of in vivo testing: Not applicable. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Clarithromycin Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Clarithromycin in plasma. Bioequivalence based on (90% CI): Clarithromycin. Waiver request of in vivo testing: Not applicable. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Clonidine Hydrochloride Tablets/Oral. Recommended studies: 1 study. 1. Type of study: fasting Design: single-dose, two-way crossover in vivo; Strength: 0.3 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Clonidine in plasma. Bioequivalence based on (90% CI): Clonidine. Waiver request of in vivo testing: 0.1 mg and 0.2 mg based on (i) acceptable bioequivalence study on the 0.3-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Clopidogrel Bisulfate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Clopidogrel in plasma. Bioequivalence based on (90% CI): Clopidogrel. Waiver request of in vivo testing: Not applicable. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Darifenacin Hydrobromide Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Darifenacin in plasma. Bioequivalence based on (90% CI): Darifenacin. Waiver request of in vivo testing: 7.5 mg based on (i) acceptable bioequivalence studies on the 15-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Darunavir Ethanolate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: single-dose of 600 mg (2 × 300 mg); Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: single-dose of 600 mg (2 × 300 mg); Subjects: Normal, healthy males and females, general population. Additional

comments: Analytes to measure (in appropriate biological fluid): Darunavir in plasma. Bioequivalence based on (90% CI): Darunavir. Waiver request of in vivo testing: Not applicable.

- Delavirdine Mesylate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Delavirdine in plasma. Bioequivalence based on (90% CI): Delavirdine. Waiver request of in vivo testing: 100 mg based on (i) acceptable bioequivalence studies on the 200-mg strength, (ii) proportional similarity of the 100 mg formulation to the 200-mg strength, and (iii) acceptable in vitro dissolution testing of all strengths.
- Desloratadine Orally Disintegrating Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Desloratadine and the active metabolite, 3-hydroxydesloratadine in plasma. Please submit the metabolite data as supportive evidence of the comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Desloratadine. Waiver request of in vivo testing: 2.5 mg based on (i) acceptable bioequivalence studies on the 5-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Desloratadine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Desloratadine and its metabolite, 3-hydroxydesloratadine. Bioequivalence based on (90% CI): Desloratadine. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: Not applicable.
- Dexmethylphenidate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Dexmethylphenidate in plasma. Bioequivalence based on (90% CI): Dexmethylphenidate. Waiver request of in vivo testing: 2.5 mg and 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Diclofenac Sodium; Misoprostol Delayed Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 75 mg/0.2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the bioequivalence study if they are pregnant. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 75 mg/0.2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the bioequivalence study if they are pregnant. Analytes to measure: Diclofenac and misoprostol's metabolite, misoprostol acid in plasma. Bioequivalence based on (90% CI): Diclofenac and misoprostol's metabolite, misoprostol acid. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 50 mg/ 0.2 mg based on (i) acceptable bioequivalence studies on the 75-mg/0.2-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Didanosine Chewable Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 2 × 200 mg (400 mg dose); Subjects: Normal, healthy males and females, general population Additional comments: Analytes to measure (in appropriate biological fluid): Didanosine in plasma using an achiral method. Bioequivalence based on (90% CI): Didanosine. Waiver request of in vivo testing: 25 mg, 50 mg, 100 mg, and 150 mg, based on (i) acceptable bioequivalence study on the 200-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Digoxin Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 0.25 mg; Subjects: Normal, healthy males and females, general population Additional comments: If reliable blood drug levels cannot be obtained using a 1 × 0.25 mg dose, you may use a single dose of 2 × 0.25 mg tablets. Please carefully monitor the study subjects for adverse events. A washout period of about 2 weeks is suggested. Please continue sample collection for approximately 6 days, that is, at least three or more terminal half-lives of the drug. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 0.25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see above comments. Analytes to measure (in appropriate biological fluid): Digoxin in plasma. Bioequivalence based on (90% CI): Digoxin. Waiver request of in vivo testing: 0.125 mg based on (i) acceptable bioequivalence studies on the 0.25-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution

testing on 12 dosage units of all strengths of the test and reference products.

- Diltiazem Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 420 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 420 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Diltiazem and the active metabolites desacetyldiltiazem and desmethyldiltiazem in plasma. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Diltiazem. Waiver request of in vivo testing: 120 mg, 180 mg, 240 mg, 300 mg, and 360 mg based on (i) acceptable bioequivalence studies on the 420-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Dipyridamole Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Dipyridamole in plasma. Bioequivalence based on (90% CI): Dipyridamole. Waiver request of in vivo testing: 25 mg and 50 mg based on (i) acceptable bioequivalence study on the 75-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Divalproex Sodium Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure: Valproic acid in plasma. Bioequivalence based on (90% CI): Valproic acid. Waiver request of in vivo testing: 250 mg based on (i) acceptable bioequivalence studies on the 500-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Donepezil Hydrochloride Orally Disintegrating Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Donepezil in plasma. Bioequivalence based on (90% CI): Donepezil. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Donepezil Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Donepezil in plasma. Bioequivalence based on (90% CI): Donepezil. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Doxazosin Mesylate Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Analytes to measure (in appropriate biological fluid): Doxazosin in plasma. Bioequivalence based on (90% CI): Doxazosin. Waiver request of in vivo testing: 4 mg based on (i) acceptable bioequivalence studies on the 8-mg strength, (ii) proportionally similar across both strengths, and (iii) acceptable in vitro dissolution testing of both strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.

- Doxycycline Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 150 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 150 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Doxycycline in plasma. Bioequivalence based on (90% CI): Doxycycline. Waiver request of in vivo testing: 50 mg, 75 mg, and 100 mg based on (i) acceptable bioequivalence studies on the 150-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Drospirenone; Estradiol Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 0.5 mg and 1 mg; Subjects: Normal, healthy postmenopausal women. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 0.5 mg and 1 mg; Subjects: Normal, healthy postmenopausal women. Additional comments: Analytes to measure (in appropriate biological fluid): Drospirenone and unconjugated estradiol, unconjugated estrone, and total estrone in plasma. Bioequivalence based on (90% CI): Drospirenone and baseline-adjusted total estrone. Statistical analysis should be performed on data both with and without baseline adjustment. Bioequivalence acceptance criteria will be based on baseline-adjusted results only. Baseline adjustment: Data of each subject and period should be adjusted for the mean of −1 hour, −0.5 hour, and predose levels for that same subject and period. If, after adjustment, any negative concentrations result, they should be set equal to zero. Waiver request of in vivo testing: Not applicable.
- Efavirenz Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Efavirenz in plasma. Bioequivalence based on (90% CI): Efavirenz. Waiver request of in vivo testing: Not applicable.
- Entacapone Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to the high inter- and intrasubject variability observed with this product, you may want to consider using a replicate study design. Since the drug product is to be used predominantly in the elderly, please include as many subjects of 60 years of age or older as possible. 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure: Entacapone in plasma. Bioequivalence based on (90% CI): Entacapone. Waiver request of in vivo testing: Not applicable.
- Entecavir Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: As an option, due to the relatively long half-life, the firm may wish to conduct this study using a parallel design. As an additional option for either the crossover or parallel design, the firm may wish to truncate the AUC at 72 hours. Analytes to measure (in appropriate biological fluid): Entecavir in plasma. Bioequivalence based on (90% CI): Entecavir. Waiver request of in vivo testing: 0.5 mg based on (i) acceptable bioequivalence studies on the 1-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Eplerenone Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Eplerenone in plasma. Bioequivalence based on (90% CI): Eplerenone. Waiver request of in vivo testing: 25 mg based on (i) acceptable bioequivalence studies on the 50-mg strength, (ii) proportionally similar to the 50-mg strength, and (iii) acceptable in vitro dissolution testing.
- Eprosartan Mesylate; Hydrochlorothiazide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 600 mg/25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Please include provisions for appropriate monitoring and intervention in the case of possible drug-related adverse events (e.g., subjects complaining of dizziness/lightheadedness should have blood pressure/heart rate assessed). 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 600 mg/25 mg; Subjects: Normal, healthy males and females, general population. Additional Comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Eprosartan and Hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Eprosartan and Hydrochlorothiazide. Waiver request of in vivo testing: 600 mg/12.5 mg, based on (i) acceptable bioequivalence studies on the 600-mg/25-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Erlotinib Hydrochloride Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 150 mg; Subjects: Normal, healthy males and females, general population. Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Any subject experiencing an adverse event should be followed until the adverse event has completely resolved. Analytes to measure (in appropriate biological fluid): Erlotinib in plasma. Bioequivalence based on (90% CI): Erlotinib. Waiver request of in vivo testing: 100 mg and 25 mg based on (i) acceptable bioequivalence studies on the 150-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Escitalopram Oxalate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Escitalopram, using an achiral assay. Bioequivalence based on (90% CI):

Escitalopram. Waiver request of in vivo testing: 5 mg and 10 mg based on (i) acceptable bioequivalence studies on the 20-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Esterified Estrogens Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 2.5 mg; Subjects: Normal, healthy post menopausal or surgically sterile females. Additional comments: Analytes to measure (in appropriate biological fluid): Estrone sulfate and Equilin sulfate in plasma. 1. Please provide baseline correction for endogenous estrone sulfate in the analysis. Please measure baseline estrone sulfate levels at −1, −0.5, and 0 hours. The mean of the predose estrone sulfate levels should be used for the baseline adjustment of the postdose levels. Any negative values obtained from baseline correction should be designated as zero (0) and any subject with baseline-adjusted predose concentrations (at time 0 hour) greater than 5% of their C_{max} should be excluded from the bioequivalence statistical analysis and the 90% confidence interval based on the remaining subjects. 2. The selected blood-sampling schedule should include sufficient time points around T_{max} for the best estimate of C_{max}, and should be sufficiently long for the best characterization of the elimination phase of both analytes (at least 96 hours). 3. The analytical assay method selected should be sufficiently sensitive and specific to measure estrone sulfate and equilin sulfate concentrations in plasma and should have a lower limit of quantitation (LLOQ) of 50 pg/mL or less for both analytes. 4. Based on the estimated half-life of the two analytes, the washout duration should be greater than five times the half-life, therefore at least a 2-week washout period between doses is recommended. Bioequivalence based on (90% CI): Estrone sulfate and Equilin sulfate. Waiver request of in vivo testing: 0.3 mg, 0.625 mg, and 1.25 mg based on (i) acceptable bioequivalence studies on the 2.5-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Eszopiclone Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 3 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 3 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Eszopiclone in plasma. Bioequivalence based on (90% CI): Eszopiclone. Waiver request of in vivo testing: 1 mg and 2 mg, based on acceptable (i) bioequivalence studies on the 3-mg tablet, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.
- Ethambutol Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Ethambutol in plasma. Bioequivalence based on (90% CI): Ethambutol. Waiver request of in vivo testing: 100 mg, based on acceptable (i) bioequivalence studies on the 400-mg strength, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.
- Ethinyl Estradiol and Levonorgestrel Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 0.03 mg/0.15 mg tablet of ethinyl estradiol and levonorgestrel; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 0.01 mg tablet of ethinyl estradiol; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Ethinyl estradiol and levonorgestrel in plasma for the combination tablets. Only ethinyl estradiol for the single component tablet. Bioequivalence based on (90% CI): Ethinyl estradiol and levonorgestrel. Waiver request of in vivo testing: Bioequivalence studies conducted on Seasonique® (ethinyl estradiol and levonorgestrel) tablets, 0.03 mg/0.15 mg, may be referenced to support a request for (a) Waiver of evidence of in vivo bioequivalence for Seasonale® (ethinyl estradiol and levonorgestrel) tablets, 0.03 mg/0.15 mg. Please submit separate applications for each RLD.
- Ethinyl Estradiol and Levonorgestrel Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 0.03 mg/0.15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Ethinyl estradiol and levonorgestrel in plasma. Only ethinyl estradiol for the single component tablet in Seasonique. Bioequivalence based on (90% CI): Ethinyl estradiol and levonorgestrel. Waiver request of in vivo testing: Bioequivalence studies conducted on Seasonique (ethinyl estradiol and levonorgestrel) Tablets, 0.03 mg/0.15 mg, may be referenced to support a request for (a) Waiver of evidence of in vivo bioequivalence for Seasonale (ethinyl estradiol and levonorgestrel) Tablets, 0.03 mg/0.15 mg. Please submit separate applications for each RLD.
- Etidronate Disodium Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Etidronate in plasma. Bioequivalence based on (90% CI): Etidronate. Waiver request of in vivo testing: 200 mg based on (i) acceptable bioequivalence study on the 400-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Exemestane Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 25 mg; Subjects: Normal, healthy postmenopausal women, general population. Additional comments: This product is indicated for use in postmenopausal women. Because of teratogenicity concerns with this product, females in these studies should not be of childbearing potential. We recommended that you attempt to include as many postmenopausal women as possible. 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 25 mg; Subjects: Normal, healthy postmenopausal women, general population.

Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Exemestane in plasma. Bioequivalence based on (90% CI): Exemestane. Waiver request of in vivo testing: Not applicable.

- Famotidine Orally Disintegrating Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Famotidine in plasma. Bioequivalence based on (90% CI): Famotidine. Waiver request of in vivo testing: 20 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Famotidine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Famotidine in plasma. Bioequivalence based on (90% CI): Famotidine. Waiver request of in vivo testing: 10 mg and 20 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Note: Separate applications should be submitted for the prescription (Rx) and over-the-counter (OTC) products. You may request (a) Waiver of in vivo bioequivalence testing for the OTC product; if you conduct the studies on the Rx product, submit acceptable dissolution data on all strengths and the formulations of the products are proportional. Please cross-reference in the OTC application the studies conducted for the Rx product. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Felbamate Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: Multipledose, two-way steady-state crossover in vivo; Strength: 600 mg; Subjects: Male and nonpregnant female epilepsy patients. Additional comments: Please also consider the following additional safety monitoring: (a) If any evidence of bone marrow (hematologic) depression occurs, felbamate treatment should be discontinued and a hematologist consulted to ensure appropriate medical care. (b) Additional criteria for exclusion from the study relative to baseline be practiced including: (i) twofold increase in the highest, 2-day prestudy seizure frequency, (ii) single generalized, tonic–clonic seizure if none occurred during pretreatment screening, and/or (iii) significant prolongation of generalized, tonic–clonic seizures. Analytes to measure: Felbamate in plasma. 1. Measurements of felbamate are requested on at least two consecutive days immediately prior to pharmacokinetic analysis days 7 and 14 to confirm steady-state concentrations of felbamate (i.e., additional consecutive measures on days 5, 6, 12, and 13). 2. Because felbamate is rapidly absorbed and reaches a peak plasma concentration within 1 to 3 hours postconsumption, please also include blood sampling at 0.25 hours after drug dosing to accurately measure the absorption/distribution phases of the felbamate pharmacokinetic profile. 3. Patients who receive multiples of 600 mg tablets of felbamate per day (1200–4800 mg/day) would be eligible for the study by continuing their established maintenance dose. Because patients will be administered different dosing regimens, the dose needs to be included in the analysis of variance (ANOVA) statistical model. Dose normalization is not advised. 4. No washout period is necessary between treatment periods. 5. You are encouraged to submit protocols for the in vivo bioequivalence studies to be conducted at steady state in patients already taking the RLD at a therapeutic dose for review prior to initiating the studies. Bioequivalence based on (90% CI): Felbamate. Waiver request of in vivo testing: 400 mg based on (i) acceptable bioequivalence studies on the 600-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Fenofibrate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 145 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 145 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Due to the difficulties with the fenofibrate assay, only the metabolite, fenofibric acid, should be measured. Bioequivalence based on (90% CI): Fenofibric Acid. Waiver request of in vivo testing: 48 mg based on (i) acceptable bioequivalence studies on the 145-mg strength, (ii) proportional similarity of the formulations 48 mg and 145-mg strengths, and (iii) acceptable in vitro dissolution testing of 48-mg and 145-mg strengths.
- Fexofenadine Hydrochloride Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 180 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Fexofenadine in plasma. Bioequivalence based on (90% CI): Fexofenadine. Waiver request of in vivo testing: 30 mg and 60 mg based on (i) acceptable bioequivalence study on the 180-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Flavoxate Hydrochloride Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Flavoxate and the metabolite, 3-methylflavone-8-carboxylic acid in plasma. Bioequivalence based on (90% CI): Flavoxate or the metabolite, 3 methyl-flavone-8-carboxylic acid. If flavoxate can be reliably measured, a confidence interval approach for bioequivalence determination should be used for flavoxate. If flavoxate cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for 3-methylflavone-8-carboxylic acid. Waiver request of in vivo testing: Not applicable.
- Fluconazole Tablet/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Fluconazole in plasma. Bioequivalence based on (90% CI): Fluconazole. Waiver request of in vivo testing: 50 mg, 100 mg, and 150 mg based on (i) acceptable bioequivalence study on the 200-mg strength, (ii) proportional similarity of the

formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Fluvastatin Sodium Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to the teratogenicity concerns with fluvastatin sodium, female subjects enrolled in these studies should not be pregnant. 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Fluvastatin in plasma (achiral assay). Bioequivalence based on (90% CI): Fluvastatin. Waiver request of in vivo testing: Not applicable. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.
- Fosamprenavir Calcium Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 700 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 700 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Amprenavir (not the prodrug fosamprenavir) in plasma. Bioequivalence based on (90% CI): Amprenavir. Waiver request of in vivo testing: Not applicable.
- Fosinopril Sodium; Hydrochlorothiazide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 20/12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the studies if they are pregnant. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 20/12.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the studies if they are pregnant. Analytes to measure (in appropriate biological fluid): The metabolite of fosinopril, fosinoprilat and hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Fosinoprilat and Hydrochlorothiazide. Waiver request of in vivo testing: 10 mg/12.5 mg based on (i) acceptable bioequivalence studies on the 20-/12.5-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Fosinopril Sodium Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Metabolite fosinoprilat in plasma. Bioequivalence based on (90% CI): Metabolite fosinoprilat. Waiver request of in vivo testing: 10 mg, and 20 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Gabapentin Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Gabapentin in plasma. Bioequivalence based on (90% CI): Gabapentin. Waiver request of in vivo testing: 100 mg, 300 mg, 400 mg, and 600 mg based on (i) acceptable bioequivalence studies on the 800-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Gemifloxacin Mesylate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 320 mg (base equivalent); Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Females should not be lactating. Subjects should not have a history of prolongation of the QTC interval, or ongoing proarrhythmic conditions such as clinically significant bradycardia or acute myocardial ischemia. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 320 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional Comments: Females should not be lactating. Subjects should not have a history of prolongation of the QTC interval, or ongoing proarrhythmic conditions such as clinically significant bradycardia or acute myocardial ischemia. Analytes to measure (in appropriate biological fluid): Gemifloxacin in plasma. Bioequivalence based on (90% CI): Gemifloxacin. Waiver request of in vivo testing: Not applicable.
- Glimepiride/Rosiglitazone Maleate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1 mg/4 mg; Subjects: Normal, healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Additional Comments: Because of the potential for hypoglycemia from BE studies using the 4-mg dose of glimepiride tablets, in vivo BE study of the 1 mg glimepiride/4 mg rosiglitazone maleate tablets is recommended. In addition, each dose in the study should be administered with 240 mL of 20% glucose solution to minimize hypoglycemic effects. After dosing, 60 mL of 20% glucose solution should be given to each subject every 15 minutes for the following 4 hours 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1 mg/4 mg; Subjects: Normal, healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior

to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Additional comments: Please see additional comments above. Analytes to measure (in appropriate biological fluid): Glimepiride and Rosiglitazone in plasma. Bioequivalence based on (90% CI): Glimepiride and Rosiglitazone. Waiver request of in vivo testing: 2 mg/4 mg, 4 mg/4 mg, 2 mg/8 mg, and 4 mg/8 mg tablets, based on acceptable (i) bioequivalence studies on the 1-mg/4-mg tablet; (ii) proportional similarity of the formulations; and (iii) acceptable in vitro dissolution testing of all strengths.

- Glimepiride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Because of the potential for hypoglycemia from using a dose of 4 mg of glimepiride tablets, you should conduct the bioequivalence studies using the 1 mg dose. Each dose in the studies should be administered with 240 mL of 20% glucose solution to minimize hypoglycemic effects. After dosing, 60 mL of 20% glucose solution should be given to each subject every 15 minutes for the following 4 hours. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please comment above. Analytes to measure: Glimepiride in plasma. Bioequivalence based on (90% CI): Glimepiride. Waiver request of in vivo testing: 2 mg and 4 mg based on (i) acceptable bioequivalence studies on the 1-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Glipizide; Metformin Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg/500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Since the drug product causes hypoglycemia, it is recommended that subjects receive 60 mL of 20% glucose solution in water after each dose and every 15 minutes for 4 hours during fasting and fed bioequivalence studies. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg/500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Glipizide and metformin in plasma. Bioequivalence based on (90% CI): Glipizide and metformin. Waiver request of in vivo testing: 2.5 mg/250 mg and 2.5 mg/500 mg based on (i) acceptable bioequivalence studies on the 5-mg/500-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Glyburide; Metformin Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 5 mg/500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: The drug products should be administered with 240 mL of 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 5 mg/500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: The drug products should be administered with 240 mL of 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. Analytes to measure: Glyburide and Metformin. Bioequivalence based on (90% CI): Glyburide and Metformin. Waiver request of in vivo testing: 1.25 mg/250 mg and 2.5 mg/500 mg based on (i) acceptable bioequivalence studies on the 5-mg/500-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Granisetron Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Granisetron in plasma. Bioequivalence based on (90% CI): Granisetron. Waiver request of in vivo testing: Not applicable.
- Hydrochlorothiazide; Irbesartan Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 25 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 25 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Hydrochlorothiazide and irbesartan in plasma. Bioequivalence based on (90% CI): Hydrochlorothiazide and irbesartan. Waiver request of in vivo testing: 12.5 mg/150 mg and 12.5 mg/300 mg based on (i) acceptable bioequivalence studies on the 25-mg/300-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Lisinopril; Hydrochlorothiazide Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg/20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects enrolled in the BE studies should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg/20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Lisinopril and Hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Lisinopril and Hydrochlorothiazide. Waiver request of in vivo testing: 12.5/10 mg and 12.5 mg/20 mg based on (i) acceptable bioequivalence studies on the 25-mg/20-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Hydrochlorothiazide; Losartan Potassium Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 25 mg/100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 25 mg/100 mg; Subjects: Normal, healthy males and females, general population. Additional

comments: Please see comments above. Analytes to measure: Hydrochlorothiazide, losartan, and its carboxylic metabolite in plasma. For the carboxylic acid metabolite, the following data should be submitted: (1) individual and mean concentration, (2) individual and mean pharmacokinetic parameters, and (3) geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Hydrochlorothiazide and Losartan. Waiver request of in vivo testing: 12.5 mg/50 mg and 12.5 mg/100 mg based on (i) acceptable bioequivalence studies on the 25-mg/100-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Hydrochlorothiazide; Olmesartan Medoxomil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 25 mg/40 mg Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: The labeling for this drug contains a black box regarding pregnancy and fetal/neonatal morbidity and mortality. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 25 mg/40 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Hydrochlorothiazide and Olmesartan in plasma. Bioequivalence based on (90% CI): Hydrochlorothiazide and Olmesartan. Waiver request of in vivo testing: 12.5-mg/40-mg and 12.5-mg/20-mg strengths based on (i) acceptable bioequivalence studies on the 25-mg/40-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Hydrochlorothiazide; Valsartan Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg/160 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg/160 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Valsartan and hydrochlorothiazide in plasma. Bioequivalence based on (90% CI): Valsartan and hydrochlorothiazide. Waiver request of in vivo testing: 12.5 mg/80 mg and 12.5 mg/160 mg based on (i) acceptable bioequivalence studies on the 25-mg/160-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Irbesartan Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects should be excluded from the bioequivalence studies if they are pregnant. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population Additional comments: Please see comment above. Analytes to measure: Irbesartan in plasma. Bioequivalence based on (90% CI): Irbesartan. Waiver request of in vivo testing: 75 mg and 150 mg based on (i) acceptable bioequivalence studies on the 300-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Isosorbide Mononitrate Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way, crossover in vivo; Strength: 120 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-way, crossover in vivo; Strength: 120 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Isosorbide mononitrate in plasma. Bioequivalence based on (90% CI): Isosorbide mononitrate. Waiver request of in vivo testing: 30 mg and 60 mg based on (i) acceptable bioequivalence studies on the 120-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Isradipine Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way, crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-way, crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Isradipine in plasma. Bioequivalence based on (90% CI): Isradipine. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Lamivudine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid):

Lamivudine in plasma. Bioequivalence based on (90% CI): Lamivudine. Waiver request of in vivo testing: 150 mg based on (i) acceptable bioequivalence studies on the 300-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Lamivudine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of Study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Lamivudine in plasma. Bioequivalence based on (90% CI): Lamivudine. Waiver request of in vivo testing: Not applicable.
- Lamivudine; Zidovudine Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 150 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 150 mg/300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Lamivudine and Zidovudine in plasma. Bioequivalence based on (90% CI): Lamivudine and Zidovudine. Waiver request of in vivo testing: Not applicable. Products at this Web site conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Lamotrigine Chewable Dispersible Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: Single-dose of 50 mg (2 × 25 mg); Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: Single-dose of 50 mg (2 × 25 mg); Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Lamotrigine in plasma. Please utilize a validated analytical method such as LC-MS/MS to reliably measure plasma lamotrigine concentrations. An LLOQ of 10 ng/mL is recommended to adequately characterize the pharmacokinetics at 50 mg study dose. Bioequivalence based on (90% CI): Lamotrigine. Waiver request of in vivo testing: 2 mg and 5 mg based on (i) acceptable bioequivalence studies on the 25-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Products at this Web site conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products.
- Lamotrigine Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: Single-dose of 50 mg (2 × 25 mg); Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, studies on the highest strength are not recommended. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: Single dose of 50 mg (2 × 25 mg); Subjects: Normal, healthy males and females, general population. Additional comments: See comment above. Analytes to measure (in appropriate biological fluid): Lamotrigine in plasma. Please utilize a validated analytical method such as LC-MS/MS to reliably measure plasma lamotrigine concentrations. An LLOQ of 10 ng/mL is recommended to adequately characterize the pharmacokinetics at 50 mg study dose. Bioequivalence based on (90% CI): Lamotrigine. Waiver request of in vivo testing: 100 mg, 150 mg, and 200 mg based on (i) acceptable bioequivalence studies on the 25-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please find the dissolution information for this product at this Web site and conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Leflunomide Tablets/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Only female subjects who are unable to bear children should be included in the study and male subjects wishing to father a child during the study should be excluded from the study. Since the half-life of the metabolite A77 1726 is very long, you may consider bioequivalence studies with parallel designs. 3. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Please measure only the leflunomide's metabolite, A77 1726, in plasma. Bioequivalence based on (90% CI): The metabolite of leflunomide, A77 1726. Waiver request of in vivo testing: 10 mg based on (i) acceptable bioequivalence studies on the 20-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Levonorgestrel Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 0.75 mg; Subjects: Normal, healthy females, general population. Additional comments: Analytes to measure: Levonorgestrel in plasma. Bioequivalence based on (90% CI): Levonorgestrel. Waiver request of in vivo testing: Not applicable.
- Lidocaine Patch/Topical. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, in vivo, using three topical patches; Strength: 5%, 700 mg/patch; Subjects: Normal, healthy males and females, general population. Additional comments: Apply three topical patches (2100 mg total dose) simultaneously over a 12-hour period. You may use a smaller number of patches provided the plasma concentrations of lidocaine are measurable to adequately characterize the pharmacokinetic profile of lidocaine for bioequivalence assessment based on the 90% confidence interval criteria. Please include a 24-hour postdose sampling time in the bioequivalence study. In addition to pharmacokinetic data, please report the "apparent dose" delivered. The apparent dose can be determined by subtracting the remaining amount of lidocaine in each patch (used patch) from the manufactured amount. The amount of adhesive residue from each patch left on the skin should be analyzed and included in the calculation. Analytes to measure: Lidocaine in plasma. Please utilize a validated analytical method such as LC-MS/MS to

reliably measure plasma lidocaine concentrations. An LLOQ of 0.20 ng/mL is recommended to adequately characterize the pharmacokinetics at the 2100 mg study dose. Bioequivalence based on (90% CI): Lidocaine. 2. Type of study: Skin irritation/sensitization study Design: Single-dose, in vivo (preceded by an induction phase and a rest period); Strength: 5%, 700 mg/patch; Subjects: Normal, healthy males and females, general population. Additional comments: Specific recommendations are provided below for the skin irritation/sensitization/adhesion study. General comments: Please note that the name of RLD is designated as lidocaine topical patch, 5%. This designation is based on the concentration of lidocaine in the adhesive, which is 5%. Please formulate your product to contain 5% of lidocaine in the adhesive, to have the same surface area and the same total amount of lidocaine in the patch as the RLD.

- Linezolid Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional Comments: Analytes to measure (in appropriate biological fluid): Linezolid in plasma. Bioequivalence based on (90% CI): Linezolid. Waiver request of in vivo testing: Not applicable.
- Liothyronine Sodium Tablets/Oral. Recommended studies: 1 study. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Dose and Strength: 100 μg (2 × 50 μg); Subjects: Normal, healthy males and females, general population. Additional comments: Baseline levels of liothyronine should be measured at 3 predose time points (−30 minutes, −15 minutes, and 0 minute). The mean of the three predose samples should be subtracted from each measured postdose concentration. Analytes to measure (in appropriate biological fluid): Total (free + bound) liothyronine in plasma. Bioequivalence based on (90% CI): Total (free + bound) liothyronine in plasma after baseline correction. Waiver request of in vivo testing: 25 μg and 5 μg based on (i) acceptable bioequivalence studies on the 50 μg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Lisinopril Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Lisinopril in plasma. Bioequivalence based on (90% CI): Lisinopril. Waiver request of in vivo testing: 2.5 mg, 5 mg, 10 mg, 20 mg, and 30 mg, based on acceptable (i) bioequivalence studies on the 40-mg strength, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.
- Lopinavir; Ritonavir Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg/50 mg (400 mg/100 mg dose); Subjects: Normal, healthy males and females, general population. Additional comments: Pregnant and lactating women should be excluded from participation in studies. Women must have a negative baseline pregnancy test prior to receiving the drug. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg/50 mg (400 mg/100 mg dose); Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Lopinavir and ritonavir in plasma. Bioequivalence based on (90% CI): Lopinavir and ritonavir. Waiver request of in vivo testing: Not applicable.
- Loratadine Orally Disintegrating Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Loratadine and the active metabolite, descarboethoxyloratadine, in plasma. Please submit the metabolite data as supportive evidence of the comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Loratadine. Waiver request of in vivo testing: Not applicable.
- Losartan Potassium Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Pregnant women should be excluded from participation in the bioequivalence studies. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: See comment above. Analytes to measure (in appropriate biological fluid): Losartan and the metabolite carboxylic acid in plasma. Bioequivalence based on (90% CI): Losartan. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the carboxylic acid metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 25 mg and 50 mg based on (i) acceptable bioequivalence studies on the 100-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Mefloquine Hydrochloride Tablets/Oral. Recommended studies: 1 study. Type of study: Fed Design: Single-dose, parallel design in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Mefloquine has been shown to cause esophagitis/gastritis when administered under fasting conditions. A fasting bioequivalence study is not recommended. Analytes to measure: Mefloquine in plasma. Bioequivalence

based on (90% CI): Mefloquine. Waiver request of in vivo testing: Not applicable.

- Meloxicam Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way, crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-way, crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Meloxicam in plasma. Bioequivalence based on (90% CI): Meloxicam. Waiver request of in vivo testing: 7.5 mg based on (i) acceptable bioequivalence studies on the 15-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Products at this Web site conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products. Specifications of the application.
- Memantine Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Females should not be of childbearing potential. 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Females should not be of childbearing potential. Additional comments: Analytes to measure (in appropriate biological fluid): Memantine in plasma. Bioequivalence based on (90% CI): Memantine. Waiver request of in vivo testing: 5 mg, based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) formulation proportionality of 10-mg and 5-mg strengths, and (iii) acceptable dissolution testing on both strengths.
- Mercaptopurine Tablet/Oral. Recommended studies: 1 study. Submission of an investigational new drug application is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as Mercaptopurine (see 21 CFR § 320.31). Type of study: Steady-state study in patients; Strength: 50 mg; Studies may be conducted at steady state in patients receiving therapeutic doses (usually 100–200 mg/day in the average adult) or maintenance daily doses (usually 50–100 mg/day in the average adult). Patients should be in a stable regimen using the same dosage unit (multiples of the same strength). Additional comments: Patients with inherited deficiency of the enzyme thiopurine methyl transferase must be excluded from these studies. The protocol may exclude concomitant chemotherapy and should exclude prior exposure to doxorubicin. The informed consent should include a description of the known genotoxicity of 6-mercaptopurine in human cells and animal models. Analytes to measure (in appropriate biological fluid): Mercaptopurine in plasma. Bioequivalence based on (90% CI): Mercaptopurine. Waiver request of in vivo testing: Not applicable.
- Mesalamine Enema/Rectal. Recommended studies: 1 study. The following study is recommended to establish bioequivalence of mesalamine rectal enema provided that the test product is qualitatively (Q1) and quantitatively (Q2) the same as the RLD: Type of study: Fasting Design: Single-dose, two-way crossover in vivo or replicate design; Strength: 4 G/60 mL; Subjects: Normal, healthy males and females, general population. Additional comments: The proposed generic and RLD formulations should have comparable particle size. Analytes to measure (in appropriate biological fluid: Mesalamine (5-ASA) in plasma. Bioequivalence based on (90% CI): Mesalamine (5-ASA). Waiver request of in vivo testing: Not applicable. In vitro dissolution testing under the following conditions should be submitted to support documentation of bioequivalence: Please conduct comparative dissolution testing on 12 dosage units of the test and reference products using 900 mL of the following media: 0.1 N HCl, and buffers at pH 4.5, pH 6.8, and pH 7.2 using Apparatus II (paddle) at 25 and 50 rpm. Please ensure that the dissolution method is adequate to distinguish mesalamine dissolved in dissolution media from drug particles. You may modify the filtration method in the dissolution testing, if necessary.
- Mesalamine Suppository/Rectal. Recommended studies: 3 studies. 1. Type of study: Bioequivalence study with clinical end points Design: Parallel design, three arm (test, reference, and placebo) in vivo; Strengths: 500 mg and 1000 mg; Subjects: Patients with ulcerative proctitis. Additional comments: Please submit a protocol to the Clinical Review Team for recommendations on study design. 2. Type of study: Bioequivalence studies with pharmacokinetic end points (fasting) Design: Single-dose, two-way crossover in vivo; Strengths: 500 mg 1000 mg, comparing to the respective strengths of the RLD; Subjects: Normal, healthy males and females, general population. Additional comments: Because the 500-mg and 1000-mg strengths are not proportionally similar, a bioequivalence study with clinical end points and a bioequivalence study with pharmacokinetic end points (fasting) will be needed for each strength product, if you wish to develop each strength. Analytes to measure (pharmacokinetic study): Mesalamine in plasma Bioequivalence (pharmacokinetic study) based on (90% CI): Mesalamine. Waiver request of in vivo testing: Not applicable.
- Metaxalone Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 800 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Metaxalone in plasma. Bioequivalence based on (90% CI): Metaxalone. Waiver request of in vivo testing: 400 mg based on (i) acceptable bioequivalence studies on the 800-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please note that Metaxalone Tablets, 400 mg, have been discontinued from the market. If you would like to market the 400-mg strength, please submit a Citizen Petition pursuant to 21 CFR 314.122, requesting that the FDA determine whether this strength was discontinued due to safety and/or effectiveness reasons. Please follow the Citizen Petition format outlined in 21 CFR 10.20 and 10.30.
- Metformin Hydrochloride Extended-release Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 750 mg; Subjects: Normal, healthy males and females, general population Additional Comments: The drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 750 mg; Subjects: Normal, healthy males and females, general population Additional comments: Please

see comment above. Analytes to measure (in appropriate biological fluid): Metformin in plasma. Bioequivalence based on (90% CI): Metformin. Waiver request of in vivo testing: 500 mg based on (i) acceptable bioequivalence studies on the 750-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Metformin Hydrochloride; Pioglitazone Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 850 mg metformin HCl and 15 mg pioglitazone HCl (as the base); Subjects: Normal, healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Additional comments: To avoid hypoglycemic episodes in healthy volunteers, the drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 850 mg metformin HCl and 15 mg pioglitazone HCl (as the base); Subjects: Normal, healthy males and females, general population. Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Additional comments: To avoid hypoglycemic episodes in healthy volunteers, the drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing." Analytes to measure (in appropriate biological fluid): Metformin, Pioglitazone, and Hydroxypioglitazone (M-IV) in plasma. Bioequivalence based on (90% CI): Metformin and pioglitazone. Waiver request of in vivo testing: (500 mg and 15 mg) Metformin HCl, Pioglitazone HCl tablets, based on (i) acceptable bioequivalence study on the (850 mg and 15 mg) tablet, and (ii) acceptable in vitro dissolution testing of all strengths.
- Metoprolol Succinate Extended Release Tablets/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. 3. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Analytes to measure (in appropriate biological fluid): Metoprolol in plasma. Bioequivalence based on (90% CI): Metoprolol. Waiver request of in vivo testing: 25 mg, 100 mg tablets, based on (i) acceptable bioequivalence studies on the 50-mg and 200-mg strengths, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2 and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation. Because of concerns of dose dumping from this drug product when taken with alcohol, please conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium, as follows: Testing Conditions: 900 mL, 0.1 N HCl, Apparatus II (paddle) at 50 rpm, with and without the alcohol (see below): Test 1: 12 units tested according to the proposed method (with 0.1 N HCl), with data collected every 15 minutes for a total of 2 hours. Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range, and %CV on both strengths.
- Minocycline Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 135 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 135 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Minocycline in plasma. Bioequivalence based on (90% CI): Minocycline. Waiver request of in vivo testing: 45 mg and 90 mg based on (i) acceptable bioequivalence studies on the 135-mg strength, (ii) proportionally similar 45 mg and 90 mg formulations to the 135-mg strength, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.
- Mirtazapine Orally Disintegrating Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting

Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, studies on the lower strength are recommended. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population Additional comments: Please see above comment. Analytes to measure: Mirtazapine in plasma. Bioequivalence based on (90% CI): Mirtazapine. Waiver request of in vivo testing: 30 mg and 45 mg based on (i) acceptable bioequivalence studies on the 15-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Modafinil Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Modafinil using an achiral assay. Bioequivalence based on (90% CI): Modafinil. Waiver request of in vivo testing: 100 mg based on (i) acceptable bioequivalence studies on the 200-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Moexipril Hydrochloride Tablet/Oral. Recommended studies: 1 study. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 15 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Pregnant women should be excluded from participation in the bioequivalence study. Analytes to measure (in appropriate biological fluid): Moexipril in plasma. Bioequivalence based on (90% CI): Moexipril. Waiver request of in vivo testing: 7.5 mg based on (i) acceptable bioequivalence studies on the 15-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Montelukast Sodium Chewable Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Montelukast in plasma. Bioequivalence based on (90% CI): Montelukast. Waiver request of in vivo testing: 4 mg based on (i) acceptable bioequivalence studies on the 5-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Mycophenolate Mofetil Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional Comments: 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Mycophenolate mofetil, and the active metabolite, mycophenolic acid in plasma. Bioequivalence based on (90% CI): Mycophenolate mofetil. If mycophenolate mofetil plasma concentrations can be reliably measured and its pharmacokinetics accurately determined, please analyze the data for the parent compound using the confidence interval approach. The data for the active metabolite can be used as supportive evidence. However, if you can demonstrate that it is not possible to measure mycophenolate mofetil in plasma accurately and reliably, please analyze the metabolite using the confidence interval approach. Waiver request of in vivo testing: Not applicable.
- Nabumetone Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 750 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 750 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: 6-methoxy-2-naphthylacetic acid (6-MNA). Bioequivalence based on (90% CI): 6-methoxy-2-naphthyl-acetic acid (6-MNA). Waiver request of in vivo testing: 500 mg based on (i) acceptable bioequivalence studies on the 750-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Nateglinide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 120 mg; Subjects: Normal, healthy males and females, general population. Additional comments: All subjects should fast overnight for at least 10 hours prior to dosing and for 4 hours after dosing. A single oral dose (120 mg) should be administered with 240 mL of 20% glucose solution. Since, multiple plasma concentration peaks were often observed under fasting conditions, please ensure that the same sampling schedule is followed during the study for both test and reference drug administration. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 120 mg; Subjects: Normal, healthy males and females, general population Additional comments: A single oral dose (120 mg) should be administered with 240 mL of water 30 minutes after start of a standard high-fat FDA breakfast. Subjects should start the recommended meal 30 minutes prior to administration of the drug product. Study subjects should eat this meal in 30 minutes or less; however, the drug product should be administered 30 minutes after start of the meal. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Nateglinide in plasma. Bioequivalence based on (90% CI): Nateglinide. Waiver request of in vivo testing: 60 mg, based on (i) acceptable bioequivalence studies on the 120-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Nelfinavir Mesylate Tablets/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 625 mg; Subjects: Normal, healthy males and females, general population. Additional comments: High pharmacokinetic variability has been observed with

nelfinavir when administered to fasting subjects. Thus, it is the firm's responsibility to enroll an adequate number of subjects to demonstrate bioequivalence. Since nelfinavir appears to be a highly variable drug when administered under fasting conditions, conducting a replicate-design study as an alternative to a two-way crossover study may be considered. A replicate study design has the advantage that fewer subjects can be used than in a two-way crossover study. The FDA recommends that a replicate design bioequivalence study use the following two sequences: ABAB (Test Reference Test Reference) and BABA (Reference Test Reference Test). 2. Type of study: Fasting Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see above. 3. Type of study: Fed Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 625 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see above. Analytes to measure (in appropriate biological fluid): Nelfinavir in plasma. Please develop a method of adequate sensitivity to accurately measure nelfinavir concentrations in plasma. If it is not possible to accurately measure nelfinavir plasma concentrations following administration of a single dosage unit, it is acceptable to administer a higher dose. A single dose as high as 1250 mg may be safely administered to healthy, normal subjects. Bioequivalence based on (90% CI): Nelfinavir. Waiver request of in vivo testing: Not applicable.

- Nevirapine Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, randomized, two-treatment, one-period, parallel, open-label in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns of severe life-threatening skin reactions and hepatotoxicity, single-dose parallel study designs in healthy volunteers are recommended. 2. Type of study: Fed Design: Single-dose, randomized, two-treatment, one-period, parallel, open-label in vivo; Strength: 200 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Nevirapine in plasma. Bioequivalence based on (90% CI): Nevirapine. Waiver request of in vivo testing: Not applicable.
- Olanzapine Orally Disintegrating Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, studies should be conducted using the 5-mg strength. 2. Type of study: Fed Design: Single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see above comment. Analytes to measure: Olanzapine in plasma. Bioequivalence based on (90% CI): Olanzapine. Waiver request of in vivo testing: 10 mg, 15 mg, and 20 mg based on (i) acceptable bioequivalence studies on the 5-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Product at this Web site.
- Olmesartan Medoxomil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Labeling for this drug contains a black box regarding pregnancy and fetal/neonatal morbidity and mortality. 2. Type of study: Fed Design: Single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Olmesartan in plasma. Bioequivalence based on (90% CI): Olmesartan. Waiver request of in vivo testing: 20 mg and 5 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Omeprazole, Sodium Bicarbonate, and Magnesium Hydroxide Chewable Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 40 mg/600 mg/700 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Omeprazole in plasma. Bioequivalence based on (90% CI): Omeprazole. Waiver request of in vivo testing: 20 mg/600 mg/700 mg based on (i) acceptable bioequivalence studies on the 40-mg/600-mg/700-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Omeprazole Magnesium Delayed-release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Omeprazole in plasma. Bioequivalence based on (90% CI): Omeprazole. Waiver request of in vivo testing: Not applicable.
- Ondansetron Orally Disintegrating Tablet. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Ondansetron in plasma. Bioequivalence based on (90% CI): Ondansetron. Waiver request of in vivo testing: 4 mg based on (i) acceptable bioequivalence studies on the 8-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Ondansetron Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 24 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 24 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Ondansetron in plasma. Bioequivalence based on (90% CI): Ondansetron. Waiver request of in vivo testing: 4 and 8 mg based on (i)

acceptable bioequivalence studies on the 24-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Oxcarbazepine Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Oxcarbazepine and active metabolite 10-monohydroxy derivative in plasma using a chiral assay. Bioequivalence based on (90% CI): Oxcarbazepine. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 150 mg and 300 mg based on (i) acceptable bioequivalence studies on the 600-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Oxymorphone Hydrochloride Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please use a narcotic antagonist such as naltrexone if the study involves healthy subjects. You should consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Oxymorphone and its metabolite, 6-OH-oxymorphone in plasma. Bioequivalence based on (90% CI): Oxymorphone. For 6-OH-oxymorphone, please submit individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 5 mg, 10 mg, and 20 mg based on (i) acceptable bioequivalence studies of the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 phosphate buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, 4 and every 2 hours thereafter, until at least 80% of the labeled content is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets. Because of concerns of dose dumping from this drug product when taken with alcohol, please conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium, as follows: Testing Conditions: 900 mL, 0.1 N HCl, Apparatus I (basket) at 75 rpm, with and without the alcohol (see below): Test 1: 12 units tested according to the proposed method (with 0.1 N HCl), with data collected every 15 minutes for a total of 2 hours. Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range, and %CV on both strengths.
- Oxymorphone Hydrochloride Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please use a narcotic antagonist such as naltrexone if the study involves healthy subjects. You should consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist. Analytes to measure (in appropriate biological fluid): Oxymorphone and its metabolite, 6-OH-oxymorphone in plasma. For 6-OH-oxymorphone, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Oxymorphone. Waiver request of in vivo testing: 5 mg, based on acceptable (i) bioequivalence studies on the 10-mg strength, (ii) proportional similarity of the formulations, and (iii) acceptable in vitro dissolution testing of all strengths.
- Paliperidone Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 6 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 6 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Paliperidone in plasma. Bioequivalence based on (90% CI): Paliperidone. Waiver request of in vivo testing: 3 mg and 9 mg based on (i) acceptable bioequivalence studies of the 6-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, 6.8 buffer, and water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets.

- Pantoprazole Sodium Delayed Release Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Pantoprazole in plasma. Bioequivalence based on (90% CI): Pantoprazole. Waiver request of in vivo testing: 20 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Perindopril Erbumine Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Female subjects enrolled in the BE studies should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Perindopril and the active metabolite, perindoprilat in plasma. Bioequivalence based on (90% CI): Perindopril. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 2 mg and 4 mg based on (i) acceptable bioequivalence studies on the 8-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Phenytoin Chewable Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg dose (6 × 50 mg) and use a washout period of at least 14 days; Subjects: Normal, healthy males and females, general population. Additional comments: The tablets should be swallowed whole. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300-mg dose (6 × 50 mg) and use a washout period of at least 14 days; Subjects: Normal, healthy males and females, general population. Additional Comments: The tablets should be swallowed whole. Analytes to measure (in appropriate biological fluid): Phenytoin in plasma. Bioequivalence based on (90% CI): Phenytoin. Waiver request of in vivo testing: Not applicable.
- Pilocarpine Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 7.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 7.5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Pilocarpine and the metabolite, pilocarpic acid in plasma. Pilocarpine has been shown to be unstable in heparinized plasma and convert to pilocarpic acid during storage. Therefore, you should pay attention to the stabilization of pilocarpine and separation of the drug from its metabolites in the assay development and validation. Recent literature states that the use of EDTA as an anticoagulant during blood sampling may be helpful in stabilizing pilocarpine. The stability of pilocarpine in plasma samples and the assay specificity of pilocarpine, especially in relation to its metabolites and plasma endogenous components, should be clearly demonstrated in the assay method validation report submitted to the FDA. Bioequivalence based on (90% CI): Pilocarpine. If pilocarpine can be reliably measured, a confidence interval approach for bioequivalence determination should be used for pilocarpine. If pilocarpine cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for pilocarpic acid. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 7.5-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Pimozide Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Pimozide in plasma Pimozide has a long terminal elimination half-life. Please ensure adequate washout periods between treatments in the crossover studies. You may also consider using a parallel study design due to pimozide's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC0–t or AUC–inf. Please collect sufficient blood samples in the bioequivalence study to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (t_{max}). Bioequivalence based on (90% CI): Pimozide. Waiver request of in vivo testing: 1 mg based on (i) acceptable bioequivalence studies on the 2-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Pravastatin Sodium Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional Comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Pravastatin in plasma. Bioequivalence based on (90% CI): Pravastatin. Waiver request of in vivo testing: 10 mg, 20 mg, and 40 mg based on (i) acceptable bioequivalence studies on the 80-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Quetiapine Fumarate Tablet/Oral. Recommended studies: 3 studies. 1. Type of study: Fasting Design: single-dose, in –vivo; Strength: 25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please include careful safety precautions in your protocols, including adequate monitoring of vital signs and adverse events, stopping criteria in the event of an unacceptable degree of hypotension or tachycardia, and appropriate evaluation and management of adverse events. Please assure

that the investigator(s) will be vigilant in recognizing and managing any unacceptable clinical or laboratory findings. It is recommended that a study protocol be submitted for review before initiating a bioequivalence study for this product. 2. Type of study: Fed Design: single-dose, in vivo; Strength: 25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. 3. Type of study and design: Steady-state, in vivo; Strength: 300 mg; Subjects: Schizophrenic patients already receiving quetiapine in a stable regimen. Additional comments: Please see comments above. Analytes to measure: Quetiapine in plasma. Bioequivalence based on (90% CI): Quetiapine. Waiver request of in vivo testing: 50 mg, 100 mg, 150 mg, 200 mg, and 400 mg based on (i) acceptable bioequivalence studies on the 25-mg and 300-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products.

- Quinapril Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way, crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Pregnant women should be excluded from participation in bioequivalence studies with ACE inhibitors. 2. Type of study: Fed Design: single-dose, two-way, crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population Additional comments: Pregnant women should be excluded from participation in bioequivalence studies with ACE inhibitors. Analytes to measure: Quinapril and the metabolite, Quinaprilat in plasma. Bioequivalence based on (90% CI): Quinapril. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 5 mg, 10 mg, and 20 mg based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Raloxifene Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 60 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 60 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Raloxifene and the metabolites, raloxifene-4′-glucuronide and raloxifene-6′-glucuronide in plasma. Bioequivalence based on (90% CI): Raloxifene. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: Not applicable.
- Ribavirin Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Ribavirin in plasma. Bioequivalence based on (90% CI): Ribavirin. Waiver request of in vivo testing: 200 mg, and 400-mg strengths based on (i) acceptable bioequivalence studies on the 600-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Riluzole Tablets/Oral. Recommended studies: 1 study. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Riluzole in plasma. Bioequivalence based on (90% CI): Riluzole. Waiver request of in vivo testing: Not applicable.
- Risedronate Sodium; Calcium Carbonate Tablets/Oral (co-packaged). Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 35 mg (risedronate sodium tablet); Subjects: Normal, healthy males and females, general population. Additional comments: As an option, due to the relatively long half-life, the firm may wish to conduct this study using a parallel design. As an additional option for either the crossover or parallel design, the firm may wish to truncate the AUC at 72 hours. Analytes to measure (in appropriate biological fluid): Risedronate in plasma. Bioequivalence based on (90% CI): Risedronate. Waiver request of in vivo testing: Not applicable. For calcium carbonate table please conduct comparative dissolution testing on 12 dosage units.
- Risedronate Sodium Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 35 mg; Subjects: Normal, healthy males and females, general population. Additional comments: As an option, due to the relatively long half-life, the firm may wish to conduct this study using a parallel design. As an additional option for either the crossover or parallel design, the firm may wish to truncate the AUC at 72 hours. Analytes to measure (in appropriate biological fluid): Risedronate in plasma. Bioequivalence based on (90% CI): Risedronate. Waiver request of in vivo testing: 5 mg and 30 mg based on (i) acceptable bioequivalence study on the 35-mg and 75-mg strengths, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Risperidone Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, bioequivalence studies should be conducted using the 1-mg strength. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Risperidone in plasma. Bioequivalence based on (90% CI): Risperidone. Waiver request of in vivo testing: 0.25 mg, 0.5 mg, 2 mg, 3 mg,

and 4 mg based on (i) acceptable bioequivalence studies on the 1-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Rizatriptan Benzoate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Rizatriptan in plasma. Bioequivalence based on (90% CI): Rizatriptan. Waiver request of in vivo testing: 5 mg, based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Rosiglitazone Maleate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 8 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Rosiglitazone in plasma. Bioequivalence based on (90% CI): Rosiglitazone. Waiver request of in vivo testing: 2 mg and 4 mg, based on (i) acceptable bioequivalence studies on the 8-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Rosuvastatin Calcium Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 40 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Rosuvastatin in plasma. Bioequivalence based on (90% CI): Rosuvastatin. Waiver requests of in vivo testing: 5-mg, 10-mg, and 20-mg strengths based on (i) acceptable bioequivalence studies on the 40-mg strength, (ii) proportional similarity across all strengths, and (iii) acceptable dissolution testing of all strengths.
- Saquinavir Mesylate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Saquinavir in plasma. Bioequivalence based on (90% CI): Saquinavir. Waiver request of in vivo testing: Not applicable.
- Sertraline Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, bioequivalence studies should be conducted on the 100-mg strength. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Sertraline in plasma. Bioequivalence based on (90% CI): Sertraline. Waiver request of in vivo testing: 25 mg, 50 mg, 150 mg, and 200 mg based on (i) acceptable bioequivalence studies on the 100-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Sildenafil Citrate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males. Additional comments: Analytes to measure (in appropriate biological fluid): Sildenafil and active metabolite piperazine N-desmethylsildenafil in plasma. Bioequivalence based on (90% CI): Sildenafil. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: Individual and mean concentrations; Individual and mean pharmacokinetic parameters and Geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 25 mg and 50 mg based on (i) acceptable bioequivalence studies on the 100-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Simvastatin Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Simvastatin and its β-hydroxyacid metabolite in plasma. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the β-hydroxy metabolite of simvastatin, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Bioequivalence based on (90% CI): Simvastatin. Waiver request of in vivo testing: 5 mg, 10 mg, 20 mg, and 40 mg based on (i) acceptable bioequivalence studies on the 80-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products using the method specified in the USP method.
- Sirolimus Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Sirolimus in plasma. Bioequivalence based on (90% CI): Sirolimus. Waiver request of in vivo testing: 1 mg based on (i) acceptable bioequivalence studies on the 2-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Solifenacin Succinate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, parallel in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Note: As an option, you may conduct this study using a single-dose, two-way crossover design. As an additional option for either the crossover or parallel design, you may truncate the AUC at 72 hours, provided the drug demonstrates low intrasubject variability in distribution and clearance. 2. Type of Study: Fed Design: single-dose, parallel in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Solifenacin in plasma. Bioequivalence based on (90% CI): Solifenacin. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Sumatriptan Succinate Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Sumatriptan in plasma. Bioequivalence based on (90% CI): Sumatriptan. Waiver request of in vivo testing: 25 mg and 50 mg, based on (i) acceptable bioequivalence studies on the 100-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Tadalafil Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males, general population. Additional comments: 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tadalafil in plasma. Bioequivalence based on (90% CI): Tadalafil. Waiver request of in vivo testing: 5 mg and 10 mg based on (i) acceptable bioequivalence studies on the 20-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Telithromycin Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: The study design should include a screen for signs and symptoms of possible hepatotoxicity prior to administering each subsequent dose of telithromycin in a crossover or replicate crossover design. In order to minimize the risk of hepatotoxicity, please do not exceed a 400-mg dose in the BE study. Subjects who consume alcohol should be excluded from BE studies of telithromycin. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 400 mg; Subjects: Normal, healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Telithromycin in plasma. Bioequivalence based on (90% CI): Telithromycin. Waiver request of in vivo testing: 300 mg based on (i) acceptable bioequivalence studies on the 400-mg strength, (ii) proportionally similar across both strengths, and (iii) acceptable in vitro dissolution testing of both strengths.
- Telmisartan Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 80 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Telmisartan in plasma. Bioequivalence based on (90% CI): Telmisartan. Waiver request of in vivo testing: 20 mg and 40 mg, based on (i) acceptable bioequivalence studies on the 80-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Tenofovir Disoproxil Fumarate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tenofovir in serum. Bioequivalence based on (90% CI): Tenofovir. Waiver request of in vivo testing: Not applicable.
- Terbinafine Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Randomized, single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Terbinafine in plasma. Bioequivalence based on (90% CI): Terbinafine. Waiver request of in vivo testing: Not applicable.
- Testosterone Extended Release Tablets/Buccal. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 30 mg; Subjects: Testosterone-deficient (hypogonadal) males. Additional comments: Subjects should not currently be receiving any treatment for their hypogonadism. The inclusion criterion for testosterone-deficient (hypogonadal) males is serum testosterone levels below 2.5 ng/mL. At least three predose levels will serve as baseline. A "fed" BE study is not recommended because the product is a buccal adhesive, not to be ingested. This obviates the need for oral dose dumping assessment due to food. 2. Type of study: In vitro adhesion comparative performance testing study Design: A tensiometry study is recommended to compare the peak detachment force for test and reference products. Water is recommended between the buccal tablets and the base plate of the tensiometer. The loading weight and length

of time the loading weight is applied to press the buccal tablet into contact with the base plate should be specified. Following removal of the weight, the rate at which the buccal tablet is pulled away from the base plate should be specified. The peak detachment force should be measured as the force required to detach the buccal tablet from the base plate. The comparative adhesion test should be conducted using 12 individual units of the test and reference products. Prior to conducting studies for submission to the ANDA, the firm should determine appropriate loading weight, length of time the loading weight is applied to press the buccal tablet into contact with the base plate of the tensiometer, and the rate at which the buccal tablet is pulled away from the base plate. These studies should be conducted to assure the appropriateness of the test conditions to the test and reference products. Analytes to measure (in appropriate biological fluid): Total testosterone in plasma. Bioequivalence based on (90% CI): Baseline-adjusted testosterone. Waiver request of in vivo testing: Not applicable.

- Ticlopidine Hydrochloride Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 250 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Ticlopidine in plasma. Bioequivalence based on (90% CI): Ticlopidine. Waiver request of in vivo testing: Not applicable.
- Tinidazole Tablet/Oral. Recommended studies: 1 study. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 500 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tinidazole in plasma. Bioequivalence based on (90% CI): Tinidazole. Waiver request of in vivo testing: 250 mg based on (i) acceptable bioequivalence studies of the 40-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. Dissolution testing to document bioequivalence: Apparatus: USP Apparatus I (basket) Rotation speed: 100 rpm Medium: 0.1 N HCl (or 0.1 N HCl with NaCl) at pH 1.2, pH 4.5 acetate buffer, pH 6.8 phosphate buffer, and water Volume: 900 mL Temperature: 37°C Sample times: 5, 10, 15, 20, 25, 30, and 40 minutes or as needed for profile comparisons. Additional comments: All raw data (test and reference products) should be submitted with means at each sampling point, the range (minimum and maximum values), the percentage of coefficient of variation (%CV), and f2 value tabulated (if appropriate). The dissolution testing should be conducted on 12 units from the same lot numbers that are used in the in vivo bioequivalence study.
- Tolterodine Tartrate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: Randomized, single-dose, two-treatment, two-period, two-sequenced crossover in vivo; Strength: 2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: Randomized, single-dose, two-treatment, two-period, two-sequenced crossover in vivo; Strength: 2 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tolterodine and the active metabolite, 5-hydroxymethyltolterodine (5-OHM) in plasma. Bioequivalence based on (90% CI): Tolterodine. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 1 mg based on (i) acceptable bioequivalence studies on the 2-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Topiramate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns, studies should be conducted on the 25-mg strength. Animal studies with topiramate have demonstrated selective developmental toxicity, including teratogenicity. Although no studies have been conducted in pregnant women taking topiramate, in postmarketing experience, cases of hypospadias have been reported in male infants exposed in utero to topiramate, with or without other anticonvulsants; however, a causal relationship with topiramate has not been established. Therefore, the following precautions are recommended for the bioequivalence study: Pregnant women should be excluded from the study, and a negative pregnancy test should be required within 24 hours before dosing for all women of childbearing potential. Women of childbearing potential should be enrolled only if using an effective method of contraception. Written informed consent must include the finding of birth defects in animal studies and the unknown risk to a human fetus if exposed to this drug. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 25 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Topiramate in plasma. Bioequivalence based on (90% CI): Topiramate. Waiver request of in vivo testing: 50 mg, 100 mg, and 200 mg based on (i) acceptable bioequivalence studies on the 25-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Torsemide Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Due to safety concerns associated with administering Torsemide Tablets, 100 mg, to healthy subjects, in vivo bioequivalence studies should be conducted on the 20-mg strength. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Torsemide in plasma. Bioequivalence based on (90% CI): Torsemide. Waiver request of in vivo testing: 5 mg, 10 mg, and 100 mg, based on (i) acceptable bioequivalence studies on the 20-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Tramadol Hydrochloride; Acetaminophen Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting

Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 37.5 mg/325 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 37.5 mg/325 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tramadol using an achiral assay and acetaminophen. Bioequivalence based on (90% CI): Tramadol and acetaminophen. Waiver request of in vivo testing: Not applicable.

- Tramadol Extended Release Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 100 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Tramadol in plasma by achiral assay (nonstereospecific method). Bioequivalence based on (90% CI): Tramadol. Waiver request of in vivo testing: 200 mg and 300 mg based on (i) acceptable bioequivalence studies on the 100-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation. Because of concerns of dose dumping from this drug product when taken with alcohol, please conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium, as follows: Testing conditions: 900 mL, 0.1 N HCl, Apparatus I (basket) at 75 rpm, with and without the alcohol (see below): Test 1: 12 units tested according to the proposed method (with 0.1 N HCl), with data collected every 15 minutes for a total of 2 hours. Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours. Both test and RLD products must be tested accordingly and data must be provided on individual unit, means, range, and %CV on both strengths.
- Tramadol Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 50 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Tramadol in plasma using an achiral assay. Bioequivalence based on (90% CI): Tramadol. Waiver request of in vivo testing: Not applicable.
- Trandolapril Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 4 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 4 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure: Trandolapril and its active metabolite, trandolaprilat in plasma. Bioequivalence based on (90% CI): Trandolapril. Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}. Waiver request of in vivo testing: 1 mg and 2 mg based on (i) acceptable bioequivalence studies on the 4-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Trospium Chloride Tablet/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Analytes to measure (in appropriate biological fluid): Trospium in plasma. Bioequivalence based on (90% CI): Trospium. Waiver request of in vivo testing: Not applicable.
- Valacyclovir Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1000 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1000 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Valacyclovir and its metabolite, acyclovir, in both studies. If valacyclovir plasma concentrations can be reliably measured and its pharmacokinetic parameters accurately determined, you should analyze the valacyclovir data using the confidence interval approach. The acyclovir data can be used to provide supportive evidence of comparable therapeutic outcome. Bioequivalence based on (90% CI): Valacyclovir. If valacyclovir cannot be reliably measured, you should analyze the acyclovir data obtained from these studies using the confidence interval approach. Waiver request of in vivo testing: 500 mg based on (i) acceptable bioequivalence studies on the 1000-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Valsartan Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 320 mg; Subjects: Normal, healthy males and females, general population. Additional comments: A dose of 320 mg can be

safely administered to healthy subjects. Please include provisions for appropriate monitoring and intervention in the case of possible drug-related adverse events (e.g., subjects complaining of dizziness/lightheadedness should have blood pressure/heart rate assessed). Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 320 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Valsartan in plasma. Bioequivalence based on (90% CI): Valsartan. Waiver request of in vivo testing: 40 mg, 80 mg, and 160 mg based on (i) acceptable bioequivalence studies on the 320-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

- Vardenafil Hydrochloride Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males, general population. Additional comments: 2. Type of Study: Fed Design: single-dose, two-way crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Vardenafil in plasma. Bioequivalence based on (90% CI): Vardenafil. Waiver request of in vivo testing: 2.5 mg, 5 mg, and 10 mg, based on (i) acceptable bioequivalence studies on the 20-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Varenicline Tartrate Tablet/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1.0 mg; Subjects: Normal, healthy males and females, general population, smokers, and nonsmokers may be used. Additional comments: Females should not be pregnant, and if applicable, should practice abstention or contraception during the study. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 1.0 mg; Subjects: Normal, healthy males and females, general population, smokers, and nonsmokers may be used. Additional comments: Please see comments above. Analytes to measure (in appropriate biological fluid): Varenicline in plasma. Bioequivalence based on (90% CI): Varenicline. Waiver request of in vivo testing: 0.5 mg, based on (i) acceptable bioequivalence studies of the 1-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Zafirlukast Tablets/Oral. Recommended studies: 1 study. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 20 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Zafirlukast in plasma. Bioequivalence based on (90% CI): Zafirlukast. Waiver request of in vivo testing: 10 mg based on acceptable (i) bioequivalence studies on the 20-mg tablet, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.
- Zalcitabine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 0.75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 0.75 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Zalcitabine in plasma. Bioequivalence based on (90% CI): Zalcitabine. Waiver request of in vivo testing: 0.375 mg based on (i) acceptable bioequivalence studies on the 0.75-mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Zaleplon Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Patients should be advised not to drive if they are experiencing drowsiness and/or dizziness at the end of the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Zaleplon in plasma. Bioequivalence based on (90% CI): Zaleplon. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.
- Zidovudine Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 300 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Zidovudine in plasma. Bioequivalence based on (90% CI): Zidovudine. Waiver request of in vivo testing: Not applicable. Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products.
- Zileuton Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 600 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure (in appropriate biological fluid): Zileuton in plasma. Bioequivalence based on (90% CI): Zileuton. Waiver request of in vivo testing: Not applicable.
- Zolmitriptan Orally Disintegrating Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: The whole tablet should be placed on the tongue and allowed to disintegrate for 30 seconds. After 30 seconds, all subjects should consume 240 mL of water. 2. Type of study: Fed Design: single-dose, two-treatment, two-period crossover in vivo; Strength: 5 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Please see comment above. Analytes to measure (in appropriate biological fluid): Zolmitriptan in plasma. Bioequivalence based on (90% CI): Zolmitriptan. Waiver request of in vivo

testing: 2.5 mg based on acceptable (i) bioequivalence studies on the 5-mg strength, and (ii) proportional similarity of the formulations and (iii) acceptable in vitro dissolution testing of all strengths.

- Zolpidem Tablets/Oral. Recommended studies: 2 studies. 1. Type of study: Fasting Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Patients should be advised not to drive if they are experiencing drowsiness and/or dizziness at the end of the study. 2. Type of study: Fed Design: single-dose, two-way crossover in vivo; Strength: 10 mg; Subjects: Normal, healthy males and females, general population. Additional comments: Analytes to measure: Zolpidem in plasma. Bioequivalence based on (90% CI): Zolpidem. Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10-mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

GMP Audit Template, EU Guidelines (http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol4_en.htm)

		Compliance 1 2 3[a]	Remarks	EU-Guide
1	**PERSONNEL**			
1.1	Qualified personnel available?	☐ ☐ ☐		2.1
1.2	Organization charts available?	☐ ☐ ☐		2.2
1.3	Job descriptions available?	☐ ☐ ☐		2.2
1.4	Responsibilities clearly defined?	☐ ☐ ☐		2.2
	Key personnel			
	Responsible persons designated for:			
1.5	• Production?	☐ ☐ ☐		2.5
1.6	• Quality control?	☐ ☐ ☐		2.6
1.7	Are they independent from each other?	☐ ☐ ☐		2.3
1.8	Are joint functions clearly defined?	☐ ☐ ☐		2.7
1.9	Are the responsible persons working full time?	☐ ☐ ☐		2.3
1.10	Have the responsible persons the appropriate formation, knowledge, and experience?	☐ ☐ ☐		2.1/2.2
1.11	Have the relevant departments enough personnel?	☐ ☐ ☐		2.1
	Training			
1.12	Continuous training programs for the production and QC staff?	☐ ☐ ☐		2.8
1.13	Initial job training for all employees?	☐ ☐ ☐		2.9
1.14	Teaching aids (videos, slides, brochures) available?	☐ ☐ ☐		2.9
1.15	External training courses for the staff?	☐ ☐ ☐		2.9
1.16	Training records?	☐ ☐ ☐		2.9
1.17	Special training in sensitive areas? (sterile prod., toxic subs.)	☐ ☐ ☐		2.10
1.18	Information for visitors to the manufacturing area?	☐ ☐ ☐		2.11
2	**HYGIENE**			
	Personnel hygiene			
	Detailed written hygiene programs for:			
2.1	• clothing?	☐ ☐ ☐		2.13
2.2	• use of washrooms?	☐ ☐ ☐		2.13
2.3	• behaviour in production areas?	☐ ☐ ☐		2.13
2.4	Precautions against sick or personnel with open wounds in production?	☐ ☐ ☐		2.14
	Medical examination			
2.5	• on recruitment?	☐ ☐ ☐		2.15
2.6	• regular reexaminations?	☐ ☐ ☐		2.15

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Duty of notification after:			
2.7	• trips to tropical countries?	☐ ☐ ☐		2.15
2.8	• cases of contagious illness in the family?	☐ ☐ ☐		2.15
2.9	Instructions for appropriate working clothes?	☐ ☐ ☐		2.16
2.10	Absence of food and drinks (chewing gum) in the working area?	☐ ☐ ☐		2.17
2.11	Measures against contact with open product (gloves, etc.)?	☐ ☐ ☐		2.18
2.12	Instructions for hand washing in production?	☐ ☐ ☐		2.19
2.13	Change of clothes when entering and leaving the production area?	☐ ☐ ☐		5.19
2.14	Change rooms and toilets easily within reach?	☐ ☐ ☐		3.31
2.15	Toilets and restrooms sufficiently separated from production areas?	☐ ☐ ☐		3.30/3.31
2.16	Workshops separate from production areas?	☐ ☐ ☐		3.32
2.17	Laboratory animal rooms totally segregated from production rooms?	☐ ☐ ☐		3.33
3	**WAREHOUSE**			
	Rooms, general:			
3.1	Suitable for the intended use?	☐ ☐ ☐		3
3.2	• adequate size?	☐ ☐ ☐		3
3.3	• clean?	☐ ☐ ☐		3
3.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
3.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
3.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
3.7	Appropriate lighting and air conditioning?	☐ ☐ ☐		3.3
3.8	Recording of temperature and humidity?	☐ ☐ ☐		
3.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
3.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, special requirements			
	Type of warehousing:			
3.11	Separation of goods sufficient?	☐ ☐ ☐		3.18
3.12	Provision for different storage temperatures?	☐ ☐ ☐		3.19
3.13	Goods receiving zone weather protected?	☐ ☐ ☐		3.20
3.14	Cleaning zone for incoming goods?	☐ ☐ ☐		3.20
3.15	Separate quarantine area with controlled access?	☐ ☐ ☐		3.21
3.16	Separate, protected sampling area?	☐ ☐ ☐		3.22
	Separate and safe storage of:			
3.17	• returned goods?	☐ ☐ ☐		3.23
3.18	• rejected goods?	☐ ☐ ☐		3.23
3.19	Separate and safe storage of highly active, toxic, or dangerous substances?	☐ ☐ ☐		3.24
3.20	Safe storage of narcotics?	☐ ☐ ☐		3.24
3.21	Safe storage of printed packaging materials?	☐ ☐ ☐		3.25
3.22	Security measurements against theft?	☐ ☐ ☐		3.25

		Compliance 1 2 3	Remarks	EU-Guide
3.23	Smoke detectors?	☐ ☐ ☐		3.25
3.24	Fire extinguishing system?	☐ ☐ ☐		3.25
	Operations:			
3.25	Reception, sampling, and labeling according to written procedures?	☐ ☐ ☐		5.2
3.26	Is a sampling plan available?	☐ ☐ ☐		Suppl. 4
3.27	Cleaning of incoming containers?	☐ ☐ ☐		5.3
3.28	Investigation and recording of damaged deliveries?	☐ ☐ ☐		5.4
3.29	FIFO principle?	☐ ☐ ☐		5.7
3.30	Inventory system?	☐ ☐ ☐		5.8
3.31	The location of materials can be detected at all times?	☐ ☐ ☐		
3.32	Incoming goods: containers and seals intact?	☐ ☐ ☐		5.27
3.33	Incoming goods: conformity with bill of delivery?	☐ ☐ ☐		5.27
	Labeling of incoming containers with:			
3.34	• internal name and code?	☐ ☐ ☐		5.29
3.35	• allocated batch number?	☐ ☐ ☐		5.29
3.36	• quarantine status?	☐ ☐ ☐		5.29
3.37	• expiry date or reanalysis date?	☐ ☐ ☐		5.29
3.38	Identity test for each incoming container?	☐ ☐ ☐		5.29
3.39	Are the sampled containers marked?	☐ ☐ ☐		5.30
3.40	Are reference samples taken?	☐ ☐ ☐		5.30
3.41	Safe storage of printed packaging materials?	☐ ☐ ☐		5.41
3.42	Lot tracing of all packaging materials possible?	☐ ☐ ☐		5.42
3.43	Are excessive packaging materials destroyed?	☐ ☐ ☐		5.43
	Release of starting materials by:			
	Physical/inventory checks on raw materials, packaging materials, and finished goods:			

	Item:	Stocks: Physical:	Stocks: Inventory:	Storage conditions:	

4	**DISPENSING/ASSEMBLING**			
	Rooms, general:			
4.1	Suitable for the intended use?	☐ ☐ ☐		3
4.2	• adequate size?	☐ ☐ ☐		3
4.3	• clean?	☐ ☐ ☐		3
4.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
4.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2

		Compliance 1 2 3[a]	Remarks	EU-Guide
4.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
4.7	Appropriate lighting and air conditioning?	☐ ☐ ☐		3.3
4.8	Recording of temperature and humidity?	☐ ☐ ☐		
4.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
4.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, special requirements:			
4.11	Segregated from production and warehouse?	☐ ☐ ☐		3.13
4.12	Separate weighing cabins?	☐ ☐ ☐		3.13
4.13	Separate AHU for each cabin?	☐ ☐ ☐		3.12
	Air pressure gradient from weighing cabin → corridor:			3.3
4.14	Dust extraction systems available?	☐ ☐ ☐		5.11
	Operations:			
4.15	Balances regularly calibrated?	☐ ☐ ☐		3.41
4.16	Only pharmaceutical raw materials in this area?	☐ ☐ ☐		5.17
4.17	Check on remains from previous materials before entering of new materials into a weighing cabin?	☐ ☐ ☐		5.9/5.35
4.18	Only one material in one cabin?	☐ ☐ ☐		5.9
4.19	Are dispensed materials correct labeled?	☐ ☐ ☐		5.29
4.20	Only released products in the dispensing?	☐ ☐ ☐		5.31
4.21	Cleaning SOPs for the dispensing?	☐ ☐ ☐		4.28
4.22	Previously dispensed material recorded on weighing protocol?	☐ ☐ ☐		4.8
4.23	Safety measures against mix-ups during assembling (e.g., cage pallets)?	☐ ☐ ☐		5.32/5.34
5	**SOLIDS MANUFACTURING**			
	Field of activity:			
	• Granulation	☐		
	• Compression	☐		
	• Encapsulation	☐		
	• Film and sugar coating	☐		
	• Visual inspection (capsules, tablets, etc.)	☐		
	• Premix (human)	☐		
	Rooms, general:			
5.1	Suitable for the intended use?	☐ ☐ ☐		3
5.2	• adequate size?	☐ ☐ ☐		3
5.3	• clean?	☐ ☐ ☐		3
5.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
5.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
5.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
5.7	Appropriate lighting and air conditioning?	☐ ☐ ☐		3.3
5.8	Recording of temperature and humidity?	☐ ☐ ☐		
5.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
5.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Rooms, special requirements:			
5.11	Separate manufacturing area for penicillins/cephalosporins or highly sensitizing substances?	☐ ☐ ☐		3.6
5.12	Only for processing of pharmaceuticals?	☐ ☐ ☐		3.6
5.13	Logical flow of materials?	☐ ☐ ☐		3.7
5.14	Walls, floors, and ceilings: smooth surface and free of cracks?	☐ ☐ ☐		3.8
5.15	Easy cleaning possible?	☐ ☐ ☐		3.10
5.16	Adequate drains with traps and grilles?	☐ ☐ ☐		3.11
5.17	Appropriate air handling system?	☐ ☐ ☐		3.12
	Air pressure gradient from working bay → corridor:			
	Classification according to EC guide?			
5.18	Appropriate dust extraction system?	☐ ☐ ☐		3.14
5.19	Appropriate lighting?	☐ ☐ ☐		3.16
5.20	Separate rest rooms?	☐ ☐ ☐		3.30
5.21	Changing rooms designed to avoid contamination?	☐ ☐ ☐		3.31
5.22	Toilets segregated from manufacturing areas?	☐ ☐ ☐		3.31
	Equipment			
5.23	Suitable for the intended use?	☐ ☐ ☐		3.34
5.24	Well maintained?	☐ ☐ ☐		3.34
5.25	Written & validated cleaning procedures?	☐ ☐ ☐		3.36
5.26	Maintenance without contamination risk (sep. area)?	☐ ☐ ☐		3.35
5.27	Equipment in contact with product: suitable materials quality?	☐ ☐ ☐		3.39
5.28	Machinery equipped with measuring and control devices?	☐ ☐ ☐		3.40
5.29	Calibration in fixed intervals acc. to written procedures?	☐ ☐ ☐		3.41
5.30	Calibration records available?	☐ ☐ ☐		3.41
5.31	Contents and flow direction marked on pipes?	☐ ☐ ☐		3.42
5.32	Pipes for distilled and demineralized water regularly monitored and sanitized?	☐ ☐ ☐		3.43
5.33	Not functioning equipment in the production area (if yes: clearly marked)?	**Y N** ☐ ☐ ☐		3.44
5.34	Status of cleanliness indicated?	☐ ☐ ☐		5.13
5.35	Previous product indicated?	☐ ☐ ☐		5.13
	Operations			
5.36	Are written and validated procedures for all manufacturing steps available?	☐ ☐ ☐		5.2
5.37	Are all manufacturing steps recorded with actual parameters?	☐ ☐ ☐		5.2
5.38	Check of each single container of the starting materials (contents, weight, identity)?	☐ ☐ ☐		5.3
5.39	Limits for yields?	☐ ☐ ☐		5.8
5.40	Only one batch of one product processed?	☐ ☐ ☐		5.9
5.41	Protection against microbial contamination?	☐ ☐ ☐		5.10
5.42	Appropriate measures against generation of dust (e.g., closed systems)?	☐ ☐ ☐		5.11

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Correct labeling of containers, materials, equipment, and rooms with:			5.12
5.43	• product name and batch no.	☐ ☐ ☐		5.12
5.44	• quarantine status?	☐ ☐ ☐		5.12
5.45	Deviations from standard procedures recorded and signed by the supervisor?	☐ ☐ ☐		5.14
5.46	Special procedures for the production of antibiotics, hormones, etc.?	☐ ☐ ☐		5.19
5.47	• Campaign production?	☐ ☐ ☐		5.19
5.48	• Special monitoring?	☐ ☐ ☐		5.19
5.49	• Validated decontamination procedure?	☐ ☐ ☐		5.19
5.50	Double check on weight?	☐ ☐ ☐		5.34
5.51	Line clearance before start of production?	☐ ☐ ☐		5.35
5.52	Investigation of deviations in yields?	☐ ☐ ☐		5.39
5.53	Validated procedures for reworking of rejected batches?	☐ ☐ ☐		5.62
5.54	Detailed procedures for the addition of previous batches?	☐ ☐ ☐		5.63
5.55	Special release procedure (QA) for those batches?	☐ ☐ ☐		5.64
5.56	Use of protective clothing (hair cover, shoes, masks, gloves)?	☐ ☐ ☐		2.16
5.57	Clothing regulation for visitors?	☐ ☐ ☐		2.11
	IPC			5.38
	Who performs IPC?			
5.58	Are IPC methods approved by QC?	☐ ☐ ☐		6.18
	Performance of IPCs:	*During Start-up?* **Yes No**	*Frequency*	*Automatic data recording?* **Yes No**
	Tablets/Kernels			
5.59	Individual weights	☐ ☐		☐ ☐
5.60	Disintegration	☐ ☐		☐ ☐
5.61	Thickness	☐ ☐		☐ ☐
5.62	Hardness	☐ ☐		☐ ☐
5.63	Friability/Abrasion	☐ ☐		☐ ☐
	Sugar/Film coated tablets			
5.64	Weights	☐ ☐		☐ ☐
5.65	Disintegration	☐ ☐		☐ ☐
5.66	Residual absolute humidity (IR or)	☐ ☐		☐ ☐
	Capsules			
5.67	Individual weights	☐ ☐		☐ ☐
5.68	Disintegration	☐ ☐		☐ ☐
	Validation			
5.69	Validation according to fixed procedures?	☐ ☐ ☐		5.21
5.70	New procedures released only after validation?	☐ ☐ ☐		5.22
	Validation of changes of			
5.71	• processes?	☐ ☐ ☐		5.23
5.72	• starting materials?	☐ ☐ ☐		5.23
5.73	• equipment?	☐ ☐ ☐		5.23

		Compliance 1 2 3[a]	Remarks	EU-Guide
5.74	Revalidation in fixed intervals?	☐ ☐ ☐		5.24
5.75	Procedures for the retrospective validation of old procedures?	☐ ☐ ☐		
6	**LIQUIDS MANUFACTURING**			
	Operations carried out:			
	• Dispensing (if different from solid)	☐ ☐ ☐		
	• Syrups and suspensions	☐ ☐ ☐		
	• Drops	☐ ☐ ☐		
	• Ointment manufacture	☐ ☐ ☐		
	• Ointment filling	☐ ☐ ☐		
	• Ampoule solution manufacture	☐ ☐ ☐		
	• Sterile or aseptic ampoule filling	☐ ☐ ☐		
	• Sterile freeze drying	☐ ☐ ☐		
	• Sterile powder filling	☐ ☐ ☐		
	Rooms, general:			
6.1	Suitable for the intended use?	☐ ☐ ☐		3
6.2	• adequate size?	☐ ☐ ☐		3
6.3	• clean?	☐ ☐ ☐		3
6.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
6.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
6.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
6.7	Appropriate lighting and air conditioning?	☐ ☐ ☐		3.3
6.8	Recording of temperature and humidity?	☐ ☐ ☐		
6.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
6.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, special requirements:			
6.11	Separate manufacturing area for penicillins/cephalosporins or highly sensitizing substances?	☐ ☐ ☐		3.6
6.12	Only for processing of pharmaceuticals?	☐ ☐ ☐		3.6
6.13	Logical flow of materials?	☐ ☐ ☐		3.7
6.14	Walls, floors, and ceilings: smooth surface and free of cracks?	☐ ☐ ☐		3.8
6.15	Easy cleaning possible?	☐ ☐ ☐		3.10
6.16	Adequate drains with traps and grilles?	☐ ☐ ☐		3.11
6.17	Appropriate air handling system with filtered air where open products are exposed to the environment?	☐ ☐ ☐		3.12
	Air pressure gradient from working bay → corridor:			
	Classification according to EC guide?			
6.18	Appropriate lighting?	☐ ☐ ☐		3.16
6.19	Separate rest rooms?	☐ ☐ ☐		3.30
6.20	Changing rooms designed to avoid contamination?	☐ ☐ ☐		3.31
6.21	Toilets segregated from manufacturing areas?	☐ ☐ ☐		3.31
	Equipment			
6.22	Suitable for the intended use?	☐ ☐ ☐		3.34
6.23	Well maintained?	☐ ☐ ☐		3.34

		Compliance 1 2 3[a]	Remarks	EU-Guide
6.24	Tanks, containers, pipework, and pumps designed for easy cleaning and sanitation (dead legs)?	☐ ☐ ☐		Suppl. 2
6.25	Written & validated cleaning procedures?	☐ ☐ ☐		3.36
6.26	Maintenance without contamination risk (sep. area)?	☐ ☐ ☐		3.35
6.27	Equipment in contact with product: suitable materials quality?	☐ ☐ ☐		3.39
6.28	Machinery equipped with measuring and control devices?	☐ ☐ ☐		3.40
6.29	Calibration in fixed intervals acc. to written procedures?	☐ ☐ ☐		3.41
6.30	Calibration records available?	☐ ☐ ☐		3.41
6.31	Contents and flow direction marked on pipes?	☐ ☐ ☐		3.42
6.32	Pipes for distilled and demineralized water regularly monitored and sanitized?	☐ ☐ ☐		3.43
6.33	Not functioning equipment in the production area (if yes: clearly marked)?	Y N ☐ ☐ ☐		3.44
6.34	Status of cleanliness indicated?	☐ ☐ ☐		5.13
6.35	Previous product indicated?	☐ ☐ ☐		5.13
	Operations			
6.36	Are written and validated procedures for all manufacturing steps available?	☐ ☐ ☐		5.2
6.37	Are all manufacturing steps recorded with actual parameters?	☐ ☐ ☐		5.2
6.38	Check of each single container of the starting materials (contents, weight, identity)?	☐ ☐ ☐		5.3
6.39	Limits for yields?	☐ ☐ ☐		5.8
6.40	Only one batch of one product processed?	☐ ☐ ☐		5.9
6.41	Protection against microbial contamination?	☐ ☐ ☐		5.10
	Correct labeling of containers, materials, equipment, and rooms with:			5.12
6.42	• product name and batch no.	☐ ☐ ☐		5.12
6.43	• quarantine status?	☐ ☐ ☐		5.12
6.44	Deviations from standard procedures recorded and signed by the supervisor?	☐ ☐ ☐		5.14
6.45	Special procedures for the production of antibiotics, hormones, etc.?	☐ ☐ ☐		5.19
6.46	• Campaign production?	☐ ☐ ☐		5.19
6.47	• Special monitoring?	☐ ☐ ☐		5.19
6.48	• Validated decontamination procedure?	☐ ☐ ☐		5.19
6.49	Double check on weight?	☐ ☐ ☐		5.34
6.50	Line clearance before start of production?	☐ ☐ ☐		5.35
6.51	Investigation of deviations in yields?	☐ ☐ ☐		5.39
6.52	Specification of max. storage time and storage conditions if products are not immediately filled or packaged?	☐ ☐ ☐		Suppl. 9
6.53	Validated procedures for reworking of rejected batches?	☐ ☐ ☐		5.62
6.54	Detailed procedures for the addition of previous batches?	☐ ☐ ☐		5.63
6.55	Special release procedure (QA) for those batches?	☐ ☐ ☐		5.64
6.56	Use of protective clothing (hair cover, shoes, masks, gloves)?	☐ ☐ ☐		2.16
6.57	Clothing regulation for visitors?	☐ ☐ ☐		2.11

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Water			
6.58	Loop system for purified water?	☐ ☐ ☐		Suppl. 4
6.59	Antimicrobial treatment of purified water?	☐ ☐ ☐		Suppl. 4
6.60	Loop system for water for injection?	☐ ☐ ☐		Suppl. 4
	Storage temperature of water for injection:			Suppl. 4
6.61	Loop system constructed to avoid deadlegs?	☐ ☐ ☐		Suppl. 4
6.62	Regular microbiological monitoring?	☐ ☐ ☐		Suppl. 4
6.63	Regular endotoxin control?	☐ ☐ ☐		Suppl. 4
	Special requirements for sterile and aseptic products			Suppl.
	Rooms and equipment			
6.64	Access of staff and materials to clean areas *only* through airlocks?	☐ ☐ ☐		1
6.66	Rooms classified according to the EC-Guide?	☐ ☐ ☐		3
	Classification for products to be sterilized:			
6.67	• Solution preparation (EC: class C, with special precautions class D):	Class:		5
6.68	• Filling (EC: under LF in class C):	Class:		5
	Classification for aseptic products:			
6.69	• Handling of starting materials that can be sterile filtered (EC: class C):	Class:		6
6.70	• Handling of starting materials that cannot be sterile filtered (EC: class A in class B):	Class:		6
6.71	Handling and filling of bulk (EC: class A in Class B):	Class:		6
6.72	All rooms easy to clean disinfect?	☐ ☐ ☐		17
6.73	Doors, windows, frames, lighting, etc. without edges?	☐ ☐ ☐		18
6.74	Suspended ceilings (if yes: sealed?)?	☐ ☐ ☐		19
6.75	Traps constructed to avoid microb. contamination?	☐ ☐ ☐		21
6.76	Appropriate constructed changing rooms?	☐ ☐ ☐		22
6.77	Measures against opening of both doors of airlocks?	☐ ☐ ☐		23
6.78	Overpressure gradient from cleanest areas to others?	☐ ☐ ☐		24
6.79	AHU validated and regularly revalidated?	☐ ☐ ☐		25
6.80	Control instruments for pressure gradient?	☐ ☐ ☐		26
6.81	Warning system for errors in air supply?	☐ ☐ ☐		26
6.82	Recording of pressure gradients?	☐ ☐ ☐		26
6.83	Do conveyor belts leave sterile areas?	☐ ☐ ☐		28
6.84	Maintenance works outside from clean areas possible?	☐ ☐ ☐		28
6.85	Cleaning and disinfection procedure after maintenance works?	☐ ☐ ☐		29
6.86	Regular revalidation of all equipment and systems?	☐ ☐ ☐		30
6.87	Water prepared, circulated, and stored to exclude microb. contamination?	☐ ☐ ☐		31
6.88	Cleaning and disinfection of rooms according to validated SOPs rooms?	☐ ☐ ☐		32
	• Disinfection methods?			
6.89	Microb. monitoring of cleaning and disinfection agents?	☐ ☐ ☐		33

		Compliance 1 2 3[a]	Remarks	EU-Guide
6.90	Microb. monitoring program of production areas?	☐ ☐ ☐		35
6.91	Results recorded and considered for the release?	☐ ☐ ☐		35
	Personnel and Hygiene			
6.92	Minimal no. of personnel in clean areas?	☐ ☐ ☐		7
6.93	Special and regular training?	☐ ☐ ☐		8
6.94	Regular medical examinations?	☐ ☐ ☐		10
6.95	Appropriate clean room clothes (material, design)?	☐ ☐ ☐		12
6.96	Protective clothes worn correctly?	☐ ☐ ☐		12
6.97	Prohibition of cosmetics, jewelry and watches?	☐ ☐ ☐		13
6.98	New clean room clothes for each working cycle?	☐ ☐ ☐		15
6.99	Appropriate washing and sterilization of clothes?	☐ ☐ ☐		16
	Operations			
6.100	Validation (media filling) in regular intervals?	☐ ☐ ☐		38
	Monitoring of water preparation system, frequency:			
6.101	• microbiological:			40
6.102	• chemical:			40
6.103	• particles:			40
6.104	• endotoxins:			40
6.105	Microbiological monitoring of starting materials?	☐ ☐ ☐		42
6.106	Max. storage times defined for sterilized equipment?	☐ ☐ ☐		45
6.107	Max. storage time defined between solution preparation and filtration?	☐ ☐ ☐		46
6.108	Material transfer to clean areas through double door autoclaves?	☐ ☐ ☐		48
	Sterilization processes			
6.109	All processes validated?	☐ ☐ ☐		50
6.110	Sterilized and not sterilized materials clearly separated?	☐ ☐ ☐		54
	Trays and boxes clearly labeled with			
6.111	• Product name and code	☐ ☐ ☐		54
6.112	• Batch no.	☐ ☐ ☐		54
6.113	• Status: sterilized or not sterilized	☐ ☐ ☐		54
	Sterilizers:			
6.114	• Recording of temp., pressure, and time?	☐ ☐ ☐		55
6.115	• Coldest point determined?	☐ ☐ ☐		55
6.116	• Independent counter check probe?	☐ ☐ ☐		55
6.117	• Heat-up time for each product determined?	☐ ☐ ☐		56
6.118	• Sterile cooling media?	☐ ☐ ☐		57
6.119	• Tightness tests for vacuum autoclaves?	☐ ☐ ☐		58
6.120	• Clean steam for steam autoclaves?	☐ ☐ ☐		58
6.121	• Circulated air with overpressure?	☐ ☐ ☐		61
6.122	• Recirculated air: sterile filtered?	☐ ☐ ☐		61
6.123	• Ethylene oxide autoclaves: humidity, temp., and time recorded?	☐ ☐ ☐		69
6.124	• Ethylene oxide autoclaves: use of bioindicators?	☐ ☐ ☐		70

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Filtration			
6.125	Double filtration?	☐ ☐ ☐		75
6.126	Integrity testing of filters immediately after use?	☐ ☐ ☐		77
6.127	Are results part of the batch protocol?	☐ ☐ ☐		77
6.128	Optical control of each single container of ampoules, vials, and infusions?	☐ ☐ ☐		82
	IPC			
6.129	Written IPC procedures and SOPs?	☐ ☐ ☐		
	Particle testing of			
6.130	• Rooms	☐ ☐ ☐		
6.131	• Primary packaging materials	☐ ☐ ☐		
6.132	• System of warning and action limits?	☐ ☐ ☐		
	Microbiological monitoring of			
6.133	• Rooms			
6.134	• Personnel			
6.135	• Euipment			
6.136	Residual O_2 of ampoules, infusions, and syrups?	☐ ☐ ☐		
6.137	Endotoxin testing of water and packaging materials?	☐ ☐ ☐		
6.138	Calibration of equipment?	☐ ☐ ☐		
6.139	Regular revalidation of equipment?	☐ ☐ ☐		
7	**PACKAGING**			
	Operations carried out • Blistering • Foil-packaging • Filling into tablet glasses • Effervescent Packaging • Powder filling • Syrup/drops filling • Ointment filling	 ☐ ☐ ☐ ☐ ☐ ☐ ☐		
	Rooms			
7.1	Suitable for the intended use?	☐ ☐ ☐		3
7.2	• adequate size?	☐ ☐ ☐		3
7.3	• clean?	☐ ☐ ☐		3
7.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
7.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
7.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
7.7	Appropriate lighting and air conditioning?	☐ ☐ ☐		3.3
7.8	Recording of temperature and humidity?	☐ ☐ ☐		
7.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
7.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
7.11	Adequate separation of the packaging lines?	☐ ☐ ☐		3.15
	Operations			
7.12	Only *one* product per line?	☐ ☐ ☐		5.44

		Compliance 1 2 3[a]	Remarks	EU-Guide
7.13	Check list for clearance before processing a new product/new batch?	☐ ☐ ☐		5.45
7.14	Adequate labeling of the lines (product name and code)?	☐ ☐ ☐		5.46
7.15	Check of all materials delivered to the line (quantity, identity, conformity with order)?	☐ ☐ ☐		5.47
7.16	Cleaning of primary packaging materials?	☐ ☐ ☐		5.48
7.17	Immediate labeling after filling?	☐ ☐ ☐		5.49
7.18	Careful check of all printing processes (code, expiry date)?	☐ ☐ ☐		5.50
7.19	Special safety measures for off-line printing?	☐ ☐ ☐		5.51
7.20	Regular checks of all control devices (code reader, counter, etc.)?	☐ ☐ ☐		5.52
7.21	Printings clear and durable?	☐ ☐ ☐		5.53
7.22	Balancing of printed packaging materials and bulk?	☐ ☐ ☐		5.56
7.23	Destruction of excessive coded packaging material after completion of an order?	☐ ☐ ☐		5.57
7.24	Are the finished products kept in quarantine until final release?	☐ ☐ ☐		5.58
7.25	Appropriate storage after release?	☐ ☐ ☐		5.60
	IPC			
7.26	Checks on identity of bulk and packaging materials?	☐ ☐ ☐		5.47
	Regular line checks on:			
7.27	• Aspect of the packages	☐ ☐ ☐		5.54a
7.28	• Completeness	☐ ☐ ☐		5.54b
7.29	• Conformity of quantity and quality of materials with packaging order	☐ ☐ ☐		5.54c
7.30	• Correct imprint	☐ ☐ ☐		5.54d
7.31	• Correct function of control devices	☐ ☐ ☐		5.54d
	Are the following IPC checks performed?			
7.32	• Leaking	☐ ☐ ☐		
7.33	• Release torque of screw caps	☐ ☐ ☐		
7.34	• pH, density, drop weight, viscosity, sedimentation	☐ ☐ ☐		
8	**DOCUMENTATION**			
	Specifications			
8.1	Specifications for raw/packaging materials available?	☐ ☐ ☐		4.10
	Do they include:			
8.2	• internal name and code	☐ ☐ ☐		4.11
8.3	• name of supplier and/or manufacturer?	☐ ☐ ☐		4.11
8.4	• reference sample (printed pack. mat.)?	☐ ☐ ☐		4.11
8.5	• sampling procedure?	☐ ☐ ☐		4.11
8.6	• qualitative/quantitative specifications with limits?	☐ ☐ ☐		4.11
8.7	• storage conditions?	☐ ☐ ☐		4.11
8.8	• maximum storage period?	☐ ☐ ☐		4.11
	Goods receiving?			
8.9	Written procedures for the reception of deliveries?	☐ ☐ ☐		4.19

		Compliance 1 2 3[a]	Remarks	EU-Guide
	Do records receipt include:			
8.10	• product name on labels and delivery note?	☐ ☐ ☐		4.20
8.11	• internal name and code?	☐ ☐ ☐		4.20
8.12	• receiving date?	☐ ☐ ☐		4.20
8.13	• name of supplier and/or manufacturer?	☐ ☐ ☐		4.20
8.14	• batch number of supplier?	☐ ☐ ☐		4.20
8.15	• total quantity and number of containers?	☐ ☐ ☐		4.20
8.16	• allocated internal batch number?	☐ ☐ ☐		4.20
8.17	SOPs for labeling, quarantine, and storage conditions of all incoming goods available?	☐ ☐ ☐		4.21
	Sampling procedures (SOPs) include:			
8.18	• authorized sampling personnel?	☐ ☐ ☐		4.22
8.19	• methods, equipment, and quantities?	☐ ☐ ☐		4.22
8.20	• safety measures?	☐ ☐ ☐		4.22
	Master formulae			
8.21	Are master formulae for each product and batch size available?	☐ ☐ ☐		4.3
8.22	Is the master formula approved and signed by the authorized persons?	☐ ☐ ☐		4.3
	The master formula includes:			
8.23	• product name and code?	☐ ☐ ☐		4.14a
8.24	• description of galenical form, dosage, and batch size?	☐ ☐ ☐		4.14b
8.25	• all active ingredients with name, code, and weight?	☐ ☐ ☐		4.14c
8.26	• all excipients used during manufacture with name, code, and weight?	☐ ☐ ☐		4.14c
8.27	• yields with limits?	☐ ☐ ☐		4.14d
	Does the working procedure include:			
8.28	• the production line?	☐ ☐ ☐		4.15a
8.29	• equipment to be used?	☐ ☐ ☐		4.15a
8.30	• reference to methods for cleaning, assembling, and calibration of machines?	☐ ☐ ☐		4.15b
8.31	• detailed stepwise manufacturing prescription?	☐ ☐ ☐		4.15c
8.32	• IPCs to be performed with limits?	☐ ☐ ☐		4.15d
8.33	• precautions to be followed?	☐ ☐ ☐		4.15e
8.34	Are batch records kept for each batch processed?	☐ ☐ ☐		4.17
	Do batch records include:			
8.35	• Protocol of line clearance?	☐ ☐ ☐		4.17
8.36	• Name of the product and batch no.?	☐ ☐ ☐		4.17a
8.37	• Date and time of start and end of production?	☐ ☐ ☐		4.17b
8.38	• Name and initials of responsible workers for each step?	☐ ☐ ☐		4.17c,d
8.39	• Batch and analytical no. and actual weight of all starting materials?	☐ ☐ ☐		4.17e
8.40	• Equipment used?	☐ ☐ ☐		4.17f
8.41	• Results of IPCs with initials of person who carries them out?	☐ ☐ ☐		4.17g
8.42	• Yields of the relevant manufacturing steps?	☐ ☐ ☐		4.17h
8.43	• Detailed notes on problems and process deviations?	☐ ☐ ☐		4.17i

		Compliance 1 2 3[a]	Remarks	EU-Guide
8.44	Records on reprocessing of batches?	☐ ☐ ☐		
	Packaging instructions:			
8.45	Packaging instructions for each product, package size, and presentation?	☐ ☐ ☐		4.16
	Do they include:			
8.46	• Product name?	☐ ☐ ☐		4.16a
8.47	• Description of galenical form and strength?	☐ ☐ ☐		4.16b
8.48	• Package size?	☐ ☐ ☐		4.17c
8.49	• List of all packaging materials with code for a standard batch size?	☐ ☐ ☐		4.17d
8.50	• Samples of printed packaging materials?	☐ ☐ ☐		4.17e
8.51	• Special precautions?	☐ ☐ ☐		4.17f
8.52	• Description of the process and equipment?	☐ ☐ ☐		4.17g
8.53	• IPCs to be performed with sampling instruction?	☐ ☐ ☐		4.17h
8.54	Are packaging batch records kept for each batch or part batch?	☐ ☐ ☐		4.18
	Do the packaging batch records include:			
8.55	• Protocol of line clearance?	☐ ☐ ☐		4.18
8.56	• Name of the product?	☐ ☐ ☐		4.18a
8.57	• Date and time when operations have been performed?	☐ ☐ ☐		4.18b
8.58	• Name of the responsible person?	☐ ☐ ☐		4.18c
8.59	• Initials of workers carrying out operations?	☐ ☐ ☐		4.18d
8.60	• Notes on identity checks and conformity with packaging instructions?	☐ ☐ ☐		4.18e
8.61	• Results of IPCs	☐ ☐ ☐		4.18e
8.62	• Details of operations and equipment used?	☐ ☐ ☐		4.18f
8.63	• Samples of printed packaging materials with codes (MFD, EXP, Batch no., etc.)?	☐ ☐ ☐		4.18g
8.64	• Record of problems and process deviations?	☐ ☐ ☐		4.18h
8.65	• Quantities of packaging materials delivered, used, destroyed, or returned?	☐ ☐ ☐		4.18i
8.66	• No. of packs consumed?	☐ ☐ ☐		4.18j
	Testing			
	Do the written testing procedures include:			
8.67	• Test methods?	☐ ☐ ☐		4.23
8.68	• Equipment for testing?	☐ ☐ ☐		4.23
8.69	Tests documented?	☐ ☐ ☐		4.23
	Others			
8.70	Procedures for release and rejection of materials and finished products?	☐ ☐ ☐		4.24
8.71	Final release by authorized person?	☐ ☐ ☐		4.24
8.72	Records about distribution of each batch?	☐ ☐ ☐		4.25
	Procedures and protocols about			
8.73	• Validation?	☐ ☐ ☐		4.26
8.74	• Set up and calibration of equipment?	☐ ☐ ☐		4.26
8.75	• Maintenance, cleaning, and disinfection?	☐ ☐ ☐		4.26

		Compliance 1 2 3[a]	Remarks	EU-Guide
8.76	• Training records?	☐ ☐ ☐		4.26
8.77	• Environmental monitoring of production areas?	☐ ☐ ☐		4.26
8.78	• Pest control?	☐ ☐ ☐		4.26
8.79	• Complaints?	☐ ☐ ☐		4.26
8.80	• Rrecalls?	☐ ☐ ☐		4.26
8.81	• Returned goods?	☐ ☐ ☐		4.26
8.82	Instructions for use of manufacturing and testing equipment?	☐ ☐ ☐		4.27
	Log books for major equipment incl. date and name of persons who performed:			
8.83	• Validation?	☐ ☐ ☐		4.28
8.84	• Calibration?	☐ ☐ ☐		4.28
8.85	• Maintenance, cleaning, and repair works?	☐ ☐ ☐		4.28
8.86	Chronological records of use of major equipment and manufacturing areas?	☐ ☐ ☐		4.29
9	**QUALITY CONTROL**			**6**
	General requirements			
9.1	Independent QC department available?	☐ ☐ ☐		6.1
9.2	Head of QC well qualified and sufficiently experienced?	☐ ☐ ☐		6.1
9.3	Qualified personnel available?	☐ ☐ ☐		2.1
9.4	Organization charts available?	☐ ☐ ☐		2.2
9.5	Job descriptions available?	☐ ☐ ☐		2.2
9.6	Responsibilities clearly defined?	☐ ☐ ☐		2.2
9.7	Continuous training programs for QC staff?	☐ ☐ ☐		2.2
9.8	Initial job training for all employees?	☐ ☐ ☐		2.9
9.9	Training records?	☐ ☐ ☐		
9.10	QC personnel admitted to the production rooms for sampling, etc.?	☐ ☐ ☐		
	QC Laboratories			
9.11	Suitable for the intended use?	☐ ☐ ☐		3.26
9.12	Laboratories of adequate size?	☐ ☐ ☐		3.26
9.13	Appropriate level of maintenance?	☐ ☐ ☐		3.1
9.14	Adequate separation from the production area?	☐ ☐ ☐		3.26
9.15	Controlled access of authorized personnel only?	☐ ☐ ☐		3.5
9.16	Special laboratory to handle biological samples available?	☐ ☐ ☐		3.29
9.17	Special laboratory to handle radioactive material available?	☐ ☐ ☐		3.29
9.18	Separate recreation rooms for the personnel available?	☐ ☐ ☐		3.30
9.19	Animal laboratories present?	☐ ☐ ☐		3.33
9.20	Animal laboratories separated from other areas?	☐ ☐ ☐		3.33
9.21	Animal laboratories equipped with a separate air handling system?	☐ ☐ ☐		3.33
	QC Documentation			
9.22	Do procedures exist for self-inspection? release or rejection of products or raw material? product complaints? product recalls?	 ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		

		Compliance 1 2 3[a]	Remarks	EU-Guide
	local stability testing?	☐ ☐ ☐		
	storage of reference samples?	☐ ☐ ☐		
	validation of analytical procedures?	☐ ☐ ☐		
9.23	Specifications available for			6.7
	raw materials?	☐ ☐ ☐		
	bulk products?	☐ ☐ ☐		
	packaging materials?	☐ ☐ ☐		
9.24	Analytical procedures for every product?	☐ ☐ ☐		
9.25	Are Basel methods followed?	☐ ☐ ☐		
9.26	Validation of locally developed test methods?	☐ ☐ ☐		
9.27	Sampling procedures available for			6.7
	raw materials?	☐ ☐ ☐		
	bulk products?	☐ ☐ ☐		
	packaging materials?	☐ ☐ ☐		
9.28	Suppliers certificates available?	☐ ☐ ☐		6.7
9.29	Calibration program for analytical instruments installed?	☐ ☐ ☐		6.7
9.30	Maintenance program for analytical instruments?	☐ ☐ ☐		6.7
9.31	Retention system for QC records?	☐ ☐ ☐		6.8
9.32	Batch documents stored for expiry + 1 year or 5 years (EEC 75/319, article 22) minimum?	☐ ☐ ☐		6.8
9.33	Are original data-like notebooks stored in addition to the batch documents?	☐ ☐ ☐		6.10
9.34	Can the original data be traced back easily and quickly from the analytical report number or batch number?	☐ ☐ ☐		6.10
9.35	Are trend analyses being performed for			6.9
	analytical results?	☐ ☐ ☐		
	yields?	☐ ☐ ☐		
	environmental monitoring data?	☐ ☐ ☐		
	Sampling			
9.36	Written procedures for taking samples?	☐ ☐ ☐		6.11
9.37	Do procedures define			
	method of sampling?	☐ ☐ ☐		
	necessary equipment?	☐ ☐ ☐		
	quantity of the sample?	☐ ☐ ☐		
	subdivision of the sample?	☐ ☐ ☐		
	sample container?	☐ ☐ ☐		
	labeling of samples?	☐ ☐ ☐		
	storage conditions?	☐ ☐ ☐		
	cleaning and storage of sampling equipment?	☐ ☐ ☐		
	identification of containers sampled	☐ ☐ ☐		
9.38	Are samples representative for the batch they are taken from? (sampling plan)	☐ ☐ ☐		6.12
9.39	Are critical steps being surveilled and validated by additional sampling (for example beginning or end of a process).	☐ ☐ ☐		6.12
9.40	Sample containers labeled with			6.13
	name of the content	☐ ☐ ☐		
	batch number	☐ ☐ ☐		
	date of sampling	☐ ☐ ☐		
	batch containers sampled	☐ ☐ ☐		
9.41	Are samples taken by QC/QA?	☐ ☐ ☐		

		Compliance 1 2 3[a]	Remarks	EU-Guide
9.42	Reference samples retained for validity plus 1 year?	☐ ☐ ☐		6.14
9.43	Storage of reference samples under the recommended storage conditions?	☐ ☐ ☐		6.14
9.44	Finished products stored in the final packaging?	☐ ☐ ☐		6.14
9.45	Quantity of the reference sample makes 1 (better 2) complete reanalysis possible?	☐ ☐ ☐		6.14
9.46	Sample room secure?	☐ ☐ ☐		
9.47	Sample room neatly organized and not overcrowded?	☐ ☐ ☐		
	Testing			
9.48	Are the applied analytical methods validated?	☐ ☐ ☐		6.15
9.49	Analytical methods in compliance with the registration?	☐ ☐ ☐		6.16
9.50	Are all results recorded and checked for correctness?	☐ ☐ ☐		6.16
9.51	Are all calculations checked?	☐ ☐ ☐		6.16
9.52	Do the testing protocols contain			6.17
	name and galenical form of material?	☐ ☐ ☐		
	batch number?	☐ ☐ ☐		
	supplier if applicable?	☐ ☐ ☐		
	specification reference?	☐ ☐ ☐		
	method reference?	☐ ☐ ☐		
	analytical results?	☐ ☐ ☐		
	reference to analytical certificates?	☐ ☐ ☐		
	date of the analysis?	☐ ☐ ☐		
	name of the analyst?	☐ ☐ ☐		
	name of the person verifying the data?	☐ ☐ ☐		
	statement of release or rejection?	☐ ☐ ☐		
	date and signature of the release person?	☐ ☐ ☐		
9.53	Are all IPC methods in production approved by QC?	☐ ☐ ☐		6.18
9.54	Are written methods available for the preparation of reagents and volumetric solutions?	☐ ☐ ☐		6.19
9.55	Is a record maintained of standardization of volumetric solutions?	☐ ☐ ☐		6.2
9.56	Are reagents for prolonged use labeled with			6.20
	date of the preparation?	☐ ☐ ☐		
	sign of the preparator?	☐ ☐ ☐		
9.57	Are unstable reagents labeled with			6.20
	expiry date?	☐ ☐ ☐		
	storage conditions?	☐ ☐ ☐		
9.58	Are volumetric solutions labeled with			6.20
	the last date of standardization?	☐ ☐ ☐		
	last current factor?	☐ ☐ ☐		
9.59	Are reference standards labeled with			6.21
	name and potency	☐ ☐ ☐		
	suppliers reference	☐ ☐ ☐		
	date of receipt	☐ ☐ ☐		
	date of expiry	☐ ☐ ☐		
9.60	Are reference standards stored properly and under the control of a designated person?	☐ ☐ ☐		
9.61	Are animals used for testing of components, materials, or products			
	quarantined before use?	☐ ☐ ☐		
	checked for suitability?	☐ ☐ ☐		
	Are records maintained showing the history of their use?	☐ ☐ ☐		

		Compliance 1 2 3[a]	Remarks	EU-Guide
10	**COMPLAINTS AND PRODUCT RECALLS**			**8**
	Complaints			8.1
10.1	Does a written complaint procedure exist?	☐ ☐ ☐		8.2
10.2	Are product complaints carefully reviewed?	☐ ☐ ☐		8.1
10.3	Is a person designated to handle complaints and to decide on measures to be taken?	☐ ☐ ☐		8.1
10.4	Is each complaint concerning a product recorded with all original details?	☐ ☐ ☐		8.3
10.5	Are product complaints thoroughly investigated?	☐ ☐ ☐		8.3
10.6	Is a responsible person of QC involved in the study?	☐ ☐ ☐		8.3
10.7	Is it considered that other batches might be concerned as well?	☐ ☐ ☐		8.4
10.8	Are decisions and measures as a result recorded?	☐ ☐ ☐		8.5
10.9	Is this record added to the corresponding batch documents?	☐ ☐ ☐		8.5
10.10	Are the complaint records regularly revised with respect to specific or recurring problems?	☐ ☐ ☐		8.6
10.11	Are the authorities informed of serious quality problems with a product?	☐ ☐ ☐		8.7
	Recalls			8.8
10.12	Does a written recall procedure exist?	☐ ☐ ☐		8.9
10.13	Is a person nominated responsible for the execution and coordination of a recall?	☐ ☐ ☐		8.8
10.14	Responsible person independent of the marketing and sales organization?	☐ ☐ ☐		8.8
10.15	Are the competent authorities informed of an imminent recall?	☐ ☐ ☐		8.11
10.16	Does the person responsible for a recall have access to the distribution records?	☐ ☐ ☐		8.12
10.17	Do the distribution records contain sufficient information on customers with addresses? phone numbers inside or outside working hours? batches and amounts delivered? medical samples?	 ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		8.12
10.18	Are recalled products stored separately in a secure area?	☐ ☐ ☐		8.13
10.19	Is a final record made including a reconciliation between the delivered and recovered quantities?	☐ ☐ ☐		8.14
10.20	Is the effectiveness of the arrangements for recalls checked critically from time to time?	☐ ☐ ☐		8.15
11	**SELF-INSPECTION**			**9**
11.1	Does a self-inspection procedure exist, which defines frequency and program?	☐ ☐ ☐		9.1
11.2	Are self-inspections carried out to check compliance with GMP rules?	☐ ☐ ☐		9.1
11.3	Are self-inspections conducted in an independent and detailed way? by designated competent persons from the company or external experts?	 ☐ ☐ ☐ ☐ ☐ ☐		9.2
11.4	Are self-inspections recorded?	☐ ☐ ☐		9.3

		Compliance 1 2 3[a]	Remarks	EU-Guide
11.5	Do reports contain the observations made during a self-inspection? proposals for corrective measures?	 ☐ ☐ ☐ ☐ ☐ ☐		9.3
11.6	Are actions subsequently taken recorded?	☐ ☐ ☐		9.3
12	**CONTRACT MANUFACTURE AND ANALYSIS**			**7**
12.1	Written contract between contract giver and contract acceptor available?	☐ ☐ ☐		7.1
12.2	Are responsibilities and duties clearly defined?	☐ ☐ ☐		7
12.3	All arrangements in accordance with the marketing authorization of the product concerned?	☐ ☐ ☐		7.2
	The contract giver			
12.4	Competence of the acceptor to carry out the work successful and according to GMP assessed?	☐ ☐ ☐		7.3
12.5	Acceptor provided with all the informations necessary to carry out the contract work?	☐ ☐ ☐		7.4
12.6	Acceptor informed of safety aspects?	☐ ☐ ☐		7.4
12.7	Conformance of products supplied by the acceptor ensured?	☐ ☐ ☐		7.5
12.8	Product released by a qualified person on the acceptor's side?	☐ ☐ ☐		7.5
	The contract acceptor			
12.9	Does the acceptor have adequate premises and equipment? knowledge and experience? competent personnel? a manufacturing authorization?	 ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		7.6
12.10	Does the acceptor ensure that all products or materials delivered to him are suitable?	☐ ☐ ☐		7.7
12.11	There must be no work passed to a third party without the permission of the giver.	☐ ☐ ☐		7.8
12.12	If a third party is involved it must have the necessary manufacturing and analytical information.	☐ ☐ ☐		7.8
	The contract			
12.13	Does the written contract specify the responsibilities?	☐ ☐ ☐		7.10
12.14	Have technical aspects been drawn up by competent persons?	☐ ☐ ☐		7.10
12.15	Release of material and check for compliance with the marketing authorization defined?	☐ ☐ ☐		7.11
12.16	Is defined who is responsible for purchasing of materials? IPC controls testing and release of materials? manufacturing and quality control? sampling? storage of batch documentation?	 ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		7.12
12.17	Are manufacturing, analytical, and distribution records available to the contract giver?	☐ ☐ ☐		7.13
12.18	Contract permits the giver to visit the facilities of the acceptor?	☐ ☐ ☐		7.14
12.19	In the case of contract analysis: Does the contract acceptor understand that he is subject to inspection by the competent authorities?	☐ ☐ ☐		7.15

		Compliance 1 2 3[a]	Remarks	EU-Guide
13	**AUDIT OF SUPPLIERS**			**2.7**
13.1	Supplier audits performed for			
	excipients?	☐ ☐ ☐		
	active substances?	☐ ☐ ☐		
	packaging material?	☐ ☐ ☐		

[a] 1. Fulfilled or available; 2. partially fulfilled; 3. not fulfilled or not available.

GLOSSARY

Acceptance criteria—Numerical limits, ranges, or other suitable measures for acceptance of test results.

Active pharmaceutical ingredient (API) *(or drug substance)*—Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

Airlock—An enclosed space with two or more doors, which is interposed between two or more rooms, for example, of differing classes of cleanliness, for the purpose of controlling the airflow between those rooms when they need to be entered. An airlock is designed for use either by people or for goods and/or equipment.

API starting material—A raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API starting materials are normally of defined chemical properties and structure.

Authorized person—The person recognized by the national regulatory authority as having the responsibility for ensuring that each batch of finished product has been manufactured, tested, and approved for release in compliance with the laws and regulations in force in that country.

Batch (or Lot)—A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval. A defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it is expected to be homogeneous. It may sometimes be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch. In the case of terminal sterilization, the batch size is determined by the capacity of the autoclave. In continuous manufacture, the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval.

Batch Number (or Lot Number)—A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined. A distinctive combination of numbers and/or letters which uniquely identifies a batch on the labels, its batch records and corresponding certificates of analysis, etc.

Batch records—All documents associated with the manufacture of a batch of bulk product or finished product. They provide a history of each batch of product and of all circumstances pertinent to the quality of the final product.

Bioburden—The level and type (e.g., objectionable or not) of micro-organisms that can be present in raw materials, API starting materials, intermediates, or APIs. Bioburden should not be considered contamination unless the levels have been exceeded or defined objectionable organisms have been detected.

Bulk product—Any product that has completed all processing stages up to, but not including, final packaging.

Calibration—The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements. The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established.

Clean area—An area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce the introduction, generation, and retention of contaminants within the area.

Computer system—A group of hardware components and associated software designed and assembled to perform a specific function or group of functions. A process or operation integrated with a computer system.

Consignment (or delivery)—The quantity of a pharmaceutical(s), made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch.

Contamination—The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or API during production, sampling, packaging or repackaging, storage, or transport.

Contract manufacturer—A manufacturer performing some aspect of manufacturing on behalf of the original manufacturer.

Critical—Describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification.

Critical operation—An operation in the manufacturing process that may cause variation in the quality of the pharmaceutical product.

Cross-contamination—Contamination of a material or product with another material or product. Contamination of a starting material, intermediate product, or finished product with another starting material or product during production.

Deviation—Departure from an approved instruction or established standard.

Drug (medicinal) product—The dosage form in the final immediate packaging intended for marketing. (Reference Q1A)

Drug substance—See Active pharmaceutical ingredient

Expiry date (or expiration date)—The date placed on the container/labels of an API designating the time during which the API is expected to remain within established shelf life specifications if stored under defined conditions, and after which it should not be used.

Finished product—A finished dosage form that has undergone all stages of manufacture, including packaging in its final container and labeling.

Impurity—Any component present in the intermediate or API that is not the desired entity.

Impurity profile—A description of the identified and unidentified impurities present in an API.

In-process control—Checks performed during production in order to monitor and, if necessary, to adjust the process to ensure that the product conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.

Intermediate—A material produced during steps of the processing of an API that undergoes further molecular change or purification before it becomes an API. Intermediates may or may not be isolated. Partly processed product that must undergo further manufacturing steps before it becomes a bulk product.

Large-volume parenterals—Sterile solutions intended for parenteral application with a volume of 100 mL or more in one container of the finished dosage form.

Lot—See Batch

Lot number—See Batch number

Manufacture—All operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage, and distribution of APIs and related controls.

Manufacturer—A company that carries out operations such as production, packaging, repackaging, labeling, and relabeling of pharmaceuticals.

Marketing authorization (product license, registration certificate)—A legal document issued by the competent drug regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labeling, and shelf life.

Master formula—A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls.

Master record—A document or set of documents that serve as a basis for the batch documentation (blank batch record).

Material—A general term used to denote raw materials (starting materials, reagents, solvents), process aids, intermediates, APIs, and packaging and labeling materials.

Mother liquor—The residual liquid which remains after the crystallization or isolation processes. A mother liquor may contain unreacted materials, intermediates, levels of the API, and/or impurities. It may be used for further processing.

Packaging—All operations, including filling and labeling, that a bulk product has to undergo in order to become a finished product. Filling of a sterile product under aseptic conditions or a product intended to be terminally sterilized, would not normally be regarded as part of packaging.

Packaging material—Any material intended to protect an intermediate or API during storage and transport. Any material, including printed material, employed in the packaging of a pharmaceutical, but excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

Pharmaceutical product—Any material or product intended for human or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form, that is, subject to control by pharmaceutical legislation in the exporting state and/or the importing state.

Procedure—A documented description of the operations to be performed, the precautions to be taken and measures to be applied directly or indirectly related to the manufacture of an intermediate or API.

Process aids—Materials, excluding solvents, used as an aid in the manufacture of an intermediate or API that do not themselves participate in a chemical or biological reaction (e.g., filter aid, activated carbon, etc.).

Process control—See In-process control

Production—All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labeling and relabeling, to completion of the finished product.

Qualification—Action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation, but the individual qualification steps alone do not constitute process validation.

Quality assurance (QA)—The sum total of the organized arrangements made with the object of ensuring that all APIs are of the quality required for their intended use and that quality systems are maintained.

Quality control (QC)—Checking or testing that specifications are met.

Quality unit(s)—An organizational unit independent of production which fulfills both quality assurance and quality control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.

Quarantine—The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection, or reprocessing.

Raw material—A general term used to denote starting materials, reagents, and solvents intended for use in the production of intermediates or APIs.

Reconciliation—A comparison between the theoretical quantity and the actual quantity.

Recovery—The introduction of all or part of previous batches (or of redistilled solvents and similar products) of the required quality into another batch at a defined stage of manufacture. It includes the removal of impurities from waste to obtain a pure substance or the recovery of used materials for a separate use.

Reference standard, primary—A substance that has been shown by an extensive set of analytical tests to be authentic material that should be of high purity.

Reference standard, secondary—A substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis.

Reprocessing—Subjecting all or part of a batch or lot of an in-process drug, bulk process intermediate (final biological bulk intermediate), or bulk product of a single batch/lot to a previous step in the validated manufacturing process due to failure to meet predetermined specifications. Reprocessing procedures are foreseen as occasionally necessary for biological drugs and, in such cases, are validated and preapproved as part of the marketing authorization.

Retest date—The date when a material should be reexamined to ensure that it is still suitable for use.

Reworking—Subjecting an in-process or bulk process intermediate (final biological bulk intermediate) or final product of a single batch to an alternate manufacturing process due to a failure to meet predetermined specifications. Reworking is an unexpected occurrence and is not preapproved as part of the marketing authorization.

Self-contained area—Premises which provide complete and total separation of all aspects of an operation, including personnel and equipment movement, with well-established procedures, controls, and monitoring. This includes physical barriers as well as separate air-handling systems, but does not necessarily imply two distinct and separate buildings.

Signature (signed)—See definition for signed

Signed (signature)—The record of the individual who performed a particular action or review. This record can be initials, full handwritten signature, personal seal, or authenticated and secure electronic signature.

Solvent—An inorganic or organic liquid used as a vehicle for the preparation of solutions or suspensions in the manufacture of an intermediate or API.

Specification—A list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.

Standard operating procedure (SOP)—An authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g., equipment operation, maintenance, and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documentation.

Starting material—Any substance of a defined quality used in the production of a pharmaceutical product, but excluding packaging materials.

Validation—A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting predetermined acceptance criteria. Action of proving, in accordance with the principles of GMP, that any procedure, process, equipment, material, activity, or system actually leads to the expected results (see also qualification).

Validation protocol—A written plan stating how validation will be conducted and defining acceptance criteria. For example, the protocol for a manufacturing process identifies processing equipment, critical process parameters/operating ranges, product characteristics, sampling, test data to be collected, number of validation runs, and acceptable test results.

Yield, expected—The quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot scale, or manufacturing data.

Yield, theoretical—The quantity that would be produced at any appropriate phase of production, based upon the quantity of material to be used, in the absence of any loss or error in actual production.

4

Guidance on Formulating Compressed Solids

The manufacturing of compressed solids is a complex process, requiring several steps to render powders compressible, yet easily dispersed, and with the active ingredient dissolved when placed at the site of administration. As a result, the formulations that deliver the drugs to the site of action, while maintaining an appropriate stability profile, are valuable. However, a formulation, as described in this volume, requires an understanding of the manufacturing environment conducive to manufacturing a compliant dosage form. The sections in this chapter highlight some of these considerations that would benefit formulators. The topics of interest are presented in alphabetical order for quick reference.

I. ABBREVIATED DIRECTIONS

Abbreviated directions are necessary, particularly where a direct compression involved is provided. However, these directions can be expanded based on examples given elsewhere. General working steps, such as sifting the material, the timing for blending lubricants, the use of stainless steel vessels, etc., are common to all.

II. ACTIVE PHARMACEUTICAL INGREDIENT

The active pharmaceutical ingredient (API) ultimately controls the quality of a product. The generic manufacturer faces a serious problem when procuring supplies of APIs coming off patent. Whereas Title 35 USC, Section 112, Paragraph 1 for patentability of invention requires that the inventor fully disclose the invention, the fact is that "full disclosure" does not necessarily mean disclosing steps that do not appear material in the production of the raw material. For example, it is routine practice (though questionable) for inventors of new chemical entities not to describe every step needed to remove impurities, to obtain the correct crystal structure (of a polymorph), or to obtain the correct particle size in the manufacturing process. As a result, generic manufacturers face serious situations when trying to reproduce and replicate a branded product. The issue of impurities is serious, and the regulatory authorities are getting tougher. In most instances, an unidentified peak can result in the rejection of an application. If the manufacturer of an API is unable to control the impurity profile, serious problems can arise in the manufacturing of the products.

III. BIO VS. PRODUCTION BATCHES

It is important that the manufacturer compare the drug substance used to manufacture the stability batch, bioequivalence batch, or clinical batch and the drug substance used for commercial batches. Therefore, the specifications, analytical methods, and test results for the lots of the drug substance used to manufacture these batches should be written precisely. Because the safety of the drug may be based upon the types and levels of impurities, and different physical characteristics may affect dissolution or content uniformity, these data must be developed.

IV. CLEANING VALIDATION

Solid drug powders can reach into deep cavities of the equipment, making the equipment difficult to clean. It is of utmost GMP importance that all equipment be entirely disassembled and thoroughly cleaned prior to switching to the manufacture of another drug. Appropriate standards of practice (SOP) validating cleanliness of equipment are required to assure compliance with the GMP. Problems arise in the use of highly potent, water-insoluble drugs, which are difficult to remove.

V. COATINGS

Tablets may be coated for a variety of reasons, including protection of the ingredients from air, moisture, or light; masking of unpleasant tastes and odors; improvement of appearance; and control of the site of drug release in the gastrointestinal tract. Classically, tablets were coated with sugar applied from aqueous suspensions containing insoluble powders, such as starch, calcium carbonate, talc, or titanium dioxide, suspended by means of acacia or gelatin. For purposes of identification and aesthetic value, the outside coatings may be colored. The finished coated tablets are polished by applying dilute solutions of wax in solvents, such as chloroform or powdered mix. Water-protective coatings consisting of substances, such as shellac or cellulose acetate phthalate are often applied out of nonaqueous solvents before the application of sugar coats. Excessive quantities should be avoided. The drawbacks of sugar coatings include a lengthy time necessary for application, the need for waterproofing, which adversely affects dissolution, and the increased bulk of the finished tablet.

These factors resulted in increased acceptance of film coatings. Film coatings consist of water-soluble or dispersible materials, such as hydroxypropyl methylcellulose, methylcellulose, hydroxypropylcellulose, carboxymethylcellulose sodium, and mixtures of cellulose acetate phthalate and polyethylene glycols (PEGs) applied out of nonaqueous or aqueous solvents. The evaporation of the solvents leaves a thin film that adheres directly to the tablet and allows it to retain the original shape, including grooves or identification codes. Where the drug may be destroyed or inactivated by the gastric juice or where it may irritate the gastric mucosa, the use of "enteric" coatings is indicated. Such coatings are intended to delay the release of the medication until the tablet passes through the stomach.

VI. COMPLIANCE WITH REGULATORY REQUIREMENTS

Compliance with the current good manufacturing practices (cGMP) in the manufacturing of solid dosage forms comprises three phases of the validation process: product development, design of the validation protocol, and demonstration runs (validation) of the equipment and process in the manufacture of full-scale commercial production batches. In all preapproval and postapproval inspections, the primary purpose is to assure compliance with validated processes.

The U.S. FDA issued specific guidelines that define process validation as establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product, while meeting its predetermined specifications and quality attributes. The three components of this definition include documented evidence, consistency, and predetermined specifications. Documented evidence includes the experiments, data, and analytical results that support the master formula, the in-process and finished product specifications, and the filed manufacturing process. With regard to consistency, several batches would have to be manufactured, using the full-scale batch size, to demonstrate that a process meets the consistency test. At least three batches are needed to demonstrate consistency.

VII. COMPRESSION PROCESS CONTROL

Compressed solids are subject to dissolution problems. As a result, compression parameters, such as hardness of tablets, are important. Generally, harder tablets are often difficult to eject and take longer to disintegrate. However, control of friability may require harder tablets. Newer compression equipment has built-in online monitoring of compressed culls. Where such systems are not available, continuous monitoring of compression is required to assure that the batch does not have highly diversified properties, including friability and hardness.

VIII. CONTENT UNIFORMITY

Control of the physical characteristics of the excipient is important because variations in such characteristics may also affect the performance of the dosage form. Changes in particle size of some excipient, for example, may affect content uniformity. Therefore, there is a need to test physical characteristics (particle size) for each batch of excipient. For many single-source excipients, particle size is a supplier specification and is usually tightly controlled. Having established a specification and not testing each lot of excipient upon receipt may be satisfactory in such cases. However, for some multisource excipients and where the dosage formulator expects to shift sources of supply, there may be differences in physical characteristics (particle size) that may affect dose uniformity and dissolution.

IX. CROSS-CONTAMINATION

Environmental controls for cross-contamination and protection of operators must be considered when creating an appropriate environment. Of prime importance are pressure differentials, relative humidity (often, total grains of moisture are measured), temperature, and air changes. The regulatory requirements for segregation of penicillin and cephalosporin are well established. Similar situations arise when hormones and oncolytics are manufactured. Highly active drugs pose another set of problems, wherein a low level of contamination can seriously affect the health of the operators and also create a cross-contamination situation. Remember, highly potent drugs can contaminate other products easily because there is always a threshold for preventing contamination. Generally, it is a good idea to manufacture potent drugs in separate areas.

X. DESEGREGATION OF POWDERS

Differences in particle sizes, particle shapes, hydrophilicities of powder surfaces, strengths of crystal lattice, polymorphic structures, environmental humidities, powder surface electrostatic charges, and the force and the nature of force applied all make a difference in how powders mix and demix. Segregation is a typical characteristic known from the example of separating chafe from hay by shaking the hay. The same process applies to mixing pharmaceutical ingredients in a mixer. The aim of mixing is to desegregate different powders, and it may require the use of some surfactants or other excipients to enhance the mixing or desegregation process. Overmixing, which increases electrostatic charges, can lead to segregation particularly after lubricants are added. Lubricants, by nature, are often hydrophobic (such as magnesium stearate) and readily develop electrostatic charge. The validation process develops a rationale for mixing times at all stages, from the initial mixing to mixing with binding solutions to blending with lubricants. To reduce charges, lubricants are not sifted through finer meshes. Segregation may also occur in a tablet machine hopper, causing serious problems of content uniformity.

XI. DISINTEGRATION TEST

A disintegration test is provided to determine compliance with the limits on disintegration stated in the individual monographs, except where the label states that the tablets or capsules are intended for use as troches, or are to be chewed, or are designed as modified-release dosage forms. Determine the type of units under testing from the labeling and from observation, and apply the appropriate procedure to six or more dosage units. Disintegration does not imply complete solution of the unit or even of its active constituent. Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus is a soft mass having no palpably firm core.

The apparatus consists of a basket-rack assembly, a 1000 mL, low-form beaker, 138 to 155 mm in height, with an inside diameter of 97 to 110 mm for the immersion fluid; a thermostatic arrangement for heating the fluid between 35°C and 39°C; and a device for raising and lowering the basket in the immersion fluid at a constant frequency rate between 29 and 32 cycles per minute through a distance of not less than 5.3 cm and not more than 5.7 cm. The volume of the fluid in the vessel is such that at the highest point of the upward stroke, the wire mesh remains at least 2.5 cm below the surface of the fluid and descends to not less than 2.5 cm from the bottom of the vessel on the downward stroke. The time

required for the upward stroke is equal to the time required for the downward stroke, and the change in stroke direction is a smooth transition, rather than an abrupt reversal of motion. The basket-rack assembly moves vertically along its axis. There is no appreciable horizontal motion or movement of the axis from the vertical.

A. Uncoated Tablets

Place one tablet in each of the six tubes of the basket, and operate the apparatus, using water maintained at $37 \pm 2^{\circ}C$ as the immersion fluid, unless otherwise specified in the individual monograph. At the end of the time limit specified in the monograph, lift the basket from the fluid, and observe the tablets: all the tablets disintegrated completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not less than 16 of the total of 18 tablets tested disintegrate completely.

B. Plain Coated Tablets

Apply the test for uncoated tablets, operating the apparatus for the time specified in the individual monograph.

C. Delayed-Release (Enteric-Coated) Tablets

Place one tablet in each of the six tubes of the basket, and if the tablet has a soluble external coating, immerse the basket in water at room temperature for 5 minutes. Then operate the apparatus using simulated gastric fluid TS maintained at $37 \pm 2^{\circ}C$ as the immersion fluid. After 1 hour of operation in simulated gastric fluid TS, lift the basket from the fluid, and observe the tablets: the tablets show no evidence of disintegration, cracking, or softening. Operate the apparatus, using simulated intestinal fluid TS maintained at $37 \pm 2^{\circ}C$ as the immersion fluid, for the time specified in the monograph. Lift the basket from the fluid, and observe the tablets: all the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not less than 16 of the total of 18 tablets tested disintegrate completely.

D. Buccal Tablets

Apply the test for uncoated tablets. After 4 hours, lift the basket from the fluid and observe the tablets: all the tablets disintegrated. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not less than 16 of the total of 18 tablets tested disintegrate completely.

E. Sublingual Tablets

Apply the test for uncoated tablets. Observe the tablets within the time limit specified in the individual monograph: all the tablets disintegrated. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not less than 16 of the total of 18 tablets tested disintegrate completely.

XII. DISSOLUTION

This test is provided to determine compliance with the dissolution requirements, where stated in the individual monograph, for a tablet or capsule dosage form. Of the types of apparatus described herein, use the one specified in the individual monograph. Where the label states that an article is enteric coated, and a dissolution or disintegration test does not specifically state that it is to be applied to enteric-coated articles, the individual monograph should include how to handle it. For gelatin-coated tablets that do not conform to the dissolution specification, repeat the test as follows. Where water or a medium with a pH of less than 6.8 is specified as the medium in the individual monograph, the same medium specified may be used with the addition of purified pepsin that results in an activity of 750,000 units or less per 1000 mL. For media with a pH of 6.8 or greater, pancreatin can be added to produce not more than 1750 USP units of protease activity per 1000 mL.

XIII. DISINTEGRATION AND DISSOLUTION

Disintegration is an essential attribute of tablets intended for administration by mouth, except for those intended to be chewed before swallowing and for some types of extended-release tablets. A disintegration test is provided, and limits on the times in which disintegration is to take place, appropriate for the types of tablets concerned, are given in the individual monographs. For drugs of limited water solubility, dissolution may be a more meaningful quality attribute than disintegration. A dissolution test is required in a number of monographs on tablets. In many cases, it is possible to correlate dissolution rates with biological availability of the active ingredient. However, such tests are useful mainly as a means of screening preliminary formulations and as a routine quality-control procedure.

XIV. DRUG SUBSTANCE CHARACTERIZATION

Characterization of the chemical and physical properties of a drug substance is one of the most important steps in the development of a solid dosage form. The identification of chemical properties, especially impurities, is very important. In addition, the physical properties of the API, such as solubility, polymorphism, hygroscopicity, particle size, density, etc., must be addressed. The literature and actual experience demonstrate that the physical quality (e.g., particle size of raw materials) can sometimes produce a significant impact on the availability and clinical effect of a dosage form drug. Therefore, it is appropriate that the physical characteristics of a drug substance be characterized, the impact of the physical characteristics be determined, and a specification for the bulk drug product be established, if necessary.

XV. DRYING PROCESS

Manufacturing formulas clearly specify how granules are to be dried. The temperature and length of drying are important, not only for losing a certain amount of moisture but also for achieving a specific granular structure. The end point of granulation is often described in terms of loss on drying (LOD), which is often characterized in terms of the Ohaus or Brabender index (e.g., LOD at 105°C for 1 hour) or an equivalent. Fluid-bed dryers and the newer granulator-vacuum dryers offer different rates of moisture loss and may form granules of different characteristics. The scale-up process should validate any changes in the equipment used and the technique used to dry granules. The validation should include compression tests and stability evaluations.

XVI. DYES IN FORMULATIONS

Manufacturers choose to include dyes in formulations for several reasons: for aesthetics, for identification, and for hiding inevitable mottling. Dyes can be included in the cores or in coating solutions when used. The Appendix to this book includes several formulations for coating solutions. Certifiable color additives (FD&C Certified) are available for use in foods or pharmaceuticals as either "dyes" or "lakes." Dyes dissolve in water and are manufactured as powders, granules, liquids, or other special-purpose forms. Lakes are the water-insoluble forms of dyes. Lakes are more stable than dyes and are ideal for coloring products containing fats and oils or items lacking sufficient moisture to dissolve dyes. Typical uses include coated tablets, cake and doughnut mixes, hard candies, and chewing gums. It is imperative that the manufacturer seek clarification of the status of a particular dye or lake before using it, particularly if the product has to be shipped to other countries. Labeling requirements include identification of all color additives. (The PDR is a good source to use to learn which colors are used in a particular product. For generic manufacturers, this is a good starting point.)

XVII. EQUIPMENT

The formulations provided do not specify equipment, and the manufacturer is supposed to select appropriate equipment for the batch size required. The selection of equipment must be based on full knowledge of the limitations of the equipment. The following sections (A–D) briefly describe some issues associated with equipment.

A. Blenders

Many solid oral dosage forms are made by direct compression. Two types of mixers are generally used: low energy and high energy. The low-energy mixers represent the classic type of slow mixers, such as ribbon blenders, tumblers, and the planetary pony pan. The high-energy mixers include some basic features of the low-energy mixer, but also contain some type of high-speed blade, commonly termed an intensifier bar or chopper.

1. Pony Pan

This mixer has historically been used for the manufacture of wet granulations. Because of its open pan or pot, granulating agents, such as starch paste, could be added while mixing. Because it is usually open at the top to allow the mixing blades to penetrate the powder, mixing operations are usually dusty and can lead to potential cross-contamination problems. The usefulness of these mixers is limited to wet granulating. With this type of mixer, there is good horizontal (side-to-side) blending. However, vertical (top-to-bottom) mixing does not occur. Powder placed in the mixer first will be poorly mixed. Segregation or demixing is also a recognized problem. To minimize this problem, some manufacturers empty the pan contents halfway through the mixing cycle in an attempt to turn the powder over at the bottom of the mixer. To alleviate the problem of the lack of mixing along the sides or walls of the pan, manufacturers often utilize a handheld steel paddle at various times during mixing. This type of mixing is difficult to control and reproduce. Thus, it would be difficult to validate.

The potential for segregation and poor mixing along the sides and particularly the bottom of the pony blender makes this type of blender less desirable for the dry blending of granulations of drug products. Consequently, whenever such dry blending is encountered, the manufacturer should be alert to potential problems with blending validation and content uniformity. Whenever in-process samples of the granulation are collected as part of an investigation or inspection, the formula card along with the weight of the dosage unit to be manufactured are needed for calculations.

2. Ribbon

In the ribbon blender, powder is mixed horizontally and vertically. Loading operations can be dusty. However, during the actual blending, it is enclosed, thereby limiting the amount of dust generated to the environment.

The major and potentially the most serious problem with the ribbon blender is that there is a "dead-spot" or zone at the discharge valve in some of these blenders. To compensate for this dead-spot, manufacturers recycle the powder from this area at some point during the mixing process. Obviously, there should be adequate and specific directions and procedures for assuring that this critical step is performed. Another concern with this mixer is poor mixing at the ends of the center horizontal mixing bar and at the shell wall because of blade clearance. The level of powder placed in this mixer is normally at the top of the outer ribbon blade, and as with other mixers, care must be taken not to overfill the mixer.

Cleaning problems, particularly at the ends of the ribbon blender where the horizontal bar enters the blender, have been identified. If manufacturers do not disassemble and clean the seals and packing between batches, they should have data to demonstrate the absence of foreign contaminants between batches of different products processed in the blender.

3. Tumbler

Common mixers of this type include the twin-shell and double cone. These mixers exert a gentle mixing action. Because of this mild action, lumps of powder will not be broken up and mixed. Powders may also clump due to static charges, and segregation can occur. Low humidity can contribute to this problem. Blending under very dry conditions was found to lead to charge buildup and segregation, while blending of some products under humid conditions led to lumping. More so than with other mixers, powder charge levels should not exceed 60% to 65% of the total volume of the mixer.

Fabricators of tumbler-type blenders identify the volume as the actual working capacity and not the actual volume of the blender. It is important to correlate the bulk density of the granulation with the working capacity of the blender.

4. High Shear (High Energy)

There are several fabricators of these mixers, including GRAL, Diosna, and Lodige or Littleford. These mixers are highly efficient and ideally suited for wet granulations. The end point of wet granulations can be determined by measurement on a gauge of the work needed to agitate the blend. The mixing vessel is enclosed, and dust only enters the environment when loading.

One of the problems associated with these mixers is the transfer or conversion of products blended in the older types of mixers to these blenders. Mixing times are going to be different, and the physical characteristics of the blend may also be different.

These mixers are efficient. For wet granulations, it is important to control the rate and amount of addition of the solvent. Because of their efficiency, drug substances may

partially dissolve and recrystallize upon drying as a different physical form.

An intensifier bar in the center of the blender, which rotates at very high speeds, breaks down smaller and harder agglomerates. A major disadvantage of this type of blender is that the extremely high speed of the intensifier bar generates considerable heat that can sometimes result in the charring of some sugar-base granulations. It should be pointed out that these same comments are applicable to other high-energy mixers, which also rely on high-speed choppers to disperse powders. Also, between-product cleaning of the blender requires disassembly of the intensifier bar.

5. Plastic Bag

Any discussion of mixers would not be complete without addressing the plastic bag. Manufacturers resorted to the blending or manufacture of a trituration in a plastic bag. Obviously, it is difficult to reproduce such a process, and there is the potential for loss of powder as a result of breakage or handling. When the plastic bag has been used, directions are usually not specific, and one would not know by reading the directions that a plastic bag was employed. The use of a plastic bag cannot be justified in the manufacture of a pharmaceutical product. In fact, it continues to be a popular method, as often mentioned in the formulations described in this treatise.

B. Dryers

Two basic types of dryers are used. One is the oven dryer, where the wet granulation is spread on trays and dried in an oven. The second dryer is the fluid-bed dryer, in which the wet granulation is "fluidized" or suspended in air. A third type recently introduced involves drying of granulations in vacuo while being mixed and processed. Generally, the fluid-bed dryer yields a more uniform granulation with spherical particles. However, this may result in compression problems that may require additional compression force to remedy these problems. It is not unusual to see manufacturers change from an oven dryer to a fluid-bed dryer. However, such a change should be validated for equivalency with conducted in vitro esting, such as hardness, disintegration, and comparative dissolution, and stability testing. Major changes in process details will require demonstration of bioequivalence.

Other issues of concern with drying include moisture uniformity and cross-contamination. Tray dryers present more moisture uniformity problems than fluid-bed dryers. Obviously, a dryer should be qualified for heat uniformity and a program developed to assure moisture uniformity in granulations at the end point of drying. With respect to fluid-bed dryers, moisture problems can occur if the granulation is not completely fluidized.

Regarding cross-contamination, oven dryers, particularly those in which air is recirculated, present cross-contamination problems because air recirculates through a common filter and duct. For fluid-bed dryers, the bag filters present cross-contamination problems. To minimize problems, manufacturers should use product-dedicated bags.

C. Tablet Compression Equipment

Another important variable in the manufacturing process is the tablet press or encapsulating machine. The newer dosage form equipment requires granulations with good flow characteristics and good uniformity. The newer tablet presses control weight variation by compression force and require uniform granulation to function correctly. Setup of the microprocessor-controlled tablet press usually includes some type of challenge to the system. For example, a short punch is sometimes placed among the other punches. If the press is operating correctly, it will sound an alarm when a lower- or higher-weight tablet is compressed.

Different tablet compression equipment can cause dose uniformity, weight uniformity, and hardness problems. For example, vibrations during tablet compression can cause segregation of the granulation in the feed hopper. The speed of the machine can affect fill of the die and tablet weight. Therefore, as previously discussed, it is important to have specific operating directions.

Many unit operations now provide for blending in totes, with discharge of the tote directly into tablet compression equipment. Because of segregation problems at the end of discharge, tablets from the end of compression should be tested for content uniformity. The use of inserts in totes was shown to minimize segregation.

With regard to the newer computer-controlled tablet compression equipment, buckets of tablets are often rejected because of potential weight variation problems. The disposition of these tablets, as well as the granulation and tablets used to set up the press, should be in accordance with written methods. Reworking processes for culls must be validated.

With regard to encapsulation operations, the hygroscopic nature of gelatin capsules and some of the granulations requires humidity controls for storage of the empty capsules and their subsequent filling. Scale-up of capsule products also presented some problems because of the different types of encapsulation equipment. Older equipment that operated on gravity fill, such as the Lilly and Parke-Davis machines, was commonly used for manufacturing capsules in clinical manufacturing areas. When formulations were scaled up to high-speed encapsulation equipment, flow problems and poor weight variation resulted. Additionally, some of the newer equipment provides for the formation of a slug, which could impact dissolution.

D. Coating Equipment

Many tablets are now coated with an aqueous film coat that is usually very soluble. Current technology provides for fixed sprays of the coating solution. The volume of coating solution, rate, and temperature can be controlled by some of the more highly automated operations. However, for many sugar-coated, enteric-coated, and delayed-release products, some portions of the coating process are not highly soluble and are performed manually. Generally, the shellac undercoat used for sugar-coated tablets presented disintegration and dissolution problems, particularly in aged samples.

With respect to poor disintegration, ferrous sulfate tablets probably represent the classical example. Over the years, there have been many recalls from many different manufacturers for poor disintegration of coated ferrous sulfate tablets. Likewise, there have been many problems with poor dissolution attributed to the coating process. Again, the shellac undercoat hardens, and even sometimes cracks, resulting in poor dissolution.

The numbers of applications of coats, volume of coating solution in a specific application, and temperature of the solution during applications are parameters that need to be addressed. For example, the temperature of the application and even heat during drying can cause dissolution failures in aged tablets. Another problem associated with the coating process concerns the heat applied to products that are sensitive to heat. For example, it was shown that estrogen tablets are heat sensitive and exhibited stability problems. Thus, it is important to control this phase of the process.

There are a few products, such as some of the antihistamine tablets, in which the drug substance is applied during the coating process. Other products require the active drug substance to be applied as a dust on tacky tablets as part of the coating process. For these products, it is particularly important to apply the drug in the coating solution in many controlled applications.

Again, it is important as part of the validation of these processes to demonstrate dose uniformity and dissolution and control the parameters of the coating process.

XVIII. EXCIPIENTS

Excipients are well defined in the official pharmacopoeia. No specific pharmaceutical grades are specified in this book, except where there is a specific reason to do so. However, it is known that different pharmacopoeia may have different specifications, such as particle size, impurities, moisture, etc. The harmonization of excipients, a global effort that is underway, would go a long way in making the choice of excipients. The manufacturer is referred to http://www.ipecamericas.org/index.html and the *Handbook of Pharmaceutical Excipients* for further advice. A large number of proprietary excipients are widely used, such as Ac-Di-Sol®, Explotab®, Aerosil®, Ludipress®, Avicel®, etc., and many of these are now part of pharmacopoeias. There is a significant advantage, though the cost is high, in using these ingredients because they offer additional benefits, often reducing processing time. Additionally, the suppliers of these ingredients are always willing to provide formulation support and have large databases, particularly pertaining to stability of drugs, that may be of great value to manufacturers. The following sections (A–F) list the most commonly used excipients in compressed solids.

A. Coating Agent

Carboxymethylcellulose, sodium cellacefate (formerly cellulose acetate phthalate), cellulose acetate, cellulose acetate phthalate (see cellacefate), ethylcellulose, ethylcellulose aqueous dispersion gelatin glaze, pharmaceutical hydroxypropyl, cellulose hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate (see hypromellose phthalate), hypromellose phthalate (formerly hydroxypropyl methylcellulose phthalate), methacrylic acid copolymer, methacrylic acid copolymer dispersion, methylcellulose PEG, polyvinyl acetate, phthalate shellac sucrose, titanium dioxide wax, carnauba wax, microcrystalline zein.

B. Glidant

Calcium silicate, magnesium silicate, silicon dioxide, colloidal talc.

C. Tablet Binder

Acacia alginic acid carboxymethylcellulose, sodium cellulose, microcrystalline dextrin ethylcellulose gelatin glucose, liquid guar gum hydroxypropyl methylcellulose, methylcellulose polyethylene oxide povidone starch, pregelatinized syrup.

D. Diluent

Calcium carbonate, calcium phosphate, dibasic calcium phosphate, tribasic calcium sulfate cellulose, microcrystalline cellulose, powdered dextrates, dextrin, dextrose, excipient, fructose, kaolin, lactitol, lactose, mannitol, sorbitol, starch, pregelatinized sucrose, sugar, compressible sugar, confectioner's sugar.

E. Disintegrant

Alginic acid cellulose, microcrystalline croscarmellose sodium, crospovidone polacrilin, potassium, sodium starch, glycolate starch, starch, pregelatinized.

F. Lubricant

Calcium stearate, glyceryl behenate, magnesium stearate, mineral oil, light PEG, sodium stearyl fumarate stearic acid, stearic acid, purified talc, vegetable oil, hydrogenated type I zinc stearate.

The choice of excipients is made based on three distinct considerations:

- Compatability with the active drug—Many excipients have active functional groups that can interact with the active drug and enhance its degradation. Even the water of hydration or moisture in the excipients can create difficulties in solid-state degradation of the active drug; so, it is not only the selection of the ingredient but also the grade (such as anhydrous or hydrous) that is important.
- Effect on efficacy—Excipients are known to alter the release patterns (e.g., a strong binder would delay break up of the tablet) and often bind the drug molecules in the gastrointestinal tract. The evaluation should be made in the full composition of ingredients because the presence of two ingredients may change their individual characteristics.
- Cost of formulation—Even though excipients contribute a small cost of the total formulation, the declining cost of APIs makes the selection of excipients based on cost an important consideration. This is particularly true when generic manufacturers are filing ANDAs knowing well that they will compete on a price basis. However, the total cost of formulation should not only be calculated on the basis of excipients. Often, the use of expensive excipients reduces process time, eliminates certain process steps, and even allows for the use of a cheaper packaging material. The manufacturer must, therefore, calculate the overall manufacturing cost. This aspect of formulation creates unique considerations by the multinational companies doing business worldwide; they are often forced to develop alternate formulations depending on the availability of excipients, manpower cost, and local environmental considerations.

The rule of thumb in the selection of excipients remains—keep it simple and at the bare minimum. The goal of excipients selection should be clearly defined—the dosage form yielding to a solution form at a predetermined rate (not necessarily the fastest in all instances).

The formulations described in this volume provide a quantitative listing of excipients recommended. An astute formulator would know the need to alter their quantity based on the type of equipment used to process them, the size of the batch processed at one time, and the quality of compressed product obtained. Therefore, all quantitative listings of excipients must be considered the best starting point, which can be adjusted and optimized, if necessary. In many instances, a range of excipients is allowed, such as in the case of a binder solution, to yield a suitable mass (as it is often described in the formulation of wet massing).

Where exact quantities of excipients are not available, but the excipients are identified for an innovator's product, this is still a better starting point than establishing the choice of excipients. Knowledge of the physicochemical

characteristics of the API takes a more pivotal role when the information available is limited. Obviously, one can readily identify the role of the identified, but not quantified, excipients. Some experimentation is required. However, as provided throughout this volume, significant knowledge can be gained by benchmarking the formulation. Other similar drugs or excipients should provide a good clue of the starting quantities. It is noteworthy that in obtaining the copies of competitor NDAs, through the Freedom of Information Act, some quantities are often redacted, leaving the formulator to guess. However, this should not be a difficult step, as long as the quantities of excipients chosen provide a similar weight, thickness, and disintegration and dissolution characteristics.

A common practice by innovator companies, as the NCE gets closer to the patent term expiry, is to patent a variety of formulations; for example, in the case of Aug-mentin®, the innovator chose to patent a different combination of amoxicillin and clavulanic acid and developed a composition for pediatric therapy. The purpose of this exercise is to keep generic competition out; the generic product in some cases may be the same, but not exact. The patent-end changes may also include changes in specification, choice of solvent systems used, or other cosmetic changes. However, a generic manufacturer would do well by just following the original formulation (for obvious reasons of regulatory compliance) because this has withstood the test of time. The author recommends that no changes should be made to an otherwise working formula, albeit this may improve processing, until such a time that the generic manufacturer has sufficient experience with the product. Most unusual things can happen when unsuspecting changes, appearing benign at the surface, are made to proven formulas. Given the cost of bioequivalence study requirements for compressed solids, changes in formulation should not be made unless essential and, even then, only for compliance purposes.

XIX. DIRECT COMPRESSION

The technology involved in direct compression assumes great importance in the tablet formulations, because it is often the cheapest means, particularly in the production of generics, that the active substance permits. The limiting factors are the physical properties of the active substance and its concentration in the tablets. Even substances such as ascorbic acid that are hardly suitable for direct compression, owing to the friability of their crystals, can normally be directly pressed into tablets at concentrations of 30% to 40%. However, this technique is not as suitable if the content of ascorbic acid is higher. This limit may be shifted upward by special direct compression auxiliaries, for example Ludipress. Two important alternatives, viz. Ludipress grades and Kollidon VA 64, can be found in the BASF line of pharmaceutical excipients for direct compression.

Ludipress is a speciality derived from lactose, Kollidon 30, and Kollidon CL. It thus combines the properties of a filler, binder, disintegrant, and flow agent and also often acts as a release accelerator. By virtue of its versatility, formulations containing it are usually very simple. It can also be combined with almost all active substances with the exception of those that enter into a chemical interaction with lactose (Maillard reaction).

Active substances, for example many analgetics, behave very differently with Ludipress when the dosage is extremely high. Acetylsalicylic acid and metamizole can be pressed when little Ludipress has been added; ibuprofen requires a larger amount; and the fraction of Ludipress required in the tablets is too large for paracetamol (= acetaminophen).

An alternative to the Ludipress grades is the outstanding dry binder Kollidon VA 64 together with excipients, for example calcium phosphate, microcrystalline cellulose, lactose, or starch, and a disintegrant, for example Kollidon CL. This combination even allows 500 mg of paracetamol to be pressed into good tablets with a weight of 700 mg.

No other dry binder has a binding power and plasticity comparable to those of Kollidon VA 64. Plasticity, in particular, is an important parameter in direct compression. This property of Kollidon VA 64 is not adversely effected by increasing the pressure. The beneficial properties of Kollidon VA 64 can also be exploited for the production of concentrated active substance that is subsequently used for direct tabletting. Kollidon VA 64 and Ludipress can also be combined with one another.

XX. FILL WEIGHTS

Fill weights are provided in all formulations. These may not coincide with scale for many reasons, as described elsewhere: differences in the salt forms, hydrates, or overages added in manufacturing and also to provide the extra margin of variation in filling during fast compression operations.

XXI. FINAL PACKAGING

A formulation design does not end with assuring that good tablets are formed; it must allow for handling during packaging, such as sliding into blister sheets or dropping into bottles. Actual fill runs must be conducted, and then the finished product must be subjected to simulated, and finally, the actual rigors of shipping before finalizing a formulation. Know that during shipping, the product may be exposed to diverse and often harsh weather conditions. Silica gel is often placed in the finished packs, or cotton is inserted, mainly to provide moisture or absorb odor (in the case of cotton).

XXII. FINAL TESTING

Finished product testing, particularly assay, content uniformity, and dissolution, is required. In the review of dissolution test results, it is important to eventually see results close to 100% dissolution. In some cases, manufacturers profile the dissolution results only to the specification. However, if lower but still acceptable results are obtained (such as 85%), it is important to continue the test. This can be performed by increasing the speed of the apparatus. If a product completely dissolves, yet only results in a value of 85%, it may indicate some problem with the test. Likewise, high dissolution results (115%) also indicate some problem with the test. Obviously, unusual or atypical results should be explained in the validation report.

XXIII. FINES

Solids, when grinded to small particle sizes (as when passing through sieves or crushing granules), yield a distribution of various particle sizes. A certain amount of very fine particles,

such as those passing #100 mesh, is required to fill in the gaps in a good compaction process; however, a large proportion of fines (as they are called) can create a problem in the flow or compaction of material. As a result, many master formulas require the reworking of fines back to granules. Any such recommendation should be carried out considering the type of processing and equipment used. These are mere suggestions; if a product compacts well, then it has the right proportion of fines.

XXIV. FORMULA EXCESSES

The difference between the scale and the quantity used for manufacturing is a result of either adjustment for the chemical form used (such as salt form for labeled base), hydrate forms (to compensate for additional water), potency variations (such as for antibiotics and biologicals), manufacturing excesses (for losses of drug during manufacturing), stability excesses (to compensate for loss during the shelf life; this is most important for vitamin products), and solvent/hydration loss (such as during manufacturing).

XXV. GEOMETRIC DILUTION

In all instances where low-dose drugs are manufactured, the mixing of ingredients should be done in a geometric dilution process; for example, a tablet containing 100 mg per tablet will first require mixing the active drug with a smaller quantity of excipient and then building up the volume to make sure the API is properly distributed. Further consistency to the product is imparted during the mixing of the granulated mixture.

XXVI. GRANULATION/MIX ANALYSIS

A critical step in the manufacture of an oral solid dosage form is the blending of the final granulation. If uniformity is not achieved at this stage, then one could assume that some dosage units would not comply with uniformity requirements. The major advantage of blend analysis (from a uniformity perspective) is that specific areas of the blender that have the greatest potential to be nonuniform can be sampled. This is particularly true of the ribbon-type blender and planetary or pony-type mixers.

In some cases, such as for large or tumbler-type blenders, it is impractical to sample from the blender directly. In such cases, granulations or blends could be sampled at the time of blender discharge or directly from drums. If sampling from drums, samples from the top, middle, and bottom of each drum should be collected.

In most cases, sampling thieves are readily available for sampling the small quantities that need to be taken from key areas of the blender or the drums. If samples larger than one dosage unit must be collected, however, adequate provisions must be made to prevent excessive handling manipulation between the time of sampling and the time of analysis.

Good science and logic would seem to dictate that sample sizes of the approximate equivalent weight of the dosage unit should be sampled in order to test for uniformity. Many industrial pharmacy and engineering texts confirm this approach. Large granulation sample sizes, such as 1 oz, will provide little information with respect to uniformity. Generally, further mixing after sampling and prior to analysis can yield misleading results.

The acceptance criteria for granulation dose uniformity testing needs to be continuously evaluated. Although many manufacturers evaluate dose uniformity using the compendia dose uniformity specifications (85–115% with an RSD of 6–7.8), such specifications should be tighter where supported by the firm's historical data on the level of blend uniformity with its equipment for a given product. In many cases, compendia assay limits for the finished product (90–110% of label claim) are broad enough for this purpose, and most manufacturers should be able to demonstrate blend assay results well within these limits. If larger sample sizes are taken for assay to evaluate total composite assay, then the specific USP or filed criteria for assay should be used.

In addition to the analysis of blends for dose uniformity and potency, blends are tested for physical characteristics.

A major physical parameter used to demonstrate equivalence between batches is the particle size profile. This is particularly important for comparison of the biobatch with production batches and should be repeated when processes are modified or changed. The particle size profile will provide useful information for demonstrating comparability.

Particle size profiles are particularly important for the tablet made by a wet granulation process. The size and even the type of granule can affect the pore size in a tablet as well as its dissolution. For example, dissolution failure may be attributed to a change in the milling screen size, yielding a granulation with larger granules. When coated, larger pores permit increased penetration into the tablet by the coating solution, resulting in slower dissolution.

Another test typically performed on the granulation, particularly when the wet granulation process is used, is loss on drying (LOD) and moisture content. If organic solvents are employed, then residual solvent residues are also tested. In the validation of a drying process, LOD levels are determined before, during, and after drying in order to demonstrate times and levels. As with processing variables, levels (specifications) are established in the development phase, with the validation phase used to confirm the adequacy of the process.

XXVII. INGREDIENT WARNING

Whereas many organic solvents are removed, traces may remain, and these may cause reactions, particularly in children; additionally, appropriate consideration should be given to the choice of using lactose for its intolerance in some of the use of sulfites or preservatives to which patients may be allergic.

XXVIII. IN-PROCESS TESTING

In-process testing is the testing performed on dosage forms during their compression/encapsulation stages to assure consistency throughout these operations. For tablets, individual tablet weights, moisture, hardness (compression force), and disintegration are performed. Because hardness and disintegration specifications are established during development and biobatch production, testing is performed to demonstrate equivalency (comparability) and consistency.

Specifications required to control the manufacturing process must be established and justified. This will require

granulation studies that would include blend uniformity, sieve analysis, and moisture. In the formulations provided in this book, the in-process milestones are not generally identified; the manufacturer is supposed to know this. Critical in-process testing stages for compressed solids are

- assuring cleanliness of equipment;
- checking and recording temperature where specified for dissolving or mixing ingredients, such as in the making of binder solutions or slurries;
- testing of granules for content uniformity, flow rate, tap density, moisture content (LOD), or other specific testing, as required;
- testing of tablets during compression for weight, thickness, friability, and disintegration;
- final testing of weight, friability, content uniformity, disintegration, and dissolution; and
- assay and finished product release.

With regard to moisture, some tablets set up (harden) upon aging as a result of poor moisture control and inadequate specifications. For example, this was shown to be a major problem with carbamazepine tablets.

XXIX. LOSS ON DRYING

This procedure determines the amount of volatile matter of any kind that is driven off under the conditions specified. Mix and accurately weigh the substance to be tested, and, unless otherwise directed in the individual monograph, conduct the determination on 1 to 2 g. If the test specimen is in the form of large crystals, reduce the particle size to about 2 mm by quickly crushing. Take a glass-stoppered, shallow weighing bottle that has been dried for 30 minutes under the same conditions to be employed in the determination. Put the test specimen in the bottle, replace the cover, and accurately weigh the bottle and the contents. By gentle, side-wise shaking distribute the test specimen as evenly as practicable to a depth of about 5 mm and not more than 10 mm in the case of bulky materials. Place the loaded bottle in the drying chamber, remove the stopper, and leave it in the chamber. Dry the test specimen at the temperature and for the time specified in the monograph. (*Note:* The temperature specified in the monograph is to be regarded as being within the range of $\pm 2^{\circ}C$ of the stated Figure.) Upon opening the chamber, close the bottle promptly, and allow it to come to room temperature in a desiccator before weighing.

If the substance melts at a lower temperature than that specified for the determination of LOD, maintain the bottle with its contents for 1 to 2 hours at a temperature $5^{\circ}C$ to $10^{\circ}C$ below the melting temperature, then dry at the specified temperature. Where the specimen under test is a tablet, use powder from not less than four tablets ground to a fine powder. Where the individual monograph directs that the LOD should be determined by thermogravimetric analysis, a sensitive electrobalance must be used. Where drying in vacuum over a desiccant is directed in the individual monograph, a vacuum desiccator or a vacuum drying pistol, or other suitable vacuum drying apparatus must be used. When drying in a desiccator is specified, exercise particular care to ensure that the desiccant is kept fully effective by frequently replacing. Where drying in a capillary-stoppered bottle in vacuum is directed in the individual monograph, use a bottle or tube fitted with a stopper having a 225 ± 25 mm diameter capillary, and maintain the heating chamber at a pressure of 5 mm or less of mercury. At the end of the heating period, admit dry air to the heating chamber, remove the bottle, and with the capillary stopper still in place, allow it to cool in a desiccator before weighing.

Many pharmacopoeial articles are hydrates or contain water in adsorbed form. As a result, the determination of the water content is important in demonstrating compliance with the pharmacopoeial standards. Generally, one of the methods given next is called for in the individual monograph, depending upon the nature of the article. In rare cases, a choice is allowed between two methods. When the article contains water of hydration, method I (titrimetric), method II (azeotropic), or method III (gravimetric) is employed, as directed in the individual monograph.

XXX. MANUFACTURING YIELDS

The formulas provided here include scale as well as quantities for 1000 tablets; often in a scale-up, yields must be calculated to extrapolate exact quantities needed for a specific batch size; yields vary because of differences in the tablet weight (within the specified range), losses in equipment, and losses to the environment. The exhaust or vacuum can carry with it a lot of product at times.

XXXI. MASTER FORMULA

This document must include specific manufacturing directions for the full-scale commercial process, including in-process and finished product specifications. The cGMP-compliant master formula will have room for direct entry onto the documents of all critical parameters, such as temperature, mixing times, LOD, etc., beside signatures of the persons responsible for complying with the specifications. No specific guidelines are provided for the formatting of this document. However, those skilled in assuring compliance with the GMP know the art of capturing most eventualities that may arise in the manufacturing of the product. The key is to assure that no individual discretions are allowed.

XXXII. MULTIPLE-ITEM ENTRIES

In the formulations provided in this book, an ingredient may appear in multiple places; this is necessary so as to identify the different quantities used at different stages and at different times for different purposes. For example, the dry form of starch may be mixed with the drug and then used in the making of a paste for granulation. Similarly, solvents are often listed in many places.

XXXIII. MULTIPLE STRENGTHS OF FORMULATIONS

The formulations disclosed in this book handle multiple strengths in two ways: one to adjust the fill weight of tablets and the other to provide a different formulation. There are specific reasons for this. Where the quantity of API is high, a simple doubling of fill weight might not work, and an adjustment to the excipients will be required. On the other hand are products where the API is less than 1% of the total weight, in which case, the formulation remains the same, with one of the

major components, such as lactose or dicalcium phosphate, providing compensation for the additional weight. Then, the tablet can be compressed at the same weight.

XXXIV. NOVEL DRUG DELIVERY SYSTEMS

From osmotically driven release of the API to wax matrices to plastic "ghosts" (e.g., Gradumet®), the compressed solid dosage forms offer a variety of possibilities for incorporating novel drug delivery systems. It should be noted that the compression force required to manufacture the dosage form can deform a structured component; on the other hand, the high compression force and the resultant rise in temperature that is inevitable can be used to create unique dosage form designs. One such example is the use of PEG 6000 or 8000 in direct compression formulations. The compression pressures in a typical tabletting machine or in a roller compactor are generally high enough to produce sufficient heat to melt the PEGs and then congeal to provide adequate binding without the need for wet massing. The author used this technique to formulate a myriad of drugs, particularly those subject to stability problems, such as vitamins. PEGs are compatible with most drugs, are cheap, and dissolve rapidly to release the drug. The author highly recommends using this technique to formulate directly compressible formulations instead of using the direct-compression-grade raw materials that are very expensive. Another technique that lends itself appropriately to solid compression is the use of solid solutions. Many drugs, when melted with water-soluble compounds, such as succinic acid, PEG, etc., congeal in a molecular dispersion, which, when placed in the gastrointestinal environment, releases the drug rapidly—it is already in a solution state. Wax embedding is another process (such as used for diltiazem) for moderating the release of drugs.

Briefly, the formulator has many tools available with which to formulate novel drug delivery systems with compression of solids. These techniques have, however, not been exploited as widely as their potential offers. The young formulators not yet biased by the need to follow a traditional route of formulating are encouraged to experiment with a myriad of possibilities, using components that have well proven their utility but in a different role. Remember, a temperature rise during the compression process is a source of energy that can be put to use.

XXXV. PARTICLE COATING

Even though solid-state compression excludes moisture, which is the primary starting point in chemical degradation, these dosage forms are not impervious to atmosphere; this protection is generally provided by coating the final compressed dosage form, such as by sealing with waxes. However, there are instances where it may be necessary to coat the particles of the drug before incorporating them into formulations. There can be several reasons for doing this, besides imparting greater stability. It is done to mask the taste, for example, in chewable tablets, to improve flow in tablets comprising a larger proportion of the active drug, to impart specific release characteristics, or to protect the gastrointestinal mucosa (such as in the case of particle-coated iron tablets). Coated particles should be treated as a specialized form of excipient, which must be properly tested for its specifications prior to incorporating in the final dosage form. Most of the particle-coating methods involve a fluid-bed system or coating on a nonpareil bead.

XXXVI. PRESERVATIVES IN COMPRESSED SOLID DOSAGE FORMULATIONS

As a rule of thumb, good formulations include only essential components. Because compressed solids have low moisture content, microbiological stability generally does not pose a problem, with few exceptions. However, in the wet granulation process, slurries or pastes are made that are water-based and are often kept for a few hours before being used, requiring the use of preservatives, particularly when gelatin is also used with starch. Generally, a standard combination of propylparabens and methylparabens would do. Preservatives are also included in compressed solids, where the compositions may be highly hygroscopic, resulting in localized liquefaction of powders that might promote microbial growth.

XXXVII. PUNCH SIZE AND SHAPE

The choice of punch size is dependent on the amount of API, the quantity of excipients needed to make it compressible, and what can be reasonably administered. Tablets ranging in weight from less than 100 mg to over 1 g are compressed in 6- to 15-mm-diameter punches. The size is also important because a proportion between thickness and diameter must be maintained. Thick tablets are difficult to eject from dyes, such as a long cylindrical product. Experienced machine operators know how well a tabletting mix compresses on one punch size and shape, and it becomes difficult to compress using other shapes and sizes. Whereas round tablets are the easiest to compress (from a technical viewpoint of design of punches to ejection), manufacturers use all different shapes, from bugs bunny-shaped vitamins to diamond-shaped Viagra® tablets.

The formulations provided in this book may have to be altered to meet the compaction requirements of different punch shapes and sizes other than those recommended here. Concave punches (giving convex tablets) are made to reduce the contact of compressed material with the wall of the die. This makes ejection of a tablet easier. However, because of the shape, there may be more picking of tablets. In several formulations described here, biplanar flat, round punches are recommended. The identification marks or logos on the tablets create additional problems in the picking of tablets. The polishing of punches remains an essential part of good tablet compressing. Often, punches wear out fast depending on the type of compression material used.

Regardless of what the supplier of a punch recommends, a punch must be replaced once it fails to provide the surface quality needed. Punches should ideally be replaced in groups and not individually (except to replace broken items).

XXXVIII. REWORKING CULLS

During the setup of machines and through rejection, especially in automated rejection systems, there may be a substantial amount of culls available. In most instances, it would be prudent to just discard them; however, for expensive APIs, reworking can be done. An internal SOP should clearly define

the proportion of rework allowed and how the calculations will be made to the BOM.

XXXIX. SCALE-UP

Whereas the formulations given in this book are robust enough to be scaled-up to most sizes, manufacturers may find the need to modify these to comply with scaled-up performance. For example, the quantity of lubricants, the amount of moisture, the size of the granules, etc., are all pertinent.

XL. SEGREGATION

Particulate solids, once mixed, have a tendency to segregate by virtue of differences in the shape, size, and density (other variables are also important) of the particles of which they are composed. This process of separation occurs during mixing as well as during subsequent handling of the completed mix. Generally, large differences in particle size, density, or shape within the mixture result in instability in the mixture. The segregation process normally requires energy input and can be reduced following mixing by careful handling. One of the most common reasons for postblending (after adding lubricants) segregation is overblending. Lubricants develop electric charge very quickly, making compression difficult and altering the dissolution profile. A critical specification in the manufacturing method is the length of blending. Follow this strictly.

XLI. SIFTING INGREDIENTS AND GRANULES

Whereas the specifications of starting materials are specified, the powders often form aggregates during storage; a point-of-use check of aggregation is needed. It is a good idea to sift all ingredients through specified sieves before adding them to mixing or blending vessels. For most raw materials, sifting through a #60 sieve (250 mm) is desired. Know that passing materials through finer sieves can generate electrostatic charges. Wet mass is passed through a #8 (2.38 mm) sieve, and dried granules are passed through a #16 (1.19 mm) mesh sieve. Lubricants should be sieved through a #60 mesh, except for magnesium stearate, which should not be shifted through an opening smaller than that of a #35 mesh. This is necessary to avoid building up electrical charges. A conversion chart for sieve sizes from U.S. Mesh to inches and microns (or millimeters) follows:

U.S. Mesh	Inches	Microns	Millimeters
3	0.2650	6730	6.730
4	0.1870	4760	4.760
5	0.1570	4000	4.000
6	0.1320	3360	3.360
7	0.1110	2830	2.830
8	0.0937	2380	2.380
10	0.0787	2000	2.000
12	0.0661	1680	1.680
14	0.0555	1410	1.410
16	0.0469	1190	1.190
18	0.0394	1000	1.000
20	0.0331	841	0.841
25	0.0280	707	0.707
	0.0232	595	0.595
	0.0197	500	0.500
	0.0165	400	0.400
	0.0138	354	0.354
	0.0117	297	0.297
	0.0098	250	0.250
	0.0083	210	0.210
	0.0070	177	0.177
	0.0059	149	0.149
	0.0049	125	0.125
	0.0041	105	0.105
	0.0035	88	0.088
	0.0029	74	0.074
	0.0024	63	0.063
	0.0021	53	0.053
	0.0017	44	0.044
	0.0015	37	0.037

XLII. SPECIFICATIONS

The development of a product and its manufacturing process and specifications, the design of the validation protocol, and the demonstration (validation) runs of the full-scale manufacturing process require scientific judgment based on good scientific data. The in-process control and product specifications are established during the product development process, with the test batch serving as the critical batch used for the establishment of specifications. Specifications, such as hardness and particle size, should be established before validation of the process; these specifications should be included in the validation protocol. The use of product development runs of the process to establish specifications and demonstrate that the system is validated often causes problems.

XLIII. STABILITY TESTING

Even though compressed solids offer a major advantage over other dosage forms in being the most stable, both chemically and physically, complete stability profiles must be developed every time any change, albeit minor, is made in the formulation, the processing conditions, the equipment used, or even the manufacturing site used. This applies not just to drugs with known stability problems, but even to highly stable drugs, such as erythromycin. Subtle alternations in formulation can bring such major unsuspected changes as prolonged disintegration and dissolution. The stability profiles are developed over a span of time to establish not only the chemical stability (providing the labeled quantity), but also the in vitro release characteristics. Stability testing is also required to be conducted in the specific temperature zone areas as dictated by compendia. This creates a significant problem for multinational companies selling products around the world, where different zone temperature stability requirements come into play. A universal formula is often difficult to design for this reason. Generic manufacturers must, therefore, take this aspect into consideration and mimic the formulations used by innovators in the world regions where these products are to be sold. Unfortunately, it is not as easy to obtain this information for formulations sold outside of the United States. Some reverse engineering may be in order to accomplish this.

XLIV. STORAGE OF IN-PROCESS MATERIAL

At several stages during the manufacturing, the bulk material would have to be kept in quarantine, awaiting QC results, such as LOD measurement, content uniformity of tabletting mix, etc. The master formula should specify the conditions of storage and the length of a validated storage period. In some instances, silica gel is to be kept in the drums storing the product. Follow these instructions carefully. In most instances, the bulk should receive a final blending turnover before filling the compression hoppers; this is necessary in order to avoid any segregation of powders during storage or during transportation to and from the storage facility.

XLV. TABLET FRIABILITY

This friability determination of compressed, uncoated tablets is generally applicable to most compressed tablets. Measurement of tablet friability supplements other physical strength measurements, such as tablet crushing strength. For tablets with a unit mass equal to or less than 650 mg, take a sample of whole tablets corresponding to 6.5 g. For tablets with a unit mass of more than 650 mg, take a sample of 10 whole tablets. The tablets should be carefully dusted prior to testing. Accurately weigh the tablet sample, and place the tablets in the drum. Rotate the drum 100 times, and remove the tablets. Remove any loose dust from the tablets, as before, and accurately weigh. If tablet size or shape causes irregular tumbling, adjust the drum base so that the base forms an angle of about 10 degrees with the benchtop, and the tablets no longer bind together when lying next to each other, which prevents them from falling freely.

Effervescent tablets and chewable tablets may have different specifications as far as friability is concerned, and these tablets normally require special packaging. In the case of hygroscopic tablets, a humidity-controlled environment (relative humidity less than 40%) is required for testing.

XLVI. TABLET MANUFACTURING

Tablets are prepared by three general methods: wet granulation, dry granulation (roll compaction or slugging), and direct compression. The purpose of wet and dry granulation is to improve flow of the mixture and to enhance its compressibility. Dry granulation (slugging) involves the compaction of powders at high pressures into large, often poorly formed tablet compacts. These compacts are then milled and screened to form a granulation of the desired particle size. The advantage of dry granulation is the elimination of heat and moisture in the processing. Dry granulations can be produced by extruding powders between hydraulically operated rollers to produce thin cakes that are subsequently screened or milled to give the desired granule size.

Excipients are available that allow production of tablets at high speeds without prior granulation steps. These directly compressible excipients consist of special physical forms of substances, such as lactose, sucrose, dextrose, or cellulose, which possess the desirable properties of fluidity and compressibility. The most widely used direct-compaction fillers are microcrystalline cellulose, anhydrous lactose, spray-dried lactose, compressible sucrose, and some forms of modified starches. Direct compression avoids many of the problems associated with wet and dry granulations. However, the inherent physical properties of the individual filler materials are highly critical, and minor variations can alter flow and compression characteristics so as to make them unsuitable for direct compression.

XLVII. TABLETS

Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They may be classed, according to the method of manufacture, as compressed tablets or molded tablets. The vast majority of all tablets manufactured are made by compression, and compressed tablets are the most widely used dosage form in the United States. Compressed tablets are prepared by the application of high pressures, utilizing steel punches and dies, to powders or granulations. Tablets can be produced in a wide variety of sizes, shapes, and surface markings, depending upon the design of the punches and dies. Capsule-shaped tablets are commonly referred to as caplets. Boluses are large tablets intended for veterinary use, usually for large animals. Molded tablets are prepared by forcing dampened powders under low pressure into die cavities. Solidification depends upon crystal bridges built up during the subsequent drying process and not upon the compaction force. Tablet triturates are small, usually cylindrical, molded, or compressed tablets. Tablet triturates were traditionally used as dispensing tablets in order to provide a convenient, measured quantity of a potent drug for compounding purposes. Such tablets are rarely used today. Hypodermic tablets are molded tablets made from completely and readily water-soluble ingredients and formerly were intended for use in making preparations for hypodermic injection. They are employed orally, or where rapid drug availability is required, such as in the case of nitroglycerin tablets, sublingually. Buccal tablets are intended to be inserted in the Buccal pouch, and sublingual tablets are intended to be inserted beneath the tongue, where the active ingredient is absorbed directly through the oral mucosa. Few drugs are readily absorbed in this way, but for those that are (such as nitroglycerin and certain steroid hormones), there are a number of advantages. Soluble, effervescent tablets are prepared by compression and contain, in addition to active ingredients, mixtures of acids (citric acid, tartaric acid) and sodium bicarbonate, which release carbon dioxide when dissolved in water. They are intended to be dissolved or dispersed in water before administration. Effervescent tablets should be stored in tightly closed containers or moisture-proof packs and should be labeled to indicate that they are not to be swallowed directly.

Chewable tablets are formulated and manufactured so that they may be chewed, producing a pleasant-tasting residue in the oral cavity that is easily swallowed and does not leave a bitter or unpleasant aftertaste. These tablets have been used in tablet formulations for children, especially in multivitamin formulations, and for the administration of antacids and selected antibiotics. Chewable tablets are prepared by compression, usually utilizing mannitol, sorbitol, or sucrose as binders and fillers, and containing colors and flavors to enhance their appearance and taste.

Most compressed tablets consist of the active ingredient and a diluent (filler), binder, disintegrating agent, and lubricant. Approved FD&C and D&C dyes or lakes (dyes adsorbed onto insoluble aluminum hydroxide), flavors, and sweetening agents may also be present. Diluents are added where the quantity of active ingredient is small or difficult to compress.

Common tablet fillers include lactose, starch, dibasic calcium phosphate, and microcrystalline cellulose. Chewable tablets often contain sucrose, mannitol, or sorbitol as fillers. Where the amount of active ingredient is small, the overall tableting properties are, in large measure, determined by the filler. Because of problems encountered with the bioavailability of hydrophobic drugs of low water solubility, water-soluble diluents are used as fillers for these tablets. Binders give adhesiveness to the powder during the preliminary granulation and to the compressed tablet. They add to the cohesive strength already available in the diluent. While binders may be added dry, they are more effective when added out of solution. Common binders include acacia, gelatin, sucrose, povidone, methylcellulose, carboxymethylcellulose, and hydrolyzed starch pastes. The most effective dry binder is microcrystalline cellulose, which is commonly used for this purpose in tablets prepared by direct compression. A disintegrating agent serves to assist in the fragmentation of the tablet after administration. The most widely used tablet disintegrating agent is starch. Chemically modified starches and cellulose, alginic acid, microcrystalline cellulose, and crosslinked povidone are also used for this purpose. Effervescent mixtures are used in soluble tablet systems as disintegrating agents. The concentration of the disintegrating agent, method of addition, and degree of compaction play roles in effectiveness. Lubricants reduce friction during the compression and ejection cycles. In addition, they aid in preventing adherence of tablet material to the dies and punches. Metallic stearates, stearic acid, hydrogenated vegetable oils, and talc are used as lubricants. Because of the nature of this function, most lubricants are hydrophobic, and as such, tend to reduce the rates of tablet disintegration and dissolution. Consequently, excessive concentrations of lubricant should be avoided. PEGs and some lauryl sulfate salts have been used as soluble lubricants, but such agents generally do not possess optimal lubricating properties, and comparatively high concentrations are usually required. Glidants are agents that improve powder fluidity, and they are commonly employed in direct compression where no granulation step is involved. The most effective glidants are the colloidal pyrogenic silicas. Colorants are often added to tablet formulations for aesthetic value or for product identification. Both D&C and FD&C dyes and lakes are used. Most dyes are photosensitive, and they fade when exposed to light. The U.S. FDA regulates the colorants employed in drugs.

XLVIII. WATER-PURIFIED USP

As a general practice, the water used in wet granulation processes should be of at least the water-purified USP grade. Other grades are acceptable, provided their use can be validated, mainly for the reasons of microbiological quality and the presence of other dissolved solids.

XLIX. WEIGHT VARIATION AND CONTENT UNIFORMITY

Tablets are required to meet a weight variation test, where the active ingredient comprises a major portion of the tablet and where control of weight may be presumed to be an adequate control of drug content uniformity. Weight variation is not an adequate indication of content uniformity, where the drug substance comprises a relatively minor portion of the tablet, or where the tablet is sugar coated. Thus, the pharmacopoeia generally requires that coated tablets and tablets containing 50 mg or less of active ingredient, comprising less than 50% by weight of the dosage-form unit, pass a content uniformity test, wherein individual tablets are assayed for actual drug content.

L. WET GRANULATION VS. DRY GRANULATION OR DIRECT COMPRESSION

Drug powders are often not easily compressible. Even if they are compressible, the small quantity that needs to be dispensed requires the adding of excipients for bulking the product; however, the addition of these compatible bulking agents may render the mixture less compressible. Books were written on the physics of powder compression. In a nutshell, the compression of powders involves the breaking of a crystal lattice and the rebonding of lattices to yield a unit structure. Binders provide the bridging gap between and among the ingredients that would rather stay away (to put it simply). With compression machines, the requirement that powders fill the compression cavities as they are compressed no longer holds. The conundrum with powders is that they must flow easily to fill the cavities, but as the particle size gets smaller, the specific surface area increases, along with interparticulate friction that keeps the powder from flowing (angle of repose), subject to the individual characteristics of the chemical. Therefore, for the powders to easily flow into compression cavities, they must be present in granular form, rather than in the form of fine powder. Powders can be converted to granular form by wetting them and drying to form the bonds between particles, particularly in the presence of binding agents (the most popular being starch). The wet granulation process, therefore, involves mixing the powders with a paste of starch (generally approximately 30%) or using polyvinylpyrrolidone (PVP) in an organic solvent to make a wet mass. In most instances, the characteristic of the wet mass is judged by how well it forms a mass as tested. The wet mass is then passed through a coarse mesh, spread on trays, and dried at 50°C to 60°C or directly placed in a fluid-bed dryer. The test of drying is that the LOD ranges from 1% to 3%. This is referred to as wet granulation. Dry granulation is a process where the active drug is mixed with ingredients that are inherently granular and compressible or are made by modifications through wet granulation, to impart good flow ability and compressibility to the mix. Several APIs are also available in direct compressible grades, often coated to impart an additional element of chemical stability. Directly compressible aspirin or ascorbic acid are good examples. The cost of APIs rendered compressible is obviously higher; however, in the long run, it is cheaper to use directly compressible powders.

LI. MULTIVARIATE METHODS IN TABLET FORMULATION

The discussion presented demonstrates that a large number of formulation variables inevitably come into play when formulating a solid dosage form; whereas, each dosage form has its own focus on overcoming inherent difficulties, the release from solid dosage forms and their desirability makes them most widely studied. Drugs are mostly administered in formulated forms and tablets account for more than 80% of all pharmaceutical dosage forms administered. The need to prepare an easily administered dose by mouth or other body cavities in a stable form and one that releases the drug on a

timely basis has been the longest challenge for the pharmaceutical industry. As a result, tablets contain a large number of excipients including fillers or diluents, binders or adhesives, disintegrants, lubricants and glidants, colors, flavors and sweeteners; it might also be necessary to add miscellaneous components such as buffers, depending on the application. What constitutes an ideal combination of these ingredients is of great value to the formulators since not only they have to prepare an effective and stable formulation but this must be done at the lowest possible cost. This evaluation is best made by using such statistical techniques as multivariate methods.

Multivariate techniques make use of statistical experimental design, especially designs that deal with optimization, where much effort is spent on obtaining detailed knowledge about the investigated domain which may include the multivariate characterization of the excipients, in terms of both physical and spectral properties, together with principal component analysis (PCA), statistical experimental design in principal properties (PPs), and partial least squares projections to latent structures (PLS) analysis.

Component analysis: An $N \times K$ data matrix consists of N rows and K columns. The samples or objects in the rows are described by measured or calculated variables given in the columns. In a graphical illustration of a data matrix, the objects are a swarm of N points in a coordinate system of K variables. In cases where a number of objects are described by many variables, the variables tend to be correlated to some extent. This is especially true for spectral variables, where a high absorbance at one wavelength is usually accompanied by similar absorbance values at neighboring wavelengths. PCA uses this correlation to describe the variation in the data with a minimum number of orthogonal components. PCA corresponds to the least squares fitting of a straight line ($A = 1$) or an A-dimensional hyperplane to the data in the K-dimensional variable space. Objects are projected onto a subspace of lower dimension and receive new identities, t-values, often referred to as PPs or scores. The variation of the objects is summarized in the ($N \times A$) matrix, which includes a score vector for each component. Score values from two principal components (PCs), together span a mathematical plane, often referred to as a score plot. Objects are projected onto the plane to form a two-dimensional model of the data. This facilitates the detection of groupings, trends, and outliers (deviating objects) in data sets. The process of detecting and diagnosing outliers is important both when fitting and interpreting the model. An outlier may be an object that does not fit very well into the model, that is, one for which the distance to the model in X is too large to be accepted. Examining the residuals of that particular object will reveal the cause of the deviation. An outlier may, alternatively, be an object that lies far away from other objects in the score plot. Since PCA is a least squares technique such an outlier may cause one of the PCs to run through it or very close to it, resulting in a skewed model. Such outliers should be removed upon identification. PCA models can be calculated using the nonlinear iterative partial least squares (NIPALS) algorithm. The first component explains as much as possible of the variance, the second component is orthogonal to the first and explains as much as possible of the residual variance, and so on. The diversity of PCA applications makes it a very powerful tool in many situations. PCA can be used as a means to discover trends, groupings, and outliers in many types of data, to classify objects, as well as to reduce the number of dimensions and descriptive variables. The features of the PCA model of most interest in any particular study will depend on the systems being investigated and the purposes of the study.

MSC and SNV: multiplicative scatter correction (MSC) is a method for linearization and scatter correction of NIR. It is assumed that the factors affecting physical light scattering of a particular wavelength differ from the chemical factors affecting light absorption. Hence, a corrected spectrum should include only chemical information. In order to normalize the scatter level an "ideal" sample, often the average of the data set is used to correct data for each of the samples. The sample spectrum is regressed onto the average in order to calculate the additive offset and the multiplicative constant. MSC should be used carefully, as all of the samples influence the correction terms, so a deviating sample could have adverse effects on the corrections. The standard normal variate transformation (SNV) as a method for removing unwanted variation from NIR spectra. In contrast to MSC, the correction is performed on an individual sample basis, thus eliminating the possible negative effects of a deviating sample. One of the drawbacks of using SNV, as well as MSC, is that potentially interesting information regarding the particle size is lost. In cases where a response matrix exists there are other methods for removing noise from spectra. The concept of orthogonal signal correction (OSC), a method for removing information in spectra that is not related to the response prior to investigation.

Missing data can be handled by NIPALS. As a rule of thumb, in order to use this approach, there should be five times as many observations in any row or column as the number of dimensions (A) being calculated. The missing values should also be randomly distributed.

Ultravariate characterization is the basis for multivariate design. Descriptive variables that are used to characterize the excipients (for example) may be either physical properties or other variables. Usually, a homogenous group of constituents are put in the same group and characterized by the same variables, where the class of excipients commonly used as lubricants are described using literature data on relevant physical properties. By applying PCA to the descriptive data, the important information is extracted in a few PCs. The PCs are often referred to as latent variables or the PPs of the data set. Each excipient is assigned a score value in each PC. Thus, the excipients are compared and related to on a continuous scale of PPs, which are assumed to reflect real differences in excipient properties and greater distances between excipients along the PCs reflect greater differences in behavior.

LII. PHYSICAL PROPERTIES

Physical properties of the excipients influence the properties of the tablet, for example particle size and bulk volume. Determining physical properties of excipients demands a systematic approach and may consume substantial resources. To establish an optimal choice of excipients, screening experiments are conducted to gain knowledge about parameters that influence the measured results. The traditional approaches to experimental design are difficult to implement when choosing factors to use in a screening study investigating more excipients than can possibly be managed in a mixture design. One alternative is to use physical properties as factors,for example viscosity or some measure of particle size, for each class of excipients. Only a limited number of descriptive variables can be used for each excipient class for a manageable number of experiments. Orthogonal factors can

also be difficult to acquire,for example, it would be difficult to find an excipient with both a large mean particle diameter (a high setting in an imaginary design) and high density (also a high setting in such a design). These factors, together with factors for example LOD and particle shape, can clearly make the task of finding excipients representing extreme settings difficult or impossible. Use of a D-optimal selection from a candidate set described in a few variables could be a feasible option. This alternative has not been investigated by the author or reported in the literature. Another alternative is to use qualitative variables. The drawback of this approach is that only a few excipients, that is, levels in the design, can be included before the number of experiments becomes unfeasibly high. Using PPs and multivariate design instead of qualitative factors is a viable alternative if many excipients are to be included in a screening study. In many cases, of course, the resulting model will be less detailed compared to a model derived from a set of experiments where physical properties of one or a few excipients are studied. Nevertheless, it should at least give a good indication of areas in the multivariate domain that should be further explored, which may be sufficient in some cases.

LIII. PARTICLE SIZE STUDIES

The particle size of new drug substance is a critical parameter as it affects every phase of formulation and its effectiveness. Appropriate particle size is required to achieve optimal dissolution rate in solid dosage forms, control sedimentation and flocculation in suspensions, small particle size (2−5 μm) is required for inhalation therapy, content uniformity, and compressibility is governed by particle size. As a result, the preformulation studies must develop a specification of particle size as early as possible in the course of studies and develop specifications that need to be adhered to throughout the studies.

Conventional methods of grinding in mortar or ball milling (where sample quantity is sufficient; generally it is not and limited to about 25–100 mg) or micronization techniques are used to reduce the particle size. The method used can have significant effect on the crystallinity, polymorphic structures (often to amorphous forms) and drug substance stability that can range from discoloration to significant chemical degradation. Changes in polymorphic forms can be determined by performing XRPD before and after milling.

Micronization where possible allows increase in the surface area to the maximum which can impact on the solubility, dissolution and as a result, bioavailability. Since the aim of most preformulation studies is to determine if a solid dosage form can be administered, knowing that reduction of particle size where it changes dissolution rates can be pivotal in decision making for the selection of dosage forms. In the process of micronization, the drug substance is fed into a confined circular chamber where it is suspended in a high velocity stream of air. Interparticulate collisions result in a size reduction. Smaller particles are removed from the chamber by the escaping air stream towards the center of the mill where they are discharged and collected. Larger particles recirculate until their particle size is reduced. Micronized particles are typically less than 10 μm in diameter. In some instances, micronization can prove counterproductive, where it results in increased aggregation (leading to reduced surface area) or alteration of crystallinity, which must be studied using such methods as microcalorimetry, dynamic vapor sorption or inverse gas chromatography.

The introduction of dynamic vapor sorption (DVS) in 1994 revolutionized the world of gravimetric moisture sorption measurement, bringing outdated, time, and labor intensive desiccator use into the modern world of cutting-edge instrumentation and overnight vapor sorption isotherms. With a resolution down to 0.1 μg, a 1% change in mass of a 10 mg sample on exposure to the humidity controlled gas flow is both easily discernable and reproducible. DVS is a valued tool for studies related to polymorphism, compound stability, bulk and surface adsorption effects of water and organic vapors. The dynamic vapor sorption studies would typically show percent mass increases but often a hysterisis loop relationship is observed where there is crystallization of compound that results in the expelling of excess moisture. This effect can be important in some formulations, such as dry powder inhaler devices, since it can cause agglomeration of the powders and variable flow properties. The DVS is useful study when amorphous forms are involved upon size reduction; in many cases, a low level of amorphous character cannot be detected by techniques such as XRPD; microcalorimetry can detect <10% amorphous content (the limit of detection is 1% or less). The amorphous content of a micronized drug can be determined by measuring the heat output caused by the water vapor inducing crystallization of the amorphous regions.

Excellent instrumentation support and advice is available through Surface Measurement Systems, http://www.smsuk.co.uk/index.php, manufacturer of DVS-Advantage and DVS-1000 and 2000 series of equipment for dynamic vapor interaction studies. The DVS-HT represents the first new generation in gravimetric vapor sorption analyzers for more than a decade by Surface Measurement Systems (5 Wharfside, Rosemont Road, Alperton, Middlesex. HA0 4PE United Kingdom).

A. Particle Size Distribution

Particle size reduction particularly mandates study of particle size distribution studies using such techniques as sieving, optical microscopy in conjunction with image analysis, electron microscopy, the coulter counter and laser diffractometers depending on the anticipated size of the particles. Whereas the size characterization is simple for spherical particles, study of irregular particles required specialized methods. The Malvern Mastersizer Series (http://www.malvern.co.uk/home/index.htm) is an example of an instrument that measures particle size by laser diffraction. The use of this technique is based on light scattered through various angles, which is directly related to the diameter of the particle. Thus, by measuring the angles and intensity of scattered light from the particles, a particle size distribution can be deduced. It should be noted that the particle diameters reported are the same as those that spherical particles would produce under similar conditions. In the former, each particle is treated as spherical and essentially opaque to the impinging laser light.

Two different light scattering methodologies can be used to characterize particles. The classical, also known as "static" or "Rayleigh" scattering or MALLS provides a direct measure of mass.

The dynamic light scattering (DLS), which is also known as "photon correlation spectroscopy" (PCS) or "quasi-elastic light scattering" (QELS), uses the scattered light to measure the rate of diffusion of the particles. This

motion data is conventionally processed to derive a size distribution for the sample, where the size is given by the "Stokes radius" or "hydrodynamic radius" of the protein particle. This hydrodynamic size depends on both mass and shape (conformation). Dynamic scattering is particularly good at sensing the presence of very small amounts of aggregated particles and studying samples containing a very large range of masses. It can be quite valuable for comparing stability of different formulations, including real-time monitoring of changes at elevated temperatures. For submicron materials, particularly colloidal particles, quasi-elastic light scattering is the preferred technique. Two theories dominate the theory of light scattering; the Fraunhofer and Mie. According to Fraunhofer theory, the particles are spherical, nonporous, and opaque; diameter greater than wavelength, particles are distant enough from each other, random motion, and all the particles diffract the light with the same efficiency, regardless of size and shape. The Mie theory takes into account the differences in refractive indices between the particles and the suspending medium. If the diameter of the particles is above 10 μm, then the size produced by utilizing each theory is essentially the same. However, discrepancies may occur when the diameter of the particles approaches that of the wavelength of the laser source.

Although laser light diffraction is a rapid and highly repeatable method in determining the particle size distributions of pharmaceutical powders, the results obtained can be affected by particle shape. The laser light scattering generally reports broader size distribution compared to image analysis. In addition, the refractive index of the particles can introduce an error of 10% under most circumstances and should be accounted for. Another laser-based instrument, relying on light scattering, is the Aerosizer (http://www.erc.ufl.edu/facility/equipment.asp?n=20). Aerosizer measures particles one at a time in the range of 0.20 to 700 microns. The particles may be in the form of a dry powder or may be sprayed from a liquid suspension as an aerosol. The particles are blown through the system and dispersed in air to a preset count rate. The Aerosizer operates on the principle of aerodynamic time of flight. The particles are accelerated by a constant, known force due to airflow and are forced through a nozzle at nearly sonic velocity. Smaller particles are accelerated at a greater rate than large particles due to a greater force-to-mass ratio. Two laser beams measure the time of flight through the measurement region by detecting the light scattered by the particles. Statistical methods are used to correlate the start and stop times of each particle in a particular size range (channel) through the measurement zone. The time of flight is used in conjunction with the density of the particles and calibration curves established to determine the size distribution of the sample.

LIV. SURFACE AREA

Since the surface area exposed to the site of administration determines how fast a particle dissolves in accordance with the Noyes–Whitney equation, these determinations are important. Also in those instances where the particle size is difficult to measure, a gross estimation of surface area is the second best parameter to have to characterize the drug. The most common methods of surface area measurement including gas adsorption (nitrogen or krypton) based on what is most commonly described as the Braunauer, Emmet and Teller, or BET, method applied either as a multipoint or single point determination.

Adsorption is defined as the concentration of gas molecules near the surface of a solid material. The adsorbed gas is called *adsorbate* and the solid where adsorption takes place is known as the *adsorbent*. Adsorption is a physical phenomenon (usually called physisorption) that occurs at any environmental condition (pressure and temperature) but only at very low temperature, it becomes measurable. Thus physisorption experiments are performed at very low temperature, usually at the boiling temperature of liquid nitrogen at atmospheric pressure. Adsorption takes place because of the presence of an intrinsic surface energy. When a material is exposed to a gas, an attractive force acts between the exposed surface of the solid and the gas molecules. The result of these forces is characterized as physical (or Van der Waals) adsorption, in contrast to the stronger chemical attractions associated with chemisorption. The surface area of a solid includes both the external surface and the internal surface of the pores.

Because of the weak bonds involved between gas molecules and the surface (less than 15 KJ/mole), adsorption is a reversible phenomenon. Gas physisorption is considered nonselective, thus filling the surface step-by-step (or layer by layer) depending on the available solid surface and the relative pressure. Filling the first layer enables the measurement of the surface area of the material, because the amount of gas adsorbed when the monolayer is saturated is proportional to the entire surface area of the sample. The complete adsorption/desorption analysis is called an adsorption isotherm.

Once the isotherm is obtained, a number of calculation models can be applied to different regions of the adsorption isotherm to evaluate the specific surface area (i.e., BET, Dubinin, Langmuir, etc.) or the micro- and mesopore volume and size distributions (i.e., BJH, DH, H&K, S&F, etc.).

The surface area of a solid material is the total surface of the sample that is in contact with the external environment. It is expressed as square meters per gram of dry sample. This parameter is strongly related to the pore size and the pore volume that is, the larger the pore volume, the larger the surface area and the smaller the pore size, the higher the surface area. The surface area results from the contribution of the internal surface area of the pores plus the external surface area of the solid or the particles (in case of powders). Whenever a significant porosity is present, the fraction of the external surface area to the total surface area is small.

LV. POROSITY

Most solid powders contain a certain void volume of empty space. This is distributed within the solid mass in the form of pores, cavities, and cracks of various shapes and sizes. The total sum of the void volume is called the porosity. Porosity strongly determines important physical properties of materials such as durability, mechanical strength, permeability, adsorption properties, etc. The knowledge of pore structure is an important step in characterizing materials, predicting their behavior.

There are two main and important typologies of pores: closed and open pores. Closed pores are completely isolated from the external surface, not allowing the access of external fluids in neither liquid nor gaseous phase. Closed pores influence parameters like density, mechanical and thermal

properties. Open pores are connected to the external surface and are therefore accessible to fluids, depending on the pore nature/size and the nature of fluid. Open pores can be further divided in dead-end or interconnected pores. Further classification is related to the pore shape, whenever is possible to determine it. The characterization of solids in terms of porosity consists in determining the following parameters:

- **Pore size:** Pore dimensions cover a very wide range. Pores are classified according to three main groups depending on the access size.
  - Micropores: less than 2 nm diameter
  - Mesopores: between 2 and 50 nm diameter
  - Macropores: larger than 50 nm diameter
- **Specific pore volume and porosity:** The internal void space in a porous material can be measured. It is generally expressed as a void volume (in cm^3 or mL) divided by a mass unit (g).
- **Pore size distribution:** It is generally represented as the relative abundance of the pore volume (as a percentage or a derivative) as a function of the pore size.
- **Bulk density:** Bulk density (or envelope density) is calculated by the ratio between the dry sample mass and the external sample volume.
- **Percentage porosity:** The percentage porosity is represented by ratio between the total pore volume and the external (envelope) sample volume multiplied by 100.
- **Surface area:** See above for discussion.

LVI. TRUE DENSITY

Density is the ratio of the mass of an object to its volume, and for solids this term describes the arrangement of molecules. The study of compaction of powders is described by the Heckel equation. The densities of molecular crystals can be increased by compression. Information about the true density of a powder can be used to predict whether a compound will cream or sediment in a suspension such as metered dose inhaler (MDI) formulation. Therefore, suspensions of compounds that have a true density less than these figures will cream (rise to the surface), and those that are denser will sediment. It should be noted, however, that the physical stability of a suspension is not merely a function of the true density of the material. The true density is thus a property of the material and is independent of the method of determination. In this respect, the determination of the true density can be determined using three methods: displacement of a liquid, displacement of a gas (pycnometry), or floatation in a liquid. The liquid displacement is tedious and tends to underestimate the true density; displacement of a gas is more accurate but needs relatively expensive instrumentation. As an alternative, the floatation method is simple to use and inexpensive.

Gas pycnometry is probably the most commonly used method in the pharmaceutical industry for measuring true density. Gas pycnometers rely on the measurement of pressure changes, as a reference volume of gas, typically helium, added to, or deleted from, the test cell.

LVII. FLOW AND COMPACTION OF POWDERS

The flow properties of a powder will determine the nature and quantity of excipients needed to prepare a compressed or powder dosage form. This refers mainly to factors such as ability to process the powder through machines. To make a quick evaluation, the compound is compressed using an infrared (IR) press and die under 10 tons of pressure with variable dwell times, and the resulting tablets are tested with regard to their crushing strength after storing the tablets for about 24 hours. If longer dwell times result in higher crushing strength then the material is likely plastic; elastic material will show capping at low dwell times; the brittle material will not show any effect of dwell times. It is recommended that the compressed tablets be subject to XPRD to record any changes in the polymorphic forms.

There appears to be a relationship between indentation hardness and the molecular structure of organic materials. However, a prerequisite for predicting indentation hardness is knowledge of the crystal structure. As a result, highly sophisticated, computational methods and extensive crystallography libraries have recently become available to study the. For example, the Pfizer Research relies on the The Cambridge Structural Database (http://www.ccdc.cam.ac.uk/), the world repository of small molecule crystal structures. The Cambridge Structural Database (CSD) is the principal product of the CCDC. It is the central focus of the CSD System, which also comprises software for database access, structure visualization and data analysis, and structural knowledge bases derived from the CSD. The CSD records bibliographic, chemical, and crystallographic information for organic molecules and metal-organic compounds whose 3D structures have been determined using X-ray diffraction or neutron diffraction. The CSD records results of single crystal studies and powder diffraction studies which yield 3D atomic coordinate data for at least all non-H atoms. In some cases, the CCDC is unable to obtain coordinates, and incomplete entries are archived to the CSD. The CSD is distributed as part of the CSD System, which includes software for search and information retrieval (ConQuest), structure visualization (Mercury), numerical analysis (Vista), database creation (PreQuest). The CSD System also incorporates IsoStar, a knowledge base of intermolecular interactions, contains data derived from both the CSD and the PDB. Some software listed above are available for free use.

X-ray microtomography such as available from Skyscan (http://www.skyscan.be/next/home.htm) is used to analyze the effect of compaction on powder particles. It allows for the noninvasive 3D analysis of resulting structures, and has shown that the structure may be controlled by choice of pyrogen and the method of solvent removal. Simple seeding of the substrate surface with drug crystals can be used initially with a view to incorporating more sophisticated substrate polymorph approaches. The Skyscan-1172 represents a new generation in desk-top X-ray micro-CT scan systems. A novel architecture in which both the sample stage and the x-ray camera are moveable allows an unprecedented combination of image resolution, sample size accommodation, scan speed, and sample throughput. This innovative flexible scanner geometry of the Skyscan-1172 is particularly advantageous over intermediate resolution levels, where scans are around 10 times faster (to obtain the same or better image quality) compared to previous scanners with a fixed source-detector design. The Skyscan-1172 features two X-ray camera options: the high-performance 10 megapixel option, and the economy 1.3 megapixel option. The former, 10 megapixel camera allows the maximum scanning versatility, with an image field width of 68 mm (in dual image camera shift mode) or 35 mm (in standard single camera image mode). A nominal resolution (pixel size) of lower than 1 μm is attainable. A scannable height of around 70 mm allows for

either large samples or automatic batch scanning of a column of smaller samples. The system obtains multiple X-ray "shadow" transmission images of the object from different angular views, as the object rotates on a high-precision stage. From these shadow images, cross-section images of the object are reconstructed by a modified Feldkamp cone-beam algorithm, creating a complete 3D representation of internal microstructure and density over a selected range of heights in the transmission images. The best micro-CT scan images are obtained from objects in which microstructure coincides with contrast in X-ray absorption of the sample's constituent materials.

LVIII. COLOR

The color of a powder sample is used to indicate presence of solvents, distribution of particle size, and other possible differences in different lots of a new lead compound. In some instances, degradation of drug can be correlated with color changes to such degree that accurate color measurements can be used as a tool to provide product specification. The compendia often describe color of substances but mostly in subjective terms. Historically, the color evaluation has been a subjective measurement; however, newer quantitative measurement systems make this a more objective process. There are two basic methods for measuring the colors of surfaces.

- The first is to imitate the analysis made by the eye in terms of responses to three stimuli. This technique, known as "tristimulus colorimetry," sets out to measure X, Y, and Z directly.
- The second method is to determine reflectance (R) for each wavelength band across the range of the spectrum to which the eye is sensitive, and then to calculate the visual responses by summing products of R and the standard values for distribution of the sensitivity of the three-color responses.

The tristimulus method has theoretical advantages where the materials to be measured are fluorescent, but there are serious practical problems in assuming that a tristimulus colorimeter exactly matches human vision, that is, in eliminating color blindness from the instrument.

Two commonly used types of color measurement equipment are a colorimeter and a spectrophotometer. A tristimulus colorimeter has three main components

- a source of illumination (usually a lamp functioning at a constant voltage);
- a combination of filters used to modify the energy distribution of the incident/reflected light; and
- a photoelectric detector that converts the reflected light into an electrical output.

Each color has a fingerprint reflectance pattern in the spectrum. The colorimeter measures color through three wide-band filters corresponding to the spectral sensitivity curves. Measurements made on a tristimulus colorimeter are normally comparative, the instrument being standardized on glass or ceramic standards. To achieve the most accurate measurements, it is necessary to use calibrated standards of similar colors to the materials to be measured. This "hitching post" technique enables reasonably accurate tristimulus values to be obtained even when the colorimeter is demonstrably colorblind. Tristimulus colorimeters are most useful for quick comparison of near-matching colors. They are not very accurate. Large differences are evident between the various instrument manufacturers. However, colorimeters are less expensive than spectrophotometers.

To get a precise measurement of color, it is advisable to use a spectrophotometer. A spectrophotometer measures the reflectance for each wavelength, and allows to calculate tristimulus values. The advantage over tristimulus colorimetry is that adequate information is obtained to calculate color values for any illuminant and that metamerism is automatically detected. Metamerism is a psychophysical phenomenon commonly defined incompletely as "two samples which match when illuminated by a particular light source and then do not match when illuminated by a different light source." In actuality, there are several types of metamerism, of which the sample and illuminant metamerism are most common. In sample metamerism, two color samples appear to match under a particular light source, and then do not match under a different light source. Illuminant metamerism appears when different light sources illuminate same sample and differences are revealed. The observer metamerism refers to where each individual perceives color slightly differently. The geometric metamerism arises when identical colors appear different when viewed at different angles, distances, light positions, etc.

In a spectrophotometer, the light is usually split into a spectrum by a prism or a diffraction grating before each wavelength band is selected for measurement. Instruments have also been developed in which narrow bands are selected by interference filters. The spectral resolution of the instrument depends on the narrowness of the bands utilized for each successive measurement. In theory, a spectrophotometer could be set up to compare reflected light directly with incident light, but it is more usual to calibrate against an opal glass standard that has been calibrated by an internationally recognized laboratory. Checks must also be made on the optical zero, for example, by measurements with a black light trap, because dust or other problems can give rise to stray light in an instrument (which would give false readings). Spectrophotometers contain monochromators and photodiodes that measure the reflectance curve of color every 10 nm or less. The analysis generates typically 30 or more data points, with which a precise color composition can be calculated.

A large number of suppliers provided colorimeters including such large array of equipment from Hunter Lab's Labscan XE with special adapter for small quantity of powders offers an excellent choice in preformulation work. The instrument has a 3-mm port and requires 0. 4-cm^3 powder to perform the testing. (http://www.hunterlab.com/)

LIX. ELECTROSTATICITY

When subjected to attrition, powders can acquire an electrostatic charge, the intensity of which is often proportional to physical force applied as static electrification of two dissimilar materials occurs by the making and breaking of surface contacts (tribo-electrification or friction electrification). Electrostatic charges are often used to induce adhesive character to bind drugs to carrier systems, for example, glass beads coated with HPMC containing drugs. The net charge on a powder may be either electropositive or electronegative depending on the direction of electron transfer. The mass charge density can vary from 10−5 to 100 μC/kg depending on the

stress, ranging from gentle sieving to micronization process. This can be determined using electric detectors to determine polarity as well as the electrostatic field. The electrostaticity results in significant changes in the powder flow properties.

Studies on tribo-electrification and potential charge buildup on equipment and particle surfaces and subsequent adhesion due to static charge often overlook the fact that all materials (whether they have a net surface charge or not) exhibit surface energy forces, that are very short range, but come into play once surfaces are "touching." These van der Waals forces are due to the dispersive and polar surface energies inherent at material boundaries. Dry powders with mass-median particle sizes larger than around 100 to 200 μm, seldom exhibit strong "cohesive" powder behavior, and such powders are usually described as "free flowing." As particle size decreases, however, the amount of surface area per unit mass increases, and surface-energy forces have a greater influence on bulk powder flow characteristics. For contacting particles that are smaller than 2 to 20 μm, such forces can be strong enough to cause small amounts of plastic deformation on particle surfaces near the points of contact—even with no applied external loads. The bulk behavior of such fine powders can be dominated by their "cohesivity." It is well known that powders comprised of finer particles are more cohesive, and, when very cohesive powders are placed in a rotating drum, they do not usually flow easily, nor do they form a smooth top surface. Instead, cohesive powders build up large overhanging "chunks" that can break off and collapse or cascade in random avalanches onto the material further down the slope. Placing the rotating drum in a centrifuge at an elevated G-level can cause a "nonflowable" cohesive powder to flow.

LX. CAKING

Powders cake due agglomeration as a result of factors such as static electricity, hygroscopicity, particle size, impurities of the powder and storage conditions, stress temperature, RH, and storage time, etc. The mechanisms involved in caking are based on the formation of five types of interparticle bonds such as bonding resulting from mechanical tangling, bonding resulting from steric effects, bonds via static electricity, bonds due to free liquid and bonds due to solid bridges. During the process of micronization, the formation of localized amorphous zones can lead to caking as these zones are more reactive to factors described above specially when exposed to moisture; the mechanisms involve moisture sorption due to surface sintering and recrystallization at well below the critical relative humidity. In most instances, increase in relative humidity begin to show some impact at values above 20% resulting in most dramatic effects above 75% to 80% relative humidity for powders that are subject to humidity effects.

LXI. POLYMORPHISM

Because polymorphism can have an effect on so many aspects of drug development, it is important to fix the polymorph (usually the stable form) as early as possible in the development cycle. Whereas, it is not necessary to create additional solid state forms by techniques or conditions unrelated to the synthetic process for the purpose of clinical trials, regulatory submission of a thorough study of the effects of solvent, temperature and possibly pressure on the stability of the solid state forms is advised. A conclusion that polymorphism does not occur with a compound must be substantiated by crystallization experiments from a range of solvents. This should also include solvents that may be involved in the manufacture of the drug product, for example, during granulation.

Whilst it is hoped that the issue of polymorphism is resolved during prenomination and early development, it can remain a concern when the synthesis of the drug is scaled-up into a larger reactor or transferred to another production site. It is not unlikely that a metastable form identified in prenomination may not be reproduced in later batches products because of some unrecorded conditions in the early phases of development. Related substances whether identified or not can significantly alter the predominance of a specific polymorph. To develop a reliable, commercial recrystallization process, the following scheme should be followed in the production of candidate drugs:

1. Selection of solvent system
2. Characterization of the polymorphic forms
3. Optimization of process times, temperature, solvent compositions, etc.
4. Examination of the chemical stability of the drug during processing
5. Manipulation of the polymorphic form, if necessary

Many analytical techniques have been used to quantitate mixtures of polymorphs, for example, XRPD has been used to quantitate the various polymorphs. Assay development requires creation of calibration curves and validation, which can be a difficult task where mixed polymorphs are present and requires study that there is no polymorphic transformation during analysis or change in the hydration of crystals, if that is also a concomitant problem. Whereas at the preformulation stage, the dosage form considerations are still developing, there is need to answer questions like how would a polymorph change should this be subject to manufacturing equipment stress like granulation or drying of granules, wet or dry granulation, and compression. In addition to the polymorphism of active drugs, the excipients like magnesium stearate can be present in various polymorphic forms that can significantly alter the behavior of active drug in the formulation stages. Studies using XRPD, IR, or SEM should be used for excipients as well as the active drug.

LXII. STABILITY STUDIES TO SELECT OPTIMAL DRUG AND EXCIPIENT COMBINATIONS

- Rapid screens of salts, solvates, hydrates, polymorphs and cocrystals.
- Large-scale preformulation and formulation studies.
- Characterization of polymers, food ingredients, and fine particles.
- Process optimization monitoring of surface and bulk chemistry.
- Quality control of incoming raw materials.
- Investigation of batch-to-batch variations in material formulations.
- At-line PAT support of production performance to specifications.

Whereas microcalorimetery remains the workhorse of studies, the use of inverse gas chromatography (IGC) is becoming more popular to determine the changes to drug substance upon micronization. The IGC differs from traditional gas chromatography insofar as the stationary phase is the

powder under investigation. The behavior of pharmaceutical solids, during either processing or use, can be noticeably affected by the surface energetics of the constituent particles. Several techniques exist to measure the surface energy, for example, sessile drop, and dynamic contact angle measurements. IGC is an alternative technique, where the powder surface is characterized by the retention behavior of minute quantities of well-characterized vapors that are injected into a column containing the material of interest. Recently published articles using IGC on pharmaceutical powders have ranged from linking surface energetic data with triboelectric charging, to study the effect of surface moisture on surface energetics. Molecular modeling has also recently been used to explore the links between IGC data and the structural and chemical factors that influence surface properties, thereby achieving predictive knowledge regarding powder behavior during processing. In this type of study, a range of nonpolar and polar adsorbates (probes) are used, for example, alkanes, from hexane to decane, acetone, diethyl ether, or ethyl acetate. The retention volume, that is, the net volume of carrier gas (nitrogen) required to elute the probe, is then measured.

IGC is a gas-phase technique for characterizing surface and bulk properties of solid materials. The principles of IGC are very simple, being the reverse of a conventional gas chromatographic (GC) experiment. A cylindrical column is uniformly packed with the solid material of interest, typically a powder, fiber, or film. A pulse or constant concentration of gas is then injected down the column at a fixed carrier gas flow rate, and the time taken for the pulse or concentration front to elute down the column is measured by a detector. A series of IGC measurements with different gas-phase probe molecules then allows access to a wide range of physicochemical properties of the solid sample.

Appendix I

Dissolution Testing Requirements of Compressed Dosage Forms

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Abacavir sulfate	Tablet	II (paddle)	75	0.1 N HCl	900	5, 10, 15, and 30	03/22/2006
Abacavir sulfate/Lamivudine	Tablet	II (paddle)	75	0.1 N HCl	900	10, 20, 30, and 45	01/03/2007
Acamprosate calcium	Tablet (delayed release)	I (basket)	180	Acid stage: 0.1 N HCl buffer stage: "citrate-sodium hydroxide" buffer pH 6.8 (150 mL of 2N NaOH, 21.014 g of citric acid and ultra-pure water to 1000 mL) (method B)	1000	120 (acid) 30, 60, 90, 120, and 180 (buffer)	12/20/2005
Acarbose	Tablet	II (paddle)	75	Water (deaerated)	900	10, 15, 20, 30, and 45	03/22/2006
Acetaminophen/butalbital	Tablet	II (paddle)	50	Water (deaerated)	900	15, 30, 45, 60, and 90	01/03/2007
Acetaminophen/butalbital/caffeine	Tablet			Refer to USP			01/14/2008
Acetaminophen/caffeine/ cihydrocodeine bitartrate	Tablet	II (paddle)	50	Water	900	10, 15, 30, 45, and 60	07/25/2007
Acetaminophen/oxycodone	Tablet			Refer to USP			01/14/2008
Acetaminophen/pentazocine HCl	Tablet	I (basket)	100	Water (deaerated)	900	10, 20, 30, 45, and 60	01/12/2004
Acetaminophen/tramadol HCl	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, 20, and 30	03/04/2006
Acyclovir	Tablet			Refer to USP			06/18/2007
Albuterol sulfate	Tablet (extended release)	II (paddle)	50	0.1 N HCl	900	1, 2, 4, and 9 hr	04/09/2007
AlendronatesSodium	Tablet			Refer to USP			01/14/2008
Alfuzosin HCl	Tablet (extended release)	II (paddle)	100	0.01 N HCl	900	1, 2, 12, and 20 hr	06/18/2007
Allopurinol	Tablet			Refer to USP			07/25/2007
Almotriptan malate	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	01/20/2006
Alosetron HCl	Tablet	II (paddle)	50 (for 1 mg) and 75 (for 0.5 mg)	Water (deaerated)	500	10, 20, 30, and 45	01/26/2006
Alprazolam	Tablet			Refer to USP			06/18/2007
Alprazolam	Tablet (extended release)	I (basket)	100	1% phosphate buffer, pH 6.0	500	1, 4, 8, and 16 hr	02/08/2007
Amantadine HCl	Tablet	II (paddle)	50	Water (deaerated)	500	10, 20, 30, 45, and 60	01/12/2004
Amiodarone HCl (test 1)	Tablet	II (paddle)	100	1% SLS in water	1000	10, 20, 30, 45, 60, and 90	01/12/2004
Amiodarone HCl (test 2)	Tablet	I (basket)	50	Acetate buffer, pH 4.0, with 1% Tween 80	900	10, 20, 30, 45, 60, and 90	01/12/2004
Amitriptyline HCl	Tablet			Refer to USP			01/14/2008
Amlodipine besylate	Tablet	II (paddle)	75	0.01 N HCl	500	10, 20, 30, 45, and 60	01/14/2004

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Amlodipine besylate/valsartan	Tablet	II (paddle)	50	For amlodipine: 0.1 N HCl, pH 1.0. For valsartan: 0.067 M phosphate buffer, pH 6.8	900 (for both Amlodipine and Valsartan)	10, 15, 30, and 45	02/19/2008
Amoxicillin/clavulanate potassium	Tablet (chewable)			Refer to USP			01/14/2008
Anastrozole	Tablet	II (paddle)	50	Water	900	5, 10, 15, 30, and 45	01/03/2007
Aripiprazole	Tablet	II (paddle)	60	pH 1.2 USP buffer (hydrochloric acid)	900	10, 20, 30, and 45	12/20/2005
Armodafinil	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	01/14/2008
Aspirin/caffeine/ orphenadrine citrate	Tablet	I (basket)	75	Water (deaerated)	900	10, 20, 30, 45, and 60	01/15/2004
Aspirin/hydrocodone bitartrate	Tablet	II (paddle)	75	Acetate buffer, pH 4.5	900	10, 20, 30, 45, 60, and 90	01/15/2004
Aspirin/meprobamate	Tablet	I (basket)	100	Water (deaerated)	900	10, 20, 30, 45, 60, and 90	01/15/2004
Aspirin/methocarbamol	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, 45, 60, and 90	01/15/2004
Atenolol	Tablet			Refer to USP			07/25/2007
Atorvastatin calcium	Tablet	II (paddle)	75	0.05 M phosphate buffer, pH 6.8	900	5, 10, 15, and 30	01/15/2004
Atovaquone	Tablet	II (paddle)	50	40% isopropanol buffered to pH 8.0 with potassium dihydrogen phosphate	900	10, 20, 30, 45, 60, and 90	06/18/2007
Atovaquone/proguanil HCl	Tablet	II (paddle) with PEAK vessels	50	40% isopropranol buffered to pH 8.0 with potassium dihydrogen phosphate	900	15, 30, 45, and 60	08/17/2006
Azithromycin	Tablet	II (paddle)	75	0.1 M phosphate buffer, pH 6.0	900	10, 20, 30, and 45	01/14/2008
Benazepril HCl	Tablet	II (paddle)	50	Water (deaerated)	500	10, 20, 30, and 45	01/16/2004
Benazepril HCl/hydrochlorothiazide	Tablet	I (basket)	100	0.1 N HCl	500	10, 20, 30, and 45	01/16/2004
Bendroflumethiazide/nadolol	Tablet			Refer to USP			07/25/2007
Benzphetamine HCl	Tablet	II (paddle)	50	Water	900	10, 20, 30, and 45	06/20/2007
Bepridil HCl	Tablet	I (basket)	100	0.1 N HCl	900	10, 20, 30, 45, and 60	01/16/2004
Bicalutamide	Tablet	II (paddle)	50	1% SLS in water	1000	10, 20, 30, 45, and 60	12/15/2005
Bisoprolol fumarate	Tablet			Refer to USP			06/18/2007
Bisoprolol fumarate/ hydrochlorothiazide	Tablet	II (paddle)	75	0.1 N HCl	900	5, 10, 20, 30, and 45	01/20/2004
Bromocriptine mesylate	Tablet			Refer to USP			07/25/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Buprenorphine HCl	Tablet (sublingual)	I (basket)	100	Water	500	2, 5, 8, 10, 15, and until at least 80% of the labeled content is dissolved	04/09/2007
Bupropion HCl	Tablet (extended release)			Refer to USP			07/25/2007
Cabergoline	Tablet	II (paddle)	50	0.1 N HCl	500	5, 10, 15, and 30	01/20/2004
Calcium acetate	Tablet			Refer to USP			01/14/2008
Candesartan cilexetil	Tablet	II (paddle)	50	0.35% polysorbate 20 in 0.05 M phosphate buffer, pH 6.5	900	10, 20, 30, 45, and 60	06/20/2007
Candesartan cilexetil (16 mg)/ hydrochlorothiazide (12.5)	Tablet	II (paddle)	50	0.35% polysorbate 20 in phosphate buffer pH 6.5	900	10, 20, 30, 45, and 60	03/04/2006
Candesartan cilexetil (32 mg)	Tablet	II (paddle)	50	0.70% Polysorbate 20 in 0.05 M phosphate buffer, pH 6.5	900	10, 20, 30, 45, and 60	06/20/2007
Candesartan cilexetil (32 mg)/ hydrochlorothiazide (12.5)	Tablet	II (paddle)	50	0.70% polysorbate 20 in phosphate buffer pH 6.5	900	15, 20, 30, 45, and 60	03/04/2006
Capecitabine	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	01/23/2004
Carbamazepine	Tablet (extended release)			Refer to USP			01/14/2008
Carbidopa/entacapone/levodopa	Tablet	I (basket)	Carbidopa and Levodopa: 50; Entacapone: 125	For both Carbidopa and Levodopa: 0.1 N HCl. For Entacapone: phosphate buffer pH 5.5	Carbidopa and Levodopa: 750 mL. Entacapone: 900 mL	10, 20, 30, 45, and 60	01/03/2007
Carbidopa/levodopa	Tablet			Refer to USP			01/14/2008
Carbidopa/levodopa	Tablet (orally disintegrating)	II (paddle)	50	0.1 N HCl	750	5, 10, 15, 30, and 45	07/25/2007
Carvedilol	Tablet	II (paddle)	50	SGF without enzyme	900	10, 20, 30, and 45	01/21/2004
Cefditoren pivoxil	Tablet	II (paddle)	75	Simulated gastric fluid without enzyme	900	5, 10, 15, 20, and 30	02/09/2006
Cefpodoxime proxetil	Tablet			Refer to USP			07/25/2007
Cefprozil	Tablet			Refer to USP			07/25/2007
Cefuroxime axetil	Tablet			Refer to USP			07/25/2007
Cetirizine HCL	Tablet (regular and chewable)	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	03/04/2006
Cetirizine HCl/pseudoephedrine HCl	Tablet (extended release)	I (basket)	100	0.1 N HCl	500	0.17, 0.25, 0.5, 1, 2, 6, and 8 hr	06/18/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Chlorambucil	Tablet	II (paddle)	75	0.1N HCl	900	10, 20, 30, and 45	08/17/2006
Chlorpheniramine maleate	Tablet (extended release)	III (reciprocating cylinder)	27 dpm	Row 1: test fluid 1 (0.1N HCl) for first hour. Row 2: test fluid 2 (phosphate buffer, pH 7.5) for fifth hour	Row 1: 250 mL. Row 2: 250 mL	1 hr for test fluid 1, and 4 hr for test fluid 2	07/25/2007
Chlorpheniramine maleate/Ibuprofen/pseudoephedrine HCl	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.5	900	10, 20, 30, and 45	02/20/2004
Chlorzoxazone	Tablet			Refer to USP			01/14/2008
Cilostazol	Tablet	II (paddle)	75	0.3% SLS in water	900	15, 30, 45, 60, and 90	08/17/2006
Cinacalcet HCl	Tablet	II (paddle)	75	0.05 N HCl	900	10, 20, 30, and 45	01/26/2006
Ciprofloxacin HCl	Tablet (extended release)	I (basket)	100	0.1 N HCl	900	1, 2, 4, and 7 hr or until at least 80% released	01/14/2008
Ciprofloxacin/ciprofloxacin HCl (AB)	Tablet (extended release)	II (paddle)	50	0.1 N HCl	900	15, 30, 60, and 120	01/14/2008
Citalopram HBr	Tablet			Refer to USP			01/14/2008
Clarithromycin	Tablet			Refer to USP			07/25/2007
Clonazepam	Tablet (orally disintegrating)	II (paddle)	50	Water	900	5, 10, 15, 30, and 45	07/25/2007
Clonidine HCl	Tablet			Refer to USP			06/18/2007
Clopidogrel bisulfate	Tablet			Refer to USP			07/25/2007
Clotrimazole	Tablet (vaginal)	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	01/24/2004
Cyclobenzaprine HCl	Tablet			Refer to USP			07/25/2007
Cyclophosphamide	Tablet	I (basket)	100	Water (deaerated)	900	10, 20, 30, 45, and 60	01/24/2004
Darifenacin hydrobromide	Tablet (extended release)	I (basket)	100	0.01M HCl comparative dissolution data should also be provided in 900 ml pH 4.5 buffer, pH 6.8 buffer, and water using apparatus I (basket) at 100 RPM.	900	1, 4, 8, 12, 16, 20, and 24 hr	01/20/2006
Darunavir ethanolate	Tablet	II (paddle)	75	2% Tween-20 in 0.05 M sodium phosphate buffer, pH 3.0	900	10, 20, 30, and 45	09/13/2007
Deferasirox	Tablet (for suspension oral)	II (paddle)	50	Phosphate buffer pH 6.8 with 0.5% Tween 20	900	10, 20, 30, and 45	06/21/2006
Delavirdine Mesylate	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.0 containing 0.6% w/v SDS	900	10, 20, 30, 45, and 60	12/03/2007
Demeclocycline HCl	Tablet			Refer to USP			07/25/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Desloratadine	Tablet	II (paddle)	50	0.1 N HCl	500	15, 20, 30, and 45	03/04/2006
Desloratadine	Tablet (orally disintegrating)	II (paddle)	50	0.1 N HCl	900	3, 6, 10, and 15	06/18/2007
Desmopressin acetate	Tablet	II (paddle)	75	Water (deaerated)	500	10, 20, 30, and 45	12/15/2005
Desogestrel/ethinyl estradiol	Tablet	II (paddle)	50	0.05% SLS in water	500	10, 20, 30, and 45	01/28/2004
Dexmethylphenidate HCl	Tablet	I (basket)	100	Water	900	10, 15, 30, and 45	06/18/2007
Diazepam	Tablet			Refer to USP			07/25/2007
Diclofenac potassium	Tablet	II (paddle)	50	SIF without enzyme	900	10, 20, 30, 45, 60, and 90	01/27/2004
Diclofenac sodium/misoprostol enteric coated (arthrotec)	Tablet (delayed release)	II (paddle) (diclo) II (paddle) (miso)	100 (diclo) 50 (miso)	Diclofenac: acid stage: 0.1 N HCl buffer stage: 750 mL 0.1N HCL + 250 mL 0.2M phos.buffer, pH 6.8 (method A) Misoprostol: water (deaerated)	Diclo: Acid: 750 Buffer:1000 Miso: 500	Diclo.: 120 (acid) 15, 30, 45, and 60 (buffer). Miso: 10, 20, and 30	12/15/2005
Didanosine	Tablet (chewable)	II (paddle)	75	Water (deaerated)	900	10, 20, 30, and 45	01/26/2004
Digoxin	Tablet			Refer to USP			06/18/2007
Diltiazem HCl	Tablet (extended release)	II (paddle)	100	Phosphate buffer, pH 5.8	900	2, 8, 14, and 24 hr	02/19/2008
Diphenhydramine citrate/ibuprofen	Tablet	II (paddle)	50	50 mM phosphate buffer, pH 6.5	900	10, 20, 30, and 45	01/14/2008
Dipyridamole	Tablet			Refer to USP			06/18/2007
Disulfiram	Tablet	II (paddle)	100	2% SDS	900	15, 30, 45, 60, 75, 90, 105, and 120	06/18/2007
Divalproex sodium	Tablet (delayed release)			Refer to USP			07/25/2007
Divalproex sodium	Tablet (extended release)	II (paddle)	100	Acid phase: 0.1 N HCl for 45 min; drug release: 0.05 M phosphate buffer with 75 mM SDS after 45 min	Acid phase:500 mL; Drug release: 900 mL	3, 9, 12, and 21 hr	06/18/2007
Donepezil HCl	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 40	01/27/2004
Donepezil HCl	Tablet (orally disintegrating (ODT))	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	03/04/2006
Doxazosin mesylate	Tablet	II (paddle)	50	0.01 N HCl	900	10, 20, 30, 45, and 60	01/27/2004
Doxazosin mesylate	Tablet (extended release)	II (paddle)	75	SGF without enzyme	900	4, 8, and 16 hr	01/03/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Doxycycline	Tablet	II (paddle)	75	0.01 N HCl	900	15, 30, 45, 60, and 90	01/14/2008
Drospirenone/estradiol	Tablet	II (paddle)	50	Water	900	10, 20, 30, and 45	01/03/2007
Efavirenz	Tablet	II (paddle)	50	2% SLS in water	1000	10, 15, 30, 45, and 60	06/18/2007
Efavirenz 600 mg; emtricitabine 200 mg; tenofovir disoproxil fumarate 300 mg	Tablet	II (paddle)	100	2% SLS in water	1000	10, 20, 30, and 45	01/03/2007
Emtricitabine/tenofovir disoproxil fumarate	Tablet	II (paddle)	50	0.01 N HCl	900	5, 10, 15, 30, and 45	01/03/2007
Entacapone	Tablet	II (paddle)	50	Phosphate buffer, pH 5.5	900	10, 20, 30, and 45	01/29/2004
Entecavir	Tablet	II (paddle)	50	Phosphate buffer pH 6.8 (50 mM)	1000	10, 20, 30, and 45	06/21/2006
Eplerenone	Tablet	II (paddle)	50	0.1 N HCl	1000	10, 20, 30, and 45	12/19/2005
Eprosartan mesylate/hydrochlorothiazide	Tablet	II (paddle)	75	0.2 M phosphate buffer, pH 7.5	1000	10, 20, 30, and 45	02/19/2008
Erlotinib HCl	Tablet	II (paddle)	75	0.1 N HCl containing 1% SDS	1000	15, 30, 45, and 60	03/22/2006
Escitalopram oxalate	Tablet	II (paddle)	75	0.1 N HCl	900	10, 20, 30, and 45	02/20/2004
Estazolam	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	01/27/2004
Esterified estrogens	Tablet	II (paddle)	50	Water	900	15, 30, 45, 60, 90, 120, and 180	02/19/2008
Estradiol	Vaginal ring	Incubator shaker	130	0.9% saline	250	1, 9, 16, 17, 18, 19, and 45 days	01/03/2007
Estradiol/norgestimate (1/0.09 mg)	Tablet	II (paddle)	50	0.3% SLS in water	500	10, 20, 30, and 45	07/09/2004
Eszopiclone	Tablet	II (paddle)	50	0.1 N HCl	500	10, 20, 30, and 45	09/13/2007
Ethambutol HCl	Tablet			Refer to USP			01/14/2008
Ethinyl estradiol/levonorgestrel	Tablet			Refer to USP			02/19/2008
Ethinyl estradiol/levonorgestrel (AB)	Tablet			Refer to USP			02/19/2008
Ethinyl estradiol/norethindrone	Tablet (chewable)	II (paddle)	75	0.09% sodium lauryl sulfate in 0.1 N HCl	500	10, 20, 30, and 45	01/14/2008
Ethinyl estradiol/norgestimate	Tablet	II (paddle)	75	0.05% Tween 20 in water	600	5, 10, 20, and 30	01/14/2008
Ethinyl estradiol/norgestimate (AB)	Tablet	II (paddle)	75	0.05% Tween 20 in water	600	10, 20, 30, and 45	01/14/2008
Ethinyl estradiol/norgestrel	Tablet	II (paddle)	75	Water with 5 ppm of Tween 80	500	10, 20, 30, 45, 60, and 90	01/28/2004
Etidronate disodium	Tablet			Refer to USP			06/18/2007
Etodolac	Tablet			Refer to USP			01/14/2008
Exemestane	Tablet	I (basket)	100	0.5%(w/v) SLS solution	900	10, 20, 30, and 45	08/17/2006

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Ezetimibe	Tablet	II (paddle)	50	0.45% SLS in 0.05 M acetate buffer, pH 4.5	500	10, 20, 30, and 45	01/14/2008
Ezetimibe/simvastatin	Tablet	II (paddle)	50	0.01M sodium phosphate, pH 7.0/0.5% SDS	900	5, 10, 20, and 30	01/03/2007
Famciclovir	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	04/09/2007
Famotidine	Tablet			Refer to USP			06/18/2007
Famotidine	Tablet (chewable)	II (paddle)	50	0.1 M phosphate buffer, pH 4.5	900	10, 20, 30, 45, and 60	01/29/2004
Famotidine	Tablet (orally disintegrating)	II (paddle)	50	Water (deaerated)	900	2, 4, 6, 8, and 10	01/29/2004
Famotidine/antacid combination berry and mint flavors	Tablet (chewable)	III (20 mesh top screen, 40 mesh bottom screen)	30 DPM	0.1 M acetate buffer, pH 4.5	900	10, 20, 39, and 45	03/04/2006
Felbamate	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, 45, 60, and 90	01/28/2004
Felodipine	Tablet (extended release)			Refer to USP			01/14/2008
Fenofibrate	Tablet	II (paddle)	50	0.05 M SLS in water	1000	10, 20, 30, and 45	01/29/2004
Fexofenadine HCl	Tablet	II (paddle)	50	0.001 N HCl	900	5, 10, 20, 30, and 45	02/19/2004
Finasteride	Tablet			Refer to USP			07/25/2007
Flavoxate HCl	Tablet	I (basket)	100	0.1 N HCl	900	5, 10, 20, and 30	01/29/2004
Fluconazole	Tablet	II (paddle)	50	Water (deaerated)	900 (for 150, 200, 300, and 400 mg tabs) 500 (for 50 and 100 mg tabs)	10, 20, 30, 45, and 60	03/04/2006
Fluoxetine HCl	Tablet	I (basket)	100	0.1 N HCl	1000	5, 10, 15, and 30	01/03/2007
Fluvastatin sodium	Tablet (extended release)	I (basket)	50	Water	900	0.5, 2, 4, and 8 hr	06/18/2007
Fluvoxamine maleate	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	01/03/2007
Fosamprenavir calcium	Tablet	II (paddle)	75	250 mM sodium acetate/acetic acid buffer pH 3.5	900	10, 20, 30, and 45	12/16/2005
Fosinopril sodium	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	01/30/2004
Fosinopril sodium/hydrochlorothiazide	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, 45, and 60	01/30/2004

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Gabapentin	Tablet	II (paddle)	50	0.06 N HCl	900	10, 20, 30, and 45	01/30/2004
Galantamine HBr	Tablet	II (paddle)	50	Water (deaerated)	500	5, 10, 20, and 30	03/04/2006
Gemfibrozil	Tablet			Refer to USP			07/25/2007
Gemifloxacin mesylate	Tablet	II (paddle)	50	0.01 N HCl	900	10, 20, 30, and 45	01/03/2007
Glimepiride	Tablet	II (paddle)	75	Phosphate buffer, pH 7.8	900	5, 10, 15, and 30	07/23/2004
Glimepiride/rosiglitazone maleate	Tablet	II (paddle)	75	0.01 M HCl with 0.5% sodium dodecyl sulfate	900	5, 10, 15, 30, 45, and 60	01/03/2007
Glipizide/metformin HCL	Tablet	II (paddle)	50	Phosphate buffer, pH 6.8	1000	10, 20,30, 45, and 60	03/04/2006
Glyburide (micronized)	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 7.5	900	10, 20, 30, 45, and 60	02/02/2004
Glyburide (nonmicronized)	Tablet	II (paddle)	75	0.05 M borate buffer, pH 9.5	500	10, 20, 30, 45, and 60	02/02/2004
Glyburide/metformin HCl	Tablet			Refer to USP			01/14/2008
Glycopyrrolate	Tablet			Refer to USP			07/25/2007
Granisetron HCl	Tablet	II (paddle)	50	Phosphate buffer, pH 6.5	500	10, 20, 30, 45, and 60	06/05/2006
Guaifenesin	Tablet (extended release)	I (basket)	75	0.1 N HCl	900	1, 2, 4, 6, and 12 hr	01/03/2007
Homatropine methylbromide/hydrocodone bitartrate	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	02/03/2004
Hydrochlorothiazide	Tablet			Refer to USP			07/25/2007
Hydrochlorothiazide/lisinopril	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, 45, and 60	02/03/2004
Hydrochlorothiazide/losartan potassium	Tablet	I (basket)	100	Water (deaerated)	900	10, 20, 30, 45, and 60	02/03/2004
Hydrochlorothiazide/Moexipril HCl	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/10/2004
Hydrochlorothiazide/olmesartan medoxomil	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.8	900	5, 10, 15, 20, 30, 45, and 60	07/09/2007
Hydrochlorothiazide/quinapril HCl	Tablet	I (basket)	100	Water (deaerated)	900	5, 10, 20, and 30	02/03/2004
Hydrochlorothiazide/valsartan	Tablet	II (paddle)	50	Phosphate buffer pH 6.8	1000	10, 20, 30, and 45	02/03/2004
Hydrocodone bitartrate/ibuprofen	Tablet	II (paddle)	50	Phosphate buffer, pH 7.2	900	5, 10, 15, and 30	02/04/2004
Hydromorphone HCl	Tablet			Refer to USP			07/25/2007
Hydroxyzine HCl	Tablet			Refer to USP			07/25/2007
Ibandronate sodium	Tablet	II (paddle)	50	Water	500	5, 10, 15, 30, and 45	01/03/2007
Ibuprofen	Tablet			Refer to USP			07/25/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Ibuprofen (chewable Tab)	Tablet (chewable)	II (paddle)	50	0.05 M phosphate buffer, pH 7.2	900	10, 20, 30, and 45	02/04/2004
Ibuprofen/oxycodone HCl	Tablet	I (basket)	100	Phosphate buffer, pH 7.2	500	10, 20, 30, and 45	04/09/2007
Imipramine HCl	Tablet			Refer to USP			01/14/2008
Irbesartan	Tablet	II (paddle)	50	0.1 N HCl	1000	10, 20, 30, and 45	12/14/2004
Irbesartan/HCTZ	Tablet	II (paddle)	50	0.1 N HCl	1000	10, 20, 30, 45, and 60	01/03/2007
Isocarboxazid	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, 45, and 60	02/04/2004
Isosorbide mononitrate	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 15, and 30	02/04/2004
Isosorbide mononitrate	Tablet (extended release)	II (paddle)	50	0.1N HCl containing 0.2% NaCl	500	1, 2, 6, 10, and 12	01/03/2007
Isradipine (10 mg)	Tablet (extended release)	II (paddle)	50	0.2% lauryl dimethylamine oxide (LDAO) in water	1000	2, 4, 8, 12, 16, and 24 hr	02/25/2004
Isradipine (5 mg)	Tablet (extended release)	II (paddle)	50	0.2% lauryl dimethylamine oxide (LDAO) in water	500	2, 4, 8, 12, 16, and 24 hr	02/25/2004
Ivermectin	Tablet	II (paddle)	50	0.5% SDS in 0.01 M monobasic sodium phosphate, pH 7.0	900	10, 20, 30, 45, and 60	02/04/2004
Ketoconazole	Tablet	I (basket)	100	Simulated gastric fluid w/o pepsin	800	15, 30, 45, 60, and 90	01/03/2007
Ketoprofen	Tablet	II (paddle)	50	SIF buffer without enzyme, pH 7.4	900	10, 20, 30, 45, and 60	02/05/2004
Lamivudine (for 100 mg and 150 mg)	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	03/22/2006
Lamivudine (for 300 mg only)	Tablet	II (paddle)	75	0.1 N HCl	900	5, 10, 15, and 30	03/22/2006
Lamivudine 150 mg/zidovudine 300 mg Tablets and abacavir sulfate 300 mg Tablets-co-packaged	Tablet	II (paddle)	75	0.1 N HCl	900	5, 10, 15, 20, 30, and 40	01/03/2007
Lamivudine/stavudine/nevirapine	Tablet	II (paddle)	75	0.1 N HCl	900	10, 20, 30, 45, and 60	01/03/2007
Lamivudine/zidovudine	Tablet	II (paddle)	75	0.1 N HCl	900	10, 20, 30, and 45	02/20/2004
Lamivudine/zidovudine + efavirenz	Tablet (copackage)	II (paddle)	Lamivudine and zidovudine: 75 efavirenz: 50	Lamivudine and zidovudine: 0.1 N HCl efavirenz: 2% SLS in water	Lamivudine and zidovudine: 1000 efavirenz: 900	10, 20, 30, and 45	01/03/2007
Lamivudine/zidovudine + nevirapine	Tablet (copackage)	II (paddle)	50	Lamivudine and zidovudine: water nevirapine: 0.06 M HCl (pH 1.2)	900	10, 15, 30, 45, and 60	01/03/2007
Lamivudine/zidovudine/nevirapine	Tablet	II (paddle)	50	0.01 N HCl	900	10, 15, 30, 45, and 60	01/03/2007
Lamotrigine	Tablet (chewable dispersible)	II (paddle)	50	0.1 N HCl	900	5, 10, 15, 20, and 30	01/14/2008

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Lamotrigine	Tablet (regular)	II (paddle)	50	0.1 N HCl	900	5, 10, 15, 20, and 30	03/04/2006
Lanthanum carbonate	Tablet (chewable)	Reciprocating cylinder (apparatus 3 modified)	10 dpm (dip rate per minute)	0.25 N HCl	900 (modified from the standard apparatus 3 vessel to achieve sink condition)	10, 20, 30, and 45	01/03/2007
Leflunomide	Tablet	II (paddle)	100	Water (deaerated)	1000	10, 20, 30, and 45	02/05/2004
Leflunomide (100 mg)	Tablet	II (paddle)	100	Water (deaerated) + 0.6% polyoxyethylene lauryl ether	1000	10, 20, 30, and 45	05/31/2007
Levetiracetam	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 15, and 30	02/05/2004
Levofloxacin	Tablet	I (basket)	100	0.1 N HCl	900	10, 20, 30, and 45	06/18/2007
Levonorgestrel	Tablet	II (paddle)	75	0.1 N HCl with 0.1% SLS	1000	10, 20, 30, 45, 60, and 90	02/05/2004
Levothyroxine sodium	Tablet			Refer to USP			07/25/2007
Lidocaine	Topical Patch	Paddle over disk (apparatus 5)	50	Acetic acid/sodium acetate buffer, pH 4.0 at 32°C	500	10, 20, 30, 60, 120, and 180	01/03/2007
Linezolid	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.8	900	5, 10, 20, 30, and 45	01/14/2008
Liothyronine sodium	Tablet			Refer to USP			06/18/2007
Lisinopril	Tablet			Refer to USP			01/14/2008
Lithium carbonate	Tablet (extended release)			Refer to USP			01/14/2008
Lomefloxacin HCl	Tablet	II (paddle)	50	0.01 N HCl	900	10, 20, 30, and 45	02/05/2004
Lopinavir/ritonavir	Tablet (combination)	II (paddle)	75	0.06 M polyoxyethylene 10 lauryl ether	900	15, 30, 60, 90, and 120	09/13/2007
Loratadine (orally disintegrating tablet)	Tablet (orally disintegrating)	I (basket)	50	SGF without enzyme	900	2, 4, 6, and 10	02/05/2004
Lorazepam	Tablet			Refer to USP			01/14/2008
Losartan potassium	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	02/06/2004
Lovastatin/niacin	Tablet (extended release)	I (basket)	100	For Niacin: water; for Lovastatin: 0.05 M phosphate buffer, pH 7.0 with 0.5% sodium dodecyl sulfate	900	For Niacin: 0.5, 1, 2, 3, 6, 9, 12, 20, and 24 hr; for Lovastatin: 15, 30, 45, and 60 min	01/14/2008

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Magnesium hydroxide/ omeprazole/sodium bicarbonate	Tablet (chewable)	II (paddle)	150	0.029 M sodium phosphate buffer w/ 0.5% SDS, pH 7.4	900	15, 30, 45, and 60	02/19/2008
Mefloquine HCl	Tablet	I (basket)	100	SGF without enzyme	900	10, 20, 30, 45, and 60	02/06/2004
Meloxicam	Tablet	II (paddle)	75	Phosphate buffer, pH 7.5	900	10, 20, 30, 45, and 60	02/20/2004
Memantine HCL	Tablet	I (basket)	100	0.1 N HCl with NaCl (12 g NaCl in 6 L water adjust pH to 1.2 with HCl)	900	10, 20, 30, and 45	12/16/2005
Mercaptopurine	Tablet	II (paddle)	50	0.1 N HCl	900	20, 30, 45, 60, 90, and 120	02/06/2004
Mesalamine	Tablet (delayed release)			Refer to USP			12/03/2007
Mesna	Tablet	II (paddle)	50	0.06 N HCl	500	5, 10, 15, 20, and 30	02/09/2004
Metaxalone	Tablet	II (paddle)	100	0.5% SLS in water	900	30, 60, 90, and 120	02/06/2004
Metformin HCl	Tablet (extended release)	I (basket)	100	Phosphate buffer, pH 6.8	1000	1, 3, 6, and 10 hr	04/09/2007
Metformin HCl/pioglitazone HCl	Tablet	II (paddle)	50	pH 2.5 McIlvaine buffer (0.1 M citric acid adjusted to pH 2.5 with 0.2 M Na_2HPO_4)	900	10, 20, 30, and 45	01/03/2007
Methimazole	Tablet			Refer to USP			01/14/2008
Metoclopramide	Tablet			Refer to USP			07/25/2007
Metolazone	Tablet	II (paddle)	75	2% SLS in 0.05 M sodium phosphate buffer, pH 7.5	900	30, 60, 90, 120, and 150	02/10/2004
Metoprolol succinate	Tablet (extended release)			Refer to USP			07/25/2007
Metoprolol tartrate	Tablet			Refer to USP			07/25/2007
Midodrine HCl	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/06/2004
Mifepristone	Tablet	II (paddle)	75	0.01 N HCl	900	5, 10, 15, 20, and 30	01/14/2008
Minocycline HCl	Tablet			Refer to USP			07/25/2007
Minocycline HCl	Tablets ER	I (basket)	100	0.1 N HCl	900	1, 2, 4, and 6 hr and until 80% of drug released	01/14/2008
Mirtazapine	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/10/2004
Mirtazapine	Tablet (orally disintegrating (ODT))	II (paddle)	50	0.1 N HCl	900	5, 10, 15, 20, and 30	03/04/2006
Misoprostol	Tablet	II (paddle)	50	Water (deaerated)	500	5, 10, 20, and 30	02/10/2004

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Modafinil	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, 45, and 60	02/10/2004
Moexipril HCl	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 15, and 30	02/10/2004
Molindone HCl	Tablet			Refer to USP			07/25/2007
Montelukast sodium	Tablet	II (paddle)	50	0.5% SDS in water	900	5, 10, 20, and 30	04/09/2007
Montelukast sodium	Tablet (chewable)	II (paddle)	50	0.5% SDS in water	900	5, 10, 20, and 30	03/04/2006
Moxifloxacin	Tablet	II (paddle)	50	0.1 N HCl	900	15, 30, 45, and 60	06/18/2007
Mycophenolate Mofetil	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/10/2004
Nabumetone	Tablet			Refer to USP			07/25/2007
Naproxen	Tablet			Refer to USP			07/25/2007
Naratriptan HCl	Tablet			Refer to USP			07/25/2007
Nateglinide	Tablet	II (paddle)	50	0.01 N HCl with 0.5% (w/v) SLS	1000	10, 20, 30, and 45	01/03/2007
Nefazodone HCl	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, 45, and 60	01/03/2007
Nelfinavir mesylate	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, 20, 30, 45, 60, and 90	01/03/2007
Neomycin Sulfate	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.8	900	15, 30, 45, and 60	01/14/2008
Nevirapine	Tablet			Refer to USP			09/13/2007
Nifedipine	Tablet (extended release)			Refer to USP			07/25/2007
Nitazoxanide	Tablet	II (paddle)	75	Phosphate buffer at pH 7.5 with 6% hexadecyltrimethyl ammonium bromide, bath temperature at 25°C	900	10, 20, 30, 45, and 60	01/03/2007
Norethindrone (AB1)	Tablet	II (paddle)	75	0.1 N HCl, 0.02% SLS	900	15, 30, 45, 60, and 75	01/03/2007
Norethindrone (AB2)	Tablet	II (paddle)	75	0.09% SLS in 0.1 N HCl (same as norethindrone/EE USP method)	500	15, 30, 45, and 60	01/03/2007
Nystatin	Tablet	II (paddle)	75	Water with 0.1% SLS	900	15, 30, 45, 60, and 90	01/03/2007
Ofloxacin	Tablet	I (basket)	100	0.1 N HCl	900	10, 20, 30, and 45	02/12/2004
Olanzapine	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 20, and 30	02/12/2004
Olanzapine (orally disintegrating)	Tablet (orally disintegrating)	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/12/2004
Olmesartan	Tablet	II (paddle)	50	0.05 M phosphate buffer, pH 6.8	900	10, 20, 30, and 45	07/09/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Omeprazole magnesium	Tablet OTC (delayed release)	II (paddle)	100	Tablets are preexposed to 300 mL of 0.1M HCL for 2 hr and then 700 mL of 0.086 M Na_2HPO_4 is added to the medium containing the capsule to give 1000 mL with pH 6.8	300 mL for the acid stage; 1000 mL for the buffer stage	Sampling started at the buffer stage 10, 20, 30, 45, and 60	01/03/2007
Ondansetron	Tablet (orally disintegrating)			Refer to USP			06/18/2007
Ondansetron HCl	Tablet	II (paddle)	50	Water (deaerated)	500	5, 10, 15, and 30	02/12/2004
Orphenadrine citrate	Tablet (extended release)	II (paddle)	50	0–1 hr: 0.1N HCl. After 1 hr: pH 7.5 buffer	800 mL for HCl, and 900 mL for buffer	0.5, 1, 2, 4, 10, and 12 hr	07/25/2007
Oxaprozin	Tablet	II (paddle)	75	0.05 M phosphate buffer, pH 7.4	1000	10, 20, 30, 45, and 60	02/12/2004
Oxcarbazepine (150 mg)	Tablet	II (paddle)	6	0.3% SDS in water	900	10, 20, 30, 45, 60, and 90	02/12/2004
Oxcarbazepine (300 mg)	Tablet	II (paddle)	60	0.6% SDS in water	900	10, 20, 30, 45, 60, and 90	02/12/2004
Oxcarbazepine (600 mg)	Tablet	II (paddle)	60	1% SDS in water	900	10, 20, 30, 45, 60, and 90	02/12/2004
Oxybutynin	Transdermal	Paddle over disk (apparatus 5)	50	Phosphate buffer, pH 4.5 at 32°C	900	1, 4, and 24 hr	01/03/2007
Oxybutynin chloride	Tablet (extended release)			Refer to USP			
Oxycodone HCl	Tablet			Refer to USP			01/14/2008
Oxycodone hydrochloride	Tablet (extended release)	I (basket)	100	SGF w/o enzymes	900	1, 4, 8, 12, and 15 hr	04/09/2007
Oxymorphone HCl	Tablet (extended release)	II (paddle)	50	pH 4.5 phosphate buffer	900	1, 4, 6, 10, and 14 hr	12/03/2007
Oxymorphone HCl	Tablets	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	01/14/2008
Paliperidone	Tablet (extended release)	Reciprocating disk (apparatus 7)	30 cycles per minute	NaCl 0.2% w/w in 0.0825 N HCl pH 1.0	50	2, 8, 14, 18, and 24 hr	12/03/2007
Pantoprazole sodium	Tablet (delayed release)	II (paddle)	100	Acid stage: 0.1 N HCl for 2 hr Buffer stage: phosphate buffer, pH 6.8	1000	1, 2 hr (acid stage) 10, 20, 30, 45, and 60 (buffer stage)	03/04/2006
Paroxetine HCl	Tablet			Refer to USP			01/14/2008
Pemoline	Tablet	II (paddle)	75	Water (deaerated)	900	10, 20, 30, 45, 60, and 90	02/13/2004

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Pergolide Mesylate	Tablet	II (paddle)	50	Simulated gastric fluid TS with cysteine without enzymes	500	10, 20, 30, and 45	03/04/2006
Perindopril erbumine	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	06/20/2007
Phenytoin	Tablet (chewable)			Refer to USP			01/14/2008
Pilocarpine HCl	Tablet	II (paddle)	50	0.1 N HCl	500	10, 20, 30, 45, and 60	01/20/2004
Pimozide	Tablet			Refer to USP			02/19/2008
Pioglitazone HCl	Tablet	II (paddle)	75	HCl-0.3 M KCl buffer, pH 2.0	900	5, 10, 15, and 30	02/13/2004
Potassium chloride	Tablet (extended release)			Refer to USP			07/25/2007
Pramipexole dihydrochloride	Tablet	II (paddle)	50	0.023 M Citrate/0.155 M phosphate buffer, pH 6.8	500	5, 10, 15, 30, and 45	10/09/2007
Pravastatin sodium	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 20, and 30	02/13/2004
Primidone	Tablet			Refer to USP			01/14/2008
Promethazine HCl	Tablet			Refer to USP			07/25/2007
Propafenone HCl	Tablet	II (paddle)	75	0.1 N HCl	900	10, 20, 30, and 45	02/13/2004
Protriptyline HCl	Tablet			Refer to USP			01/14/2008
Pseudoephedrine HCl	Tablet (extended release)			Refer to USP			01/14/2008
Quetiapine fumarate	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	02/18/2004
Quinapril HCl	Tablet			Refer to USP			07/25/2007
Rabeprazole sodium	Tablet (delayed release)	II (paddle)	100	700 mL 0.1 N HCl (acid stage), after 2 hr add 300 mL of 0.6 M Tris–HCl buffer, pH 8.0 (buffer stage). Stabilize the samples with the addition of 0.5 N NaOH	Acid: 700 buffer: 1000	10, 20, 30, and 45	04/09/2007
Raloxifene HCl	Tablet	II (paddle)	50	0.1% polysorbate 80 in water	1000	10, 20, 30, and 45	02/18/2004
Ranitidine HCl	Tablet			Refer to USP			07/25/2007
Repaglinide	Tablet			Refer to USP			07/25/2007
Ribavirin	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	02/18/2004
Rifapentine	Tablet	II (paddle)	50	0.8% SLS in phosphate buffer, pH 7.0	900	10, 20, 30, 45, 60, and 90	02/25/2004
Riluzole	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, 45, and 60	02/18/2004
Rimantadine HCl	Tablet	II (paddle)	50	Water	900	10, 20, 30, and 45	01/03/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Risedronate sodium	Tablet	II (paddle)	50	Water (deaerated)	500	10, 20, 30, and 45	02/20/2004
Risedronate sodium (75 mg)	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, and 45	09/13/2007
Risedronate sodium/ Calcium Carbonate	Tablet (Copackaged)	For Risedronate Tablets: Paddle	For Risedronate Tablets: 50	For Risedronate tablets: water. For Calcium Carbonate tablets: using USP method.	For Risedronate Tablets: 500 mL	10, 20, 30, and 45	01/03/2007
Risperidone	Tablet	II (paddle)	50	0.1 N HCl	500	10, 20, 30, 45, and 60	03/04/2006
Risperidone	Tablet (orally disintegrating)	II (paddle)	50	0.1 N HCl	500	5, 10, and 15	07/23/2004
Rizatriptan benzoate	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 15, and 30	02/18/2004
Rizatriptan benzoate	Tablet (orally disintegrating)	II (paddle)	50	Water (deaerated)	900	5, 10, and 15	02/18/2004
Ropinirole HCl	Table	I (basket)	50	Citrate buffer, pH 4.0	500	5, 10, 15, and 30	01/03/2007
Rosiglitazone maleate	Tablet	II (paddle)	50	0.01 M acetate buffer, pH 4.0	900	10, 20, 30, and 45	02/24/2004
Rosuvastatin calcium	Tablet	II (paddle)	50	0.05 M citrate buffer pH 6.6	900	10, 20, 30, and 45	12/20/2005
Saquinavir mesylate	Tablet	II (paddle)	50	Citrate buffer (pH 3.0)	900	10, 20, 30, and 45	09/13/2007
Sertraline HCl	Tablet	II (paddle)	75	0.05 M sodium acetate buffer, pH 4.5	900	10, 20, 30, and 45	02/20/2004
Sildenafil citrate	Tablet	I (basket)	100	0.01 N HCl	900	5, 10, 15, and 30	03/04/2006
Simvastatin	Tablet			Refer to USP			06/18/2007
Sirolimus	Tablet	Basket (20 mesh)	120	0.4% SLS in water	500	10, 20, 30, 45, 60, and 120	03/14/2007
Solifenacin succinate	Tablet	II (paddle)	50	Water	900	10, 15, 30, and 45	02/19/2008
Sulfamethoxazole/trimethoprim	Tablet			Refer to USP			01/14/2008
Sumatriptan succinate	Tablet	II (paddle)	30	0.01 M HCl	900	5, 10, 15, and 30	03/04/2006
Tadalafil	Tablet	II (paddle)	50	0.5% sodium lauryl sulfate	1000	10, 20, 30, and 45	01/26/2006
Telithromycin	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	01/03/2007
Telmisartan	Tablet	II (paddle)	75	Phosphate buffer, pH 7.5	900	10, 20, 30, and 45	03/04/2006
Tenofovir disoproxil fumarate	Tablet	II (paddle)	50	0.1 N HCl	900	10, 20, 30, and 45	01/03/2007
Terazosin HCl	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, 45, and 60	02/20/2004
Terbinafine HCl	Tablet	II (paddle)	50	Citrate buffer, pH 3.0 adjusted with HCl	500	10, 20, 30, and 45	02/20/2004
Testosterone	Tablet Buccal (extended release)	II (paddle, may use sinker)	60	1% sodium dodecyl sulfate in double distilled water	1000	1, 2, 4, 6, 10, 12, and 24 hr	01/03/2007
Theophylline (100 and 200 mg)	Tablet (extended release)	II (paddle)	50	SGF, pH 1.2 during first hour. SIF, pH 7.5 from end of hour 1 through 12th hour	900	1, 4, 8, and 12 hr	01/03/2007

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Theophylline (450 mg)	Tablet (extended release)	II (paddle)	50	SGF, pH 1.2 during first hour. SIF, pH 7.5 from end of hour 1 through 12th hour	900	1, 4, 8, and 12 hr	01/03/2007
Tiagabine HCl	Tablet	II (paddle)	50	Water	900	5, 10, 15, 20, and 30	01/03/2007
Ticlopidine HCl	Tablet	II (paddle)	50	Water (deaerated)	900	10, 20, 30, 45, and 60	02/19/2004
Tinidazole	Tablet	I (basket)	100	Water (deaerated)	900	10, 20, 30, and 45	01/03/2007
Tizanidine HCl	Tablet	I (basket)	100	0.1 N HCl	500	5, 10, 15, and 30	02/20/2004
Tolcapone	Tablet	II (paddle)	75	Borate buffer, pH 6.8 with 1% SLS	900	10, 20, 30, and 45	02/20/2004
Tolterodine tartrate	Tablet	II (paddle)	50	SGF without enzymes, pH 1.2	900	5, 10, 15, and 30	02/20/2004
Topiramate	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 20, and 30	02/19/2004
Toremifene citrate	Tablet	II (paddle)	50	0.02 N HCl	1000	10, 20, 30, and 45	02/20/2004
Torsemide	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	02/20/2004
Tramadol HCl	Tablet	I (basket)	100	0.1 N HCl	900	10, 20, 30, and 45	02/19/2004
Tramadol HCl	Tablet (extended release)	I (basket)	75	0.1 N HCl	900	2, 4, 8, 10, and 16 hr	01/03/2007
Trandolapril	Tablet	II (paddle)	50	Water (deaerated)	500	10, 20, 30, 45, and 60	02/20/2004
Trospium chloride	Tablet	II (paddle)	50	0.1 N HCl	1000	10, 20, 30, and 45	12/03/2007
Valganciclovir HCl	Tablet	II (paddle)	50	0.1 N HCl	900	10,15, 30, 45, and 60	06/18/2007
Valsartan (Tablet and Capsule)	Tablet	II (paddle)	50	0.067 M phosphate buffer, pH 6.8	1000	10, 20, 30, and 45	12/13/2004
Vardenafil HCl	Tablet	II (paddle)	50	0.1 N HCl	900	5, 10, 15, and 30	12/20/2005
Varenicline tartrate	Tablet	I (basket)	100	0.01 N HCl	500	5, 10, 15, and 30	12/03/2007
Venlafaxine HCl	Tablet	II (paddle)	50	Water (deaerated)	900	5, 10, 15, and 30	02/19/2004
Zafirlukast	Tablet	II (paddle)	50	1% w/v aqueous sodium dodecyl sulfate	1000	10. 30, 30, and 45	10/09/2007
Zalcitabine	Tablet			Refer to USP	900		02/19/2008
Zidovudine	Tablet			Refer to USP			07/25/2007
Zileuton	Tablet	II (paddle)	50	0.05 M SLS in water	900	10, 20, 30, 45, and 60	02/19/2004
Zolmitriptan	Tablet (orally disintegrating)	II (paddle)	50	0.1 N HCl	500	5, 10, 15, and 30	06/18/2007
Zolpidem tartrate	Tablet	II (paddle)	50	0.01 N HCl, pH 2.0	900	5, 10, 15, and 30	02/19/2004
Zolpidem tartrate	Tablet (extended release)	I (basket)	100	0.01 N HCl	500	15, 30, 90, 120, and 240	04/09/2007

Appendix II

Approved Excipients in Compressed Solid Dosage Forms

Ingredient	Dosage form	Quantity	Unit
Acacia	Oral-21; tablet	5	mg
Acacia	Oral-28; tablet	5	mg
Acacia	Buccal/sublingual; tablet	9.1	mg
Acacia	Oral; tablet, delayed action, enteric coated	10	mg
Acacia	Oral; tablet, repeat action	11.542	mg
Acacia	Oral; tablet, film coated	14.9	mg
Acacia	Oral-20; tablet	33.5	mg
Acacia	Oral; tablet, sustained action	34.4	mg
Acacia	Oral; tablet	70	mg
Acacia	Oral; tablet (immed./comp. release), uncoated, chewable	80	mg
Acacia	Oral; tablet, coated	156	mg
Acacia mucilage	Oral; tablet, coated	27.2	mg
Acesulfame potassium	Buccal; gum, chewing	2	mg
Acesulfame potassium	Sublingual; tablet	3	mg
Acesulfame potassium	Oral; tablet (immed./comp. release), uncoated, chewable	3.75	mg
Acesulfame potassium	Oral; tablet	4.4	mg
Acesulfame potassium	Oral; troche	6	mg
Acesulfame potassium	Oral; tablet, film coated	8.19	mg
Acetic acid, glacial	Oral; tablet	0.002	mg
Acetic anhydride	Oral; tablet, sustained action	0.11	mg
Acetylated monoglycerides	Oral; tablet, coated	0.28	mg
Acetylated monoglycerides	Oral; tablet, film coated	2.1	mg
Acetylated monoglycerides	Oral; tablet, sustained action	2.48	mg
Acetylated monoglycerides	Oral; tablet	3.74	mg
Acetylated monoglycerides	Oral; tablet, delayed action, enteric coated	5.17	mg
Acetyltributyl citrate	Oral; tablet	0.56	mg
Acetyltributyl citrate	Oral; tablet, enteric coated particles	18.7	mg
Acetyltributyl citrate	Oral; tablet, sustained action	57.35	mg
Acrylates copolymer	Oral; tablet (immed./comp. release), uncoated, chewable	5.05	mg
Acrylates copolymer	Oral; tablet	9.88	mg
Acrylates copolymer	Oral; tablet, orally disintegrating, delayed release	11.88	mg
Acrylates copolymer	Oral; tablet, sustained action, coated	25.18	mg
Acrylates copolymer	Oral; tablet, extended release	29.41	mg
Adipic acid	Vaginal; insert	57	mg
Agar	Oral; tablet	0.203	mg

Ingredient	Dosage form	Quantity	Unit
Albumins	Oral; tablet, film coated	4.5	mg
Alcohol	Oral; tablet, delayed action, enteric coated	71.5	mg
Alcohol	Oral; tablet	196	mg
Alcohol, dehydrated	Oral; tablet, film coated	0.75	mg
Alcohol, denatured	Oral; tablet	0.24	mg
Alginic acid	Oral; tablet, sustained action	22.25	mg
Alginic acid	Oral; tablet	32	mg
Alginic acid	Oral; tablet, film coated	52.8	mg
Alginic acid	Oral; tablet, coated	60	mg
Alginic acid	Oral; tablet (immed./comp. release), uncoated, chewable	400	mg
Alpha-tocopherol	Oral; tablet	0.3	mg
Aluminum hydroxide	Oral; tablet	15	mg
Aluminum hydroxide gel	Oral; tablet	85	mg
Aluminum hydroxide gel, dried	Oral; tablet	0.173	mg
Aluminum silicate	Oral; tablet	19.25	mg
Aluminum silicate	Oral; tablet, sustained action, coated	47	mg
Aluminum silicate	Oral; tablet, coated	50	mg
Aluminum silicate	Oral; tablet, sustained action	94	mg
Aluminum stearate	Oral; tablet	2.8	mg
Aluminum stearate	Oral; tablet, sustained action	105	mg
Alzamer-39	Oral; tablet, sustained action	10	mg
Alzamer-50	Oral; tablet, sustained action	10	mg
Alzamer-50	Oral; tablet, controlled release	32	mg
Amberlite	Oral; tablet	20	mg
Amberlite	Oral; tablet, film coated	25	mg
Amberlite IRP-69M	Oral; tablet, sustained release, film coated	18	mg
Amberlite XE-88	Oral; tablet	2.4	mg
Amberlite XE-88	Oral; tablet, coated	9	mg
Ammonium calcium alginate	Oral; tablet	10.72	mg
Ammonium chloride	Oral; tablet	4.2	mg
Ammonium chloride	Oral; tablet, film coated	8	mg
Ammonium phosphate	Sublingual; tablet	0.2	mg
Ammonium phosphate	Oral; tablet	0.4	mg
Ammonium phosphate	Oral; tablet, sustained action	0.4	mg
Anise oil	Oral; pastille	16	mg
Aquacoat	Oral; tablet	2.25	mg
Aquacoat	Oral; tablet (immed./comp. release), uncoated, chewable	13.5	mg
Aquacoat ECD	Oral; tablet	3.453	mg
Aquacoat ECD	Oral; tablet, sustained action	27.4	mg
Ascorbic acid	Oral; tablet, film coated	20	mg
Ascorbic acid	Oral; tablet	28.44	mg
Ascorbyl palmitate	Oral; tablet	0.515	mg
Aspartame	Buccal; patch, controlled release	1.1	mg

Ingredient	Dosage form	Quantity	Unit
Aspartame	Oral; tablet (immed./comp. release), film coated	5.1	mg
Aspartame	Oral; troche	6.1	mg
Aspartame	Oral; tablet, orally disintegrating, delayed release	9	mg
Aspartame	Oral; tablet	20	mg
Aspartame	Oral; tablet, film coated	20	mg
Aspartame	Oral; tablet (immed./comp. release), uncoated, effervescent	30	mg
Aspartame	Oral; tablet, orally disintegrating	36	mg
Aspartame	Oral; tablet (immed./comp. release), uncoated, chewable	65	mg
Barium sulfate	Vaginal; intrauterine device	1.42	mg
Beeswax	Oral; tablet, delayed action, enteric coated	0.1	mg
Beeswax	Oral; tablet	0.44	mg
Beeswax	Oral; tablet, coated	0.53	mg
Bentonite	Oral; tablet, coated	3.6935	mg
Bentonite	Oral; tablet	23	mg
Benzyl alcohol	Oral; tablet	1.06	mg
Benzyl alcohol	Oral; tablet, sustained action, coated	1.25	mg
Benzyl alcohol	Oral; tablet, delayed action, enteric coated	2.31	mg
Betadex	Oral-28; tablet	0.146	mg
Betadex	Oral; tablet, film coated	82.5	mg
Betadex	Oral; tablet	89.17	mg
Bismuth subcarbonate	Oral; tablet	0.0044	mg
Bismuth subcarbonate	Oral; tablet, sustained action	0.044	mg
Butylated hydroxyanisole	Oral; tablet, film coated	0.4	mg
Butylated hydroxyanisole	Oral; tablet	0.5	mg
Butylated hydroxyanisole	Sublingual; tablet	0.5	mg
Butylated hydroxytoluene	Oral; tablet, extended release	0.11	mg
Butylated hydroxytoluene	Oral; tablet (immed./comp. release), film coated	0.15	mg
Butylated hydroxytoluene	Buccal; gum, chewing	0.21	mg
Butylated hydroxytoluene	Oral; tablet, controlled release	0.21	mg
Butylated hydroxytoluene	Oral; tablet, sustained action	0.24	mg
Butylated hydroxytoluene	Oral; tablet, film coated	0.36	mg
Butylated hydroxytoluene	Oral; tablet	0.4	mg
Butylparaben	Oral; tablet, coated	0.004	mg
Butylparaben	Oral; tablet, repeat action	0.006	mg
Butylparaben	Oral; tablet, sustained action	0.04	mg
Calcium acetate	Oral-21; tablet	10	mg
Calcium acetate	Oral-28; tablet	10	mg
Calcium alginate and ammonium alginate	Oral; tablet	20	mg
Calcium carbonate	Oral; tablet, delayed action, enteric coated	8.4	mg
Calcium carbonate	Oral-21; tablet, coated	8.607	mg
Calcium carbonate	Oral-28; tablet, coated	8.607	mg
Calcium carbonate	Oral-28; tablet	9.59	mg
Calcium carbonate	Oral; tablet, coated	64.8	mg

Ingredient	Dosage form	Quantity	Unit
Calcium carbonate	Oral; tablet (immed./comp. release), film coated	132	mg
Calcium carbonate	Buccal; gum, chewing	145.5	mg
Calcium carbonate	Oral; tablet, film coated	225	mg
Calcium carbonate	Oral; tablet, sustained action	229.7	mg
Calcium carbonate	Oral; tablet	265.2	mg
Calcium carbonate	Oral; tablet (immed./comp. release), uncoated, chewable	550	mg
Calcium citrate	Oral; tablet	98.95	mg
Calcium cyclamate	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
Calcium hydroxide	Oral; tablet	35	mg
Calcium lactate	Vaginal; tablet	30	mg
Calcium phosphate	Oral-21; tablet	86	mg
Calcium phosphate	Oral; tablet, coated	93.6	mg
Calcium phosphate	Oral; tablet	160	mg
Calcium phosphate	Oral; tablet, film coated	362	mg
Calcium phosphate, dibasic	Oral; tablet, delayed action, enteric coated	46	mg
Calcium phosphate, dibasic	Oral; tablet (immed./comp. release), uncoated, chewable	50	mg
Calcium phosphate, dibasic	Oral-21; tablet	104.5	mg
Calcium phosphate, dibasic	Oral-28; tablet	104.5	mg
Calcium phosphate, dibasic	Oral; tablet (immed./comp. release), film coated	138.84	mg
Calcium phosphate, dibasic	Oral; tablet, coated	293.2	mg
Calcium phosphate, dibasic	Oral; tablet, sustained action	335	mg
Calcium phosphate, dibasic	Oral; tablet, film coated	525.56	mg
Calcium phosphate, dibasic	Oral; tablet	850	mg
Calcium phosphate, dibasic monohydrate	Oral; tablet	109.3	mg
Calcium phosphate, dibasic, dihydrate	Oral; tablet, extended release	108	mg
Calcium phosphate, dibasic, dihydrate	Oral; tablet, sustained action	189	mg
Calcium phosphate, dibasic, dihydrate	Oral; tablet, coated	488.7	mg
Calcium phosphate, dibasic, dihydrate	Oral; tablet	512	mg
Calcium phosphate, dibasic, dihydrate	Oral; tablet, film coated	635.5	mg
Calcium phosphate, tribasic	Oral; tablet, coated	21	mg
Calcium phosphate, tribasic	Oral; tablet (immed./comp. release), film coated	21.8	mg
Calcium phosphate, tribasic	Buccal/sublingual; tablet	99.2	mg
Calcium phosphate, tribasic	Oral; tablet, sustained action	100	mg
Calcium phosphate, tribasic	Oral; tablet (immed./comp. release), uncoated, chewable	130	mg
Calcium phosphate, tribasic	Oral; tablet	282	mg
Calcium phosphate, tribasic	Oral; tablet, delayed action, enteric coated	333.3	mg
Calcium pyrophosphate	Oral; tablet	298.04	mg
Calcium silicate	Oral; tablet, sustained action	15	mg
Calcium silicate	Oral; tablet, coated	143	mg
Calcium silicate	Oral; tablet	146.13	mg
Calcium silicate	Oral; tablet, film coated	182.7	mg
Calcium stearate	Oral-21; tablet	0.7	mg
Calcium stearate	Oral-28; tablet	0.7	mg

Ingredient	Dosage form	Quantity	Unit
Calcium stearate	Buccal/sublingual; tablet	1.42	mg
Calcium stearate	Sublingual; tablet	2	mg
Calcium stearate	Oral; tablet, delayed action, enteric coated	3.2	mg
Calcium stearate	Oral; tablet, film coated	16	mg
Calcium stearate	Oral; tablet, sustained action	24	mg
Calcium stearate	Oral; tablet	42.9	mg
Calcium stearate	Oral; tablet (immed./comp. release), uncoated, chewable	47.5	mg
Calcium sulfate	Oral-28; tablet	10.7	mg
Calcium sulfate	Oral; tablet, delayed action, enteric coated	75	mg
Calcium sulfate	Oral; tablet, coated	170	mg
Calcium sulfate	Oral; tablet, repeat action	235	mg
Calcium sulfate	Oral; tablet, sustained action	340	mg
Calcium sulfate	Oral; tablet	436.9	mg
Calcium sulfate	Oral; tablet, film coated	443	mg
Calcium sulfate dihydrate	Oral; tablet, sustained action, coated	29.7	mg
Calcium sulfate dihydrate	Oral; tablet, delayed action, enteric coated	87.2	mg
Calcium sulfate dihydrate	Oral-28; tablet	105.4	mg
Calcium sulfate dihydrate	Oral; tablet, coated	214.24	mg
Calcium sulfate dihydrate	Oral; tablet, repeat action	242.946	mg
Calcium sulfate dihydrate	Oral; tablet	279.309	mg
Calcium sulfate dihydrate	Oral; tablet, film coated	341	mg
Calcium sulfate, anhydrous	Oral-28; tablet	10.7	mg
Calcium sulfate, anhydrous	Oral; tablet, repeat action	86.531	mg
Calcium sulfate, anhydrous	Oral; tablet	174.5	mg
Candelilla wax	Oral; tablet, sustained action	0.16	mg
Candelilla wax	Oral; tablet (immed./comp. release), film coated	0.32	mg
Candelilla wax	Oral; tablet, extended release	0.37	mg
Candelilla wax	Oral; tablet	0.3708	mg
Candelilla wax	Oral; tablet, sustained action, coated	0.58	mg
Candelilla wax	Oral; tablet, film coated	0.8	mg
Carbomer 934	Oral; tablet, sustained action	90	mg
Carbomer 934P	Oral; tablet, orally disintegrating	0.3	mg
Carbomer 934P	Oral; tablet, sustained action	1.5	mg
Carbomer 934P	Oral; tablet, sustained action, coated	3	mg
Carbomer 934P	Buccal; tablet	9.375	mg
Carbomer 934P	Oral; tablet, extended release	15	mg
Carbomer 974P	Oral; tablet, controlled release	6.25	mg
Carbomer 974P	Oral; tablet, sustained action	6.25	mg
Carbon	Oral; tablet	0.006	mg
Carbon	Oral; tablet, coated	0.011	mg
Carboxymethyl starch	Oral; tablet	25	mg
Carboxymethylcellulose	Oral; tablet	3	mg
Carboxymethylcellulose calcium	Oral; tablet, delayed action, enteric coated	13.3	mg

Ingredient	Dosage form	Quantity	Unit
Carboxymethylcellulose calcium	Oral; tablet	29	mg
Carboxymethylcellulose calcium	Oral; tablet, film coated	241.842	mg
Carboxymethylcellulose sodium	Oral; tablet, coated	2.2	mg
Carboxymethylcellulose sodium	Oral; tablet, extended release	15	mg
Carboxymethylcellulose sodium	Oral; tablet (immed./comp. release), uncoated, chewable	24.75	mg
Carboxymethylcellulose sodium	Oral; tablet	48	mg
Carboxymethylcellulose sodium	Oral; tablet, film coated	50	mg
Carboxymethylcellulose sodium	Oral; tablet, sustained action	155	mg
Carboxypolymethylene	Oral; tablet, sustained action	195	mg
Carmine	Oral; tablet, film coated	0.377	mg
Carmine	Oral; tablet	6.8	mg
Carnauba wax	Oral; tablet, repeat action	0.046	mg
Carnauba wax	Oral-28; tablet	0.157	mg
Carnauba wax	Oral; tablet, sustained action, film coated	0.25	mg
Carnauba wax	Oral; tablet, coated	0.92	mg
Carnauba wax	Oral; tablet, film coated	5	mg
Carnauba wax	Oral; tablet (immed./comp. release), uncoated, chewable	31.129	mg
Carnauba wax	Oral; tablet	57.8	mg
Carnauba wax	Oral; tablet, sustained action, multilayer, film coated	75	mg
Carnauba wax	Oral; tablet, sustained action, coated	140	mg
Carnauba wax	Oral; tablet, delayed action, enteric coated	230	mg
Carnauba wax	Oral; tablet, extended release	290	mg
Carnauba wax	Oral; tablet, sustained action	300	mg
Carnauba yellow wax	Oral; tablet, sugar coated	0.09	mg
Carnauba yellow wax	Oral; tablet	0.18	mg
Carnauba yellow wax	Oral; tablet, coated	0.18	mg
Carnauba yellow wax	Oral; tablet, extended release	200	mg
Castor oil	Oral; tablet, coated	0.9	mg
Castor oil	Sublingual; tablet	1.6	mg
Castor oil	Oral; tablet	2	mg
Castor oil	Oral; tablet, film coated	3.06	mg
Castor oil	Oral; tablet, sustained action	23.27	mg
Castor oil hydrogenated	Oral-21; tablet	0.93	mg
Castor oil hydrogenated	Oral-28; tablet	0.93	mg
Castor oil hydrogenated	Oral; tablet, delayed action, enteric coated	1.3	mg
Castor oil hydrogenated	Sublingual; tablet	1.6	mg
Castor oil hydrogenated	Oral; tablet, film coated	3.3	mg
Castor oil hydrogenated	Oral; tablet, sustained action, coated	5	mg
Castor oil hydrogenated	Oral; tablet	37.6	mg
Castor oil hydrogenated	Oral; tablet, sustained action	295	mg
Cellacefate	Oral; tablet, film coated	15.6	mg
Cellacefate	Oral; tablet	37	mg
Cellacefate	Oral; tablet, delayed action, enteric coated	70	mg

Ingredient	Dosage form	Quantity	Unit
Cellacefate	Oral; tablet, sustained action	70	mg
Cellulose	Buccal/sublingual; tablet	4.5	mg
Cellulose	Oral; tablet, delayed action, enteric coated	16	mg
Cellulose	Oral-21; tablet	20	mg
Cellulose	Oral-28; tablet	20	mg
Cellulose	Oral; tablet, coated	40.2	mg
Cellulose	Oral; tablet, sustained action, coated	42.25	mg
Cellulose	Oral; tablet, sustained action	110.6	mg
Cellulose	Oral; tablet, film coated	391.7	mg
Cellulose	Oral; tablet	1120	mg
Cellulose acetate	Oral; tablet	2.45	mg
Cellulose acetate	Oral; tablet (immed./comp. release), uncoated, chewable	6.86	mg
Cellulose acetate	Oral; tablet, extended release	23.56	mg
Cellulose acetate	Oral; tablet, controlled release	27.39	mg
Cellulose acetate	Oral; tablet, sustained action	39	mg
Cellulose acetate	Oral; tablet, sustained action, coated	44.6	mg
Cellulose acetate CA-320S	Oral; tablet, extended release	36.02	mg
Cellulose acetate CA-398-10	Oral; tablet, extended release	47.49	mg
Cellulose microcrystalline, aqueous	Oral; tablet, delayed action, enteric coated	199.6	mg
Cellulose microcrystalline, aqueous	Oral; tablet	240	mg
Cellulose microcrystalline, aqueous	Oral; tablet, film coated	262.19	mg
Cellulose microcrystalline/ carboxymethylcellulose sodium	Oral; tablet	160	mg
Cellulose, microcrystalline	Oral; tablet, for solution	0.75	mg
Cellulose, microcrystalline	Oral; tablet, sugar coated	4.64	mg
Cellulose, microcrystalline	Oral-28; tablet, coated	10	mg
Cellulose, microcrystalline	Oral; tablet, multilayer, extended release	17.3	mg
Cellulose, microcrystalline	Oral; tablet, repeat action	25	mg
Cellulose, microcrystalline	Oral-21; tablet	28.488	mg
Cellulose, microcrystalline	Oral-28; tablet	28.488	mg
Cellulose, microcrystalline	Oral; tablet, orally disintegrating, delayed release	30	mg
Cellulose, microcrystalline	Oral; tablet, multilayer, coated	34	mg
Cellulose, microcrystalline	Sublingual; tablet	43.2	mg
Cellulose, microcrystalline	Oral; tablet, uncoated, troche	60	mg
Cellulose, microcrystalline	Oral; tablet, sustained release, film coated	62.4	mg
Cellulose, microcrystalline	Oral; tablet, sustained action, coated	100	mg
Cellulose, microcrystalline	Oral; tablet, delayed action	150	mg
Cellulose, microcrystalline	Oral; tablet, controlled release	152	mg
Cellulose, microcrystalline	Oral; tablet (immed./comp. release), film coated	240	mg
Cellulose, microcrystalline	Oral; tablet, sustained action, film coated	307.52	mg
Cellulose, microcrystalline	Oral; tablet, coated	356	mg
Cellulose, microcrystalline	Oral; tablet, sustained action	363.7	mg
Cellulose, microcrystalline	Oral; tablet, delayed action, enteric coated	375.26	mg
Cellulose, microcrystalline	Vaginal; tablet	390	mg

Ingredient	Dosage form	Quantity	Unit
Cellulose, microcrystalline	Oral; tablet, enteric coated particles	391	mg
Cellulose, microcrystalline	Oral; tablet, orally disintegrating	392.86	mg
Cellulose, microcrystalline	Oral; tablet, extended release	397.7	mg
Cellulose, microcrystalline	Oral; tablet, film coated	530	mg
Cellulose, microcrystalline	Oral; tablet (immed./comp. release), uncoated, chewable	570	mg
Cellulose, microcrystalline	Oral; tablet	1385.3	mg
Cellulose, microcrystalline 101	Oral; tablet, film coated	6.5	mg
Cellulose, microcrystalline 101	Oral; tablet, extended release	100	mg
Cellulose, microcrystalline 101	Oral; tablet	164.7	mg
Cellulose, oxidized	Oral; tablet	165.092	mg
Cellulose, powder	Oral; tablet	44	mg
Cetearyl alcohol	Oral; tablet, sustained action, film coated	62	mg
Cetearyl alcohol	Oral; tablet, sustained action	70	mg
Cetyl alcohol	Oral; tablet, sustained action	44	mg
Cetyl alcohol	Oral; tablet, sustained action, film coated	59	mg
Charcoal, activated	Oral; tablet	0.6	mg
Cherry	Oral; tablet	0.45	mg
Chromacote T 2700GN	Oral; tablet	4.74	mg
Chromacote T 2716Y	Oral; tablet	6.33	mg
Chroma-Kote T2956-Y yellow	Oral; tablet, film coated	0.912	mg
Chroma-Kote T2956-Y yellow	Oral; tablet	2.75	mg
Cinnamaldehyde	Oral; tablet	2.1	mg
Cinnamon oil	Oral; tablet (immed./comp. release), uncoated, chewable	0.001	mg
Cinnamon oil	Oral; pastille	4	mg
Citric acid	Oral; tablet, delayed action, enteric coated	1	mg
Citric acid	Oral; tablet (immed./comp. release), film coated	2.56	mg
Citric acid	Oral; tablet, orally disintegrating, delayed release	3.08	mg
Citric acid	Oral; tablet (immed./comp. release), uncoated, chewable	4.26	mg
Citric acid	Oral; tablet, extended release	5	mg
Citric acid	Sublingual; tablet	5.92	mg
Citric acid	Buccal; tablet	30	mg
Citric acid	Oral; tablet, sustained action, film coated	40	mg
Citric acid	Oral; tablet, film coated	42	mg
Citric acid	Oral; tablet, orally disintegrating	63	mg
Citric acid	Oral; tablet	78	mg
Citric acid	Oral; bar, chewable	500	mg
Citric acid monohydrate	Oral; tablet, film coated	10	mg
Citric acid monohydrate	Oral; tablet	50	mg
Citric acid, hydrous	Oral; tablet, film coated	10	mg
Coateric YPA-6-7430 white	Oral; tablet, delayed action, enteric coated	26	mg
Compressible sugar	Oral-21; tablet	8	mg
Compressible sugar	Oral-28; tablet	8	mg
Compressible sugar	Oral; tablet, coated	120	mg

Ingredient	Dosage form	Quantity	Unit
Compressible sugar	Sublingual; tablet	136	mg
Compressible sugar	Oral; tablet, sustained action	253	mg
Compressible sugar	Oral; tablet, sustained action, film coated	354	mg
Compressible sugar	Oral; tablet	360	mg
Compressible sugar	Oral; tablet (immed./comp. release), uncoated, chewable	623.5	mg
Copovidone	Oral; tablet, extended release	3.9	mg
Copovidone	Oral; tablet, orally disintegrating	4.38	mg
Copovidone	Oral; tablet, sustained action, film coated	6.1	mg
Copovidone	Oral; tablet	356.82	mg
Copovidone	Oral; tablet, film coated	853.8	mg
Corn oil	Oral; tablet, delayed action, enteric coated	0.03	mg
Corn oil	Oral; tablet, coated	0.3	mg
Corn oil	Sublingual; tablet	1.7	mg
Corn oil	Oral; tablet	20	mg
Corn syrup	Oral; tablet	14.065	mg
Cottonseed oil, hydrogenated	Oral; tablet, coated	0.6	mg
Cottonseed oil, hydrogenated	Sublingual; tablet	2	mg
Cottonseed oil, hydrogenated	Oral; tablet, delayed action, enteric coated	4	mg
Cottonseed oil, hydrogenated	Oral; tablet	34	mg
Cottonseed oil, hydrogenated	Oral; tablet, sustained action	402	mg
Croscarmellose sodium	Oral-28; tablet, coated	2	mg
Croscarmellose sodium	Oral; tablet, sugar coated	2.5	mg
Croscarmellose sodium	Oral-21; tablet	3	mg
Croscarmellose sodium	Oral-28; tablet	3	mg
Croscarmellose sodium	Sublingual; tablet	6.5	mg
Croscarmellose sodium	Oral; tablet, uncoated, troche	10	mg
Croscarmellose sodium	Oral; tablet, orally disintegrating	13	mg
Croscarmellose sodium	Oral; tablet, delayed action	14	mg
Croscarmellose sodium	Oral; tablet, extended release	15	mg
Croscarmellose sodium	Oral; tablet (immed./comp. release), uncoated, chewable	18	mg
Croscarmellose sodium	Oral; tablet, sustained action	28	mg
Croscarmellose sodium	Oral; tablet, delayed action, enteric coated	32.44	mg
Croscarmellose sodium	Oral; tablet, coated	35.2	mg
Croscarmellose sodium	Oral; tablet (immed./comp. release), film coated	50	mg
Croscarmellose sodium	Oral; tablet, film coated	165	mg
Croscarmellose sodium	Oral; tablet	180	mg
Crospovidone	Oral-21; tablet	4.45	mg
Crospovidone	Oral; tablet, multilayer, extended release	5	mg
Crospovidone	Oral; tablet, sustained action, film coated	5	mg
Crospovidone	Oral; tablet, dispersible	6	mg
Crospovidone	Sublingual; tablet	6.5	mg
Crospovidone	Oral; tablet, repeat action	10	mg
Crospovidone	Oral; tablet, orally disintegrating, delayed release	15	mg

Ingredient	Dosage form	Quantity	Unit
Crospovidone	Oral; tablet, sustained action, coated	15.4	mg
Crospovidone	Oral; tablet (immed./comp. release), film coated	17	mg
Crospovidone	Vaginal; tablet	35	mg
Crospovidone	Oral; tablet, extended release	39.2	mg
Crospovidone	Oral; tablet, delayed action, enteric coated	50	mg
Crospovidone	Oral; tablet (immed./comp. release), uncoated, chewable	100	mg
Crospovidone	Oral; tablet, enteric coated particles	130	mg
Crospovidone	Oral; tablet, sustained action	144	mg
Crospovidone	Oral; tablet, orally disintegrating	180	mg
Crospovidone	Oral; tablet, film coated	196.7	mg
Crospovidone	Oral; tablet	300	mg
Crospovidone	Oral; tablet, coated	792	mg
Crystal gum	Oral; tablet	17	mg
Cutina	Sublingual; tablet	1.6	mg
Cysteine hydrochloride	Oral; tablet, sustained action, film coated	16.2	mg
D&C black no. 1	Oral; tablet	0.08	mg
D&C blue no. 1	Oral; tablet	0.15	mg
D&C blue no. 1	Oral; tablet, film coated	0.1624	mg
D&C blue no. 1–aluminum lake	Oral; tablet	3.6	mg
D&C blue no. 2 lake	Oral; tablet, coated	0.002	mg
D&C blue no. 2 lake	Oral; tablet	0.24	mg
D&C green no. 5	Oral-21; tablet	0.0024	mg
D&C green no. 5	Oral-28; tablet	0.0024	mg
D&C green no. 5	Oral; tablet	0.015	mg
D&C red no. 19	Oral; tablet	0.005	mg
D&C red no. 27	Oral; tablet	0.04	mg
D&C red no. 3 lake	Sublingual; tablet	0.005	mg
D&C red no. 3 lake	Oral; tablet	0.5	mg
D&C red no. 30	Oral-21; tablet	0.5	mg
D&C red no. 30	Oral-28; tablet	0.5	mg
D&C red no. 30	Oral; tablet	0.75	mg
D&C red no. 30	Oral; tablet, coated	1.16	mg
D&C red no. 30	Oral; tablet (immed./comp. release), uncoated, chewable	1.46	mg
D&C red no. 30	Oral; tablet, film coated	290	mg
D&C red no. 30 lake	Oral; tablet, sustained action	0.025	mg
D&C red no. 30 lake	Oral-21; tablet	0.03	mg
D&C red no. 30 lake	Oral; tablet, delayed action, enteric coated	0.04	mg
D&C red no. 30 lake	Oral; tablet, film coated	0.064	mg
D&C red no. 30 lake	Oral; tablet, coated	0.343	mg
D&C red no. 30 lake	Oral; tablet, enteric coated particles	0.8	mg
D&C red no. 30 lake	Oral; tablet	1.5	mg
D&C red no. 30 lake	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
D&C red no. 33	Oral; tablet, coated	0.0023	mg

Ingredient	Dosage form	Quantity	Unit
D&C red no. 33	Oral; tablet	0.24	mg
D&C red no. 36	Oral; tablet	48.75	mg
D&C red no. 40	Oral; tablet	0.02	mg
D&C red no. 40 lake	Oral; tablet	0.2	mg
D&C red no. 5	Oral; tablet	0.18	mg
D&C red no. 6 lake	Oral; tablet	1.5	mg
D&C red no. 7	Oral; tablet, film coated	0.16	mg
D&C red no. 7	Oral; tablet	0.28	mg
D&C red no. 7 lake	Oral; tablet, delayed action, enteric coated	0.5	mg
D&C red no. 7 lake	Oral; tablet	0.6	mg
D&C violet no. 2 lake	Oral; tablet	0.112	mg
D&C yellow no. 10	Oral; tablet, extended release	0.03	mg
D&C yellow no. 10	Oral-28; tablet	0.09	mg
D&C yellow no. 10	Oral-21; tablet	0.12	mg
D&C yellow no. 10	Sublingual; tablet	0.23	mg
D&C yellow no. 10	Buccal; gum, chewing	1	mg
D&C yellow no. 10	Oral; tablet, delayed action, enteric coated	1.9	mg
D&C yellow no. 10	Oral; tablet, sustained action	2.01	mg
D&C yellow no. 10	Oral; tablet, coated	2.5	mg
D&C yellow no. 10	Oral; tablet	80	mg
D&C yellow no. 10	Oral; tablet, film coated	120	mg
D&C yellow no. 10 lake	Oral; tablet, sustained action	0.015	mg
D&C yellow no. 10 lake	Oral; tablet, coated	3.68	mg
D&C yellow no. 10 lake	Oral; tablet	5.2	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, delayed action, enteric coated	0.05	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, dispersible	0.13	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, sustained action, film coated	0.16	mg
D&C yellow no. 10–aluminum lake	Sublingual; tablet	0.18	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, coated	0.208	mg
D&C yellow no. 10–aluminum lake	Buccal; gum, chewing	0.35	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, film coated	0.3968	mg
D&C yellow no. 10–aluminum lake	Oral-21; tablet	0.415	mg
D&C yellow no. 10–aluminum lake	Oral-28; tablet	0.415	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, sustained release, film coated	0.8	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, extended release	1	mg
D&C yellow no. 10–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	2	mg
D&C yellow no. 10–aluminum lake	Oral; tablet, sustained action	2.33	mg
D&C yellow no. 10–aluminum lake	Oral; tablet	12.5	mg
D&C yellow no. 5	Oral; tablet	0.013	mg
D&C yellow no. 5	Sublingual; tablet	0.1	mg
D&C yellow no. 5–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	0.285	mg
D&C yellow no. 5–aluminum lake	Oral; tablet, film coated	0.59	mg
D&C yellow no. 5–aluminum lake	Oral; tablet	2.69	mg

Ingredient	Dosage form	Quantity	Unit
D&C yellow no. 6	Oral; tablet	0.005	mg
D&C yellow no. 6 lake	Sublingual; tablet	0.01	mg
D&C yellow no. 6 lake	Oral; tablet	0.5	mg
Dextrates	Oral; tablet	86.5	mg
Dextrates	Oral; tablet, sustained action	108.5	mg
Dextrates	Oral; tablet (immed./comp. release), uncoated, chewable	1066.4	mg
Dextrin	Oral; tablet, delayed action, enteric coated	9.25	mg
Dextrin	Oral; tablet	21.7	mg
Dextrose	Oral; tablet, sustained action, coated	103.95	mg
Dextrose	Sublingual; tablet	115.775	mg
Dextrose	Oral; pastille	157	mg
Dextrose	Oral; tablet	183.66	mg
Dextrose	Oral; tablet (immed./comp. release), uncoated, chewable	398	mg
Dextrose	Oral; tablet, uncoated, troche	903.5	mg
Diacetylated monoglycerides	Oral; tablet, coated	0.63	mg
Diacetylated monoglycerides	Oral; tablet, film coated	1.143	mg
Diacetylated monoglycerides	Oral; tablet, delayed action, enteric coated	1.2	mg
Diacetylated monoglycerides	Oral; tablet	9.14	mg
Dibutyl phthalate	Oral; tablet, delayed action, enteric coated	1.7	mg
Dibutyl sebacate	Oral; tablet, sustained action	1.11	mg
Dibutyl sebacate	Oral; tablet	6	mg
Dibutyl sebacate	Oral; tablet, extended release	8	mg
Diethyl phthalate	Oral; tablet (immed./comp. release), uncoated, chewable	0.5	mg
Diethyl phthalate	Oral; tablet, coated	1.25	mg
Diethyl phthalate	Oral; tablet, film coated	2.3	mg
Diethyl phthalate	Oral; tablet	4	mg
Diethyl phthalate	Oral; tablet, sustained action	12	mg
Diethyl phthalate	Oral; tablet, delayed action, enteric coated	16.8	mg
Dihydroxyaluminum sodium carbonate	Oral; tablet (immed./comp. release), uncoated, chewable	1350	mg
Diisopropylbenzothiazyl-2-sulfenamide	Oral; tablet	77	mg
Dimethyl phthalate	Oral; tablet, sustained action	0.407	mg
Dipropylene glycol	Buccal; patch, controlled release	29.9	mg
Docusate sodium	Oral; tablet, coated	0.002	mg
Docusate sodium	Oral; tablet (immed./comp. release), film coated	0.03	mg
Docusate sodium	Oral; tablet, sustained action, film coated	0.03	mg
Docusate sodium	Oral; tablet, film coated	0.5	mg
Docusate sodium	Oral; tablet	11	mg
Docusate sodium/sodium benzoate	Oral; tablet, film coated	3	mg
Docusate sodium/sodium benzoate	Oral; tablet	7	mg
Dri Klear	Oral; tablet	1.5	mg
Dri Klear 042	Oral; tablet, film coated	5.67	mg
Dri Klear 042	Oral; tablet, coated	10	mg
Dri Klear 042	Oral; tablet	18	mg

Ingredient	Dosage form	Quantity	Unit
Dri Klear LV 609527	Oral; tablet, film coated	2.256	mg
DRY FLO	Oral; tablet	27.5	mg
dry-clear LV	Oral; tablet	19.94	mg
Dusting powder	Oral; tablet, coated	22	mg
Dye black LB-1171	Oral; tablet	1.545	mg
Dye black LB-442	Oral; tablet	0.333	mg
Dye black LB-636	Oral-28; tablet	0.15	mg
Dye black LB-9972	Oral; tablet	0.19	mg
Dye blue #1	Oral; tablet	0.36	mg
Dye blue #1 Lake	Oral; tablet	15.4	mg
Dye blue #2	Oral; tablet, delayed action, enteric coated	0.0003	mg
Dye blue lake blend LB-1245	Oral; tablet	0.26	mg
Dye blue lake blend LB-332	Oral; tablet	0.11	mg
Dye blue lakolene	Oral; tablet	0.12	mg
Dye blue LB-781	Oral; tablet	2	mg
Dye brown lake	Oral; tablet	0.17	mg
Dye brown lake blend	Oral; tablet	0.258	mg
Dye brown lake blend LB-1685	Oral; tablet	0.45	mg
Dye brown lake blend LB-1792	Oral; tablet	0.22	mg
Dye brown LB-292	Oral; tablet	0.825	mg
Dye brown LB-464	Oral; tablet	1.3	mg
Dye burnt umber	Oral; tablet, film coated	0.06	mg
Dye carmine 09349	Oral; tablet, film coated	0.54	mg
Dye chroma-teric DEB-5037-ORE	Oral; tablet, delayed action, enteric coated	10	mg
Dye chroma-teric Yellow T3277-YE	Oral; tablet, delayed action, enteric coated	30.54	mg
Dye chroma-tone	Oral; tablet, film coated	1.53	mg
Dye chroma-tone PDDB-8906W	Oral; tablet	6	mg
Dye chroma-tone-P DDB-8746-OR	Oral; tablet	11.9	mg
Dye DC green #1 lake	Oral; tablet	0.649	mg
Dye DC red #2 lake	Oral; tablet	0.722	mg
Dye DC red #27 lake	Oral; tablet, film coated	0.333	mg
Dye DC red #27 lake	Oral; tablet	0.69	mg
Dye DC red #27 lake	Oral; tablet (immed./comp. release), uncoated, chewable	1.25	mg
Dye DC red #28 lake	Oral-28; tablet	0.106	mg
Dye DC red #30 HT lake	Oral; tablet, extended release	0.1	mg
Dye DC red #33 lake	Oral; tablet	0.3	mg
Dye DC red #6 barium lake	Oral; tablet	0.38	mg
Dye DC red #7 calcium lake	Sublingual; tablet	0.005	mg
Dye DC red #7 calcium lake	Oral; tablet	0.5	mg
Dye DC red lake	Oral; tablet	2.4	mg
Dye DC red LB #9570	Oral; tablet	0.85	mg
Dye DC red LB WJ-9570	Oral; tablet	0.5605	mg
Dye DC yellow #10 HT lake	Oral; tablet, sustained action	1.32	mg

Ingredient	Dosage form	Quantity	Unit
Dye DC yellow #10 HT lake	Oral; tablet	1.4	mg
Dye diolack 00F32892 yellow	Oral; tablet	2.8	mg
Dye emerald green LB	Oral; tablet	0.05	mg
Dye emerald green LB-9207	Oral; tablet	0.44	mg
Dye FDC black LB260	Oral; tablet	3	mg
Dye FDC blue #1 H.T. aluminum lake	Oral; tablet	0.288	mg
Dye FDC blue #2 HT lake	Oral; tablet	0.2	mg
Dye FDC blue #40 HT lake	Oral; tablet	0.225	mg
Dye FDC brown R LB-56069	Buccal; gum, chewing	0.14	mg
Dye FDC brown R LB-56069	Oral; tablet	0.2	mg
Dye FDC green LB-1174	Oral-21; tablet	0.3	mg
Dye FDC green LB-1174	Oral-28; tablet	0.3	mg
Dye FDC green LB-3323	Oral; tablet	1.65	mg
Dye FDC green LB-9583	Oral; tablet	0.23	mg
Dye FDC LB483	Oral; tablet	0.28	mg
Dye FDC orange LB-452	Oral; tablet	0.54	mg
Dye FDC purple LB588	Oral; tablet	0.2	mg
Dye FDC purple LB-694	Oral; tablet	0.25	mg
Dye FDC red #2 lake	Oral; tablet	0.14	mg
Dye FDC red #27 lake	Oral; tablet	0.4	mg
Dye FDC red #30 lake	Oral-21; tablet	0.03	mg
Dye FDC red #30 lake	Oral; tablet, extended release	0.315	mg
Dye FDC red #30 lake	Oral; tablet	0.4	mg
Dye FDC red #7 lake	Oral; tablet	0.06	mg
Dye FDC violet #1 lake	Oral; tablet	0.1	mg
Dye FDC yellow #10 lake	Oral-21; tablet	0.096	mg
Dye FDC yellow #10 lake	Oral-28; tablet	0.15	mg
Dye FDC yellow #10 lake	Sublingual; tablet	0.151	mg
Dye FDC yellow #10 lake	Oral; tablet (immed./comp. release), uncoated, chewable	3	mg
Dye FDC yellow #10 lake	Oral; tablet	6.52	mg
Dye FDC yellow #6 HT lake	Oral; tablet, sustained action	0.2	mg
Dye FDC yellow #6 HT lake	Oral; tablet, extended release	0.4	mg
Dye FDC yellow #6 HT lake	Oral; tablet	0.45	mg
Dye ferric oxide orange	Oral; tablet	0.5	mg
Dye green 70363	Oral; tablet	1.05	mg
Dye green AL LB-265	Oral; tablet	0.64	mg
Dye green aluminum LB	Oral; tablet	8	mg
Dye green lake blend LB-1236	Oral; tablet	0.35	mg
Dye green lake blend LB-1441	Oral; tablet	1.32	mg
Dye green lake blend LB-1644	Oral; tablet	0.26	mg
Dye green lake blend LB-333	Oral; tablet	0.11	mg
Dye green LB	Oral; tablet	0.4	mg
Dye green LB-1594	Oral; tablet	0.75	mg

Ingredient	Dosage form	Quantity	Unit
Dye green LB-1616	Oral; tablet	0.94	mg
Dye green LB-279	Oral; tablet	2	mg
Dye green LB-482	Oral; tablet	1.27	mg
Dye green LB-555	Oral; tablet	0.44	mg
Dye green LB-603	Oral; tablet	0.7	mg
Dye green LB-820	Oral; tablet	0.6	mg
Dye green LB-883	Oral; tablet	0.6	mg
Dye green PB-1543	Oral; tablet	0.02	mg
Dye green PR-1333	Oral; tablet	0.0014	ml
Dye lavender lake blend LB-1603	Oral; tablet	0.66	mg
Dye lavender LB-1356	Oral; tablet	0.03	mg
Dye mint green	Oral; tablet	0.0055	mg
Dye mint green	Oral; tablet (immed./comp. release), uncoated, chewable	0.075	mg
Dye ochre 3506	Oral; tablet, coated	0.285	mg
Dye ochre 3506	Oral; tablet	0.76	mg
Dye orange 54172	Oral; tablet	6.6	mg
Dye orange lake blend 3810	Oral; tablet	0.45	mg
Dye orange lake blend LB-1439	Oral; tablet	0.22	mg
Dye orange LB-1387	Oral; tablet, sustained action	0.4	mg
Dye orange LB-1387	Oral; tablet	0.5	mg
Dye orange LB-715	Oral; tablet	4.8	mg
Dye peach LB-1576	Oral-21; tablet	0.3	mg
Dye peach LB-1576	Oral-28; tablet	0.3	mg
Dye pink	Oral; tablet	0.3	mg
Dye pink	Oral; tablet, delayed action	7.93	mg
Dye purple LB-1902	Oral; tablet, sustained action	0.8	mg
Dye purple LB-562	Oral; tablet	0.81	mg
Dye purple LB-639	Oral; tablet	0.084	mg
Dye purple LB-694	Oral; tablet	0.125	mg
Dye red #3 lake HT	Oral; tablet	0.03	mg
Dye red #33	Oral; tablet	0.292	mg
Dye red cotolene-P	Oral; tablet	20.7	mg
Dye red lake blend 6053-R	Oral; tablet	0.6	mg
Dye red PB-1595	Oral; tablet	0.8	mg
Dye salmon LB-1668	Oral; tablet	0.2	mg
Dye spectraspray blue 50726	Oral; tablet, extended release	3.66	mg
Dye tan PB-1388	Oral; tablet	0.05	mg
Dye tan PB-1388	Oral; tablet, film coated	0.75	mg
Dye turquoise LB-1430	Oral; tablet	0.035	mg
Dye white cotolene-P	Oral; tablet	10.35	mg
Dye yellow #10	Oral; tablet	1.31	mg
Dye yellow #5 lake	Oral-21; tablet	0.1	mg
Dye yellow #5 lake	Oral; tablet	0.15	mg

Ingredient	Dosage form	Quantity	Unit
Dye yellow 70362	Oral; tablet	2.8	mg
Dye yellow lake blend LB-1769	Oral; tablet	0.13	mg
Dye yellow LB 104	Oral; tablet	0.22	mg
Dye yellow LB 9706	Oral; tablet	0.44	mg
Dye yellow LB-111	Oral; tablet	0.6	mg
Dye yellow LB-1577	Oral; tablet	5	mg
Dye yellow LB-1637	Oral; tablet	0.2	mg
Dye yellow ochre	Oral; tablet	0.24	mg
Dye yellow PB1345	Oral; tablet	0.5	mg
Dye yellow PB-1381	Oral; tablet	0.2	mg
Dye yellow WD-2014	Oral; tablet	3.07	mg
Edetate calcium disodium	Oral; tablet, film coated	0.4	mg
Edetate calcium disodium	Oral; tablet, orally disintegrating	0.775	mg
Edetate calcium disodium	Oral; tablet	4	mg
Edetate disodium	Oral; tablet, coated	0.21	mg
Edetate disodium	Oral; tablet	4	mg
Edetate disodium	Oral; tablet, film coated	4	mg
Edetate disodium	Oral; tablet, extended release	5	mg
Edetate sodium	Oral; tablet	5	mg
Edetic acid	Oral; tablet, film coated	0.2	mg
Edetic acid	Oral; tablet	4	mg
Eiderdown soap	Oral; tablet, repeat action	0.39	mg
Ethyl vanillin	Oral; tablet (immed./comp. release), uncoated, chewable	0.143	mg
Ethylcellulose	Oral-28; tablet	1.05	mg
Ethylcellulose	Oral; tablet (immed./comp. release), uncoated, chewable	8.8	mg
Ethylcellulose	Oral; tablet, sustained action, coated	15.15	mg
Ethylcellulose	Oral; tablet, orally disintegrating	17.46	mg
Ethylcellulose	Oral; tablet, coated	20	mg
Ethylcellulose	Vaginal; tablet	50	mg
Ethylcellulose	Oral; tablet, sustained action, film coated	52.5	mg
Ethylcellulose	Oral; tablet, delayed action, enteric coated	53.8	mg
Ethylcellulose	Oral; tablet, extended release	80	mg
Ethylcellulose	Oral; tablet, film coated	83	mg
Ethylcellulose	Oral; tablet	120.8	mg
Ethylcellulose	Oral; tablet, sustained action	308.8	mg
Eudragit E 100	Oral; tablet	3.5	mg
Eudragit E 100	Oral; tablet, sustained action	3.96	mg
Eudragit E 100	Oral; tablet (immed./comp. release), uncoated, chewable	4.57	mg
Eudragit E 100	Oral; tablet, film coated	7.2	mg
Eudragit E 100	Oral; tablet, orally disintegrating	214.28	mg
Eudragit L 100 - 55	Oral; tablet, extended release	4.75	mg
Eudragit L 100 - 55	Oral; tablet, delayed action	15.86	mg
Eudragit L 100 - 55	Oral; tablet, delayed action, enteric coated	17	mg

Ingredient	Dosage form	Quantity	Unit
Eudragit L 30 D	Oral; tablet, repeat action	9.45	mg
Eudragit L 30 D	Oral; tablet, sustained action, coated	15.4	mg
Eudragit L 30 D	Oral; tablet, delayed action, enteric coated	25.5	mg
Eudragit L 30 D	Oral; tablet, enteric coated particles	27.9	mg
Eudragit L 30D - 55	Oral; tablet, extended release	6.86	mg
Eudragit L 30D - 55	Oral; tablet	13.56	mg
Eudragit L 30D - 55	Oral; tablet, sustained action, coated	15	mg
Eudragit L 30D - 55	Oral; tablet, delayed action, enteric coated	140	mg
Eudragit NE 30 D	Oral; tablet, sustained action	0.35	mg
Eudragit NE 30 D	Oral; tablet	6.63	mg
Eudragit NE 30 D	Oral; tablet, sustained action, coated	30	mg
Eudragit NE 30 D	Oral; tablet, extended release	54.7	mg
Eudragit NE 30 D	Oral; tablet, controlled release	56.2	mg
Eudragit NE 30 D	Oral; tablet, coated	66	mg
Eudragit NE 40 D	Oral; tablet, sustained action, film coated	10	mg
Eudragit RL 12.5	Oral; tablet, sustained action, coated	25	mg
Eudragit RS 30 D	Oral; tablet, film coated	8	mg
Eudragit RS 30 D	Oral; tablet, controlled release	14	mg
Eudragit RS 30 D	Oral; tablet (immed./comp. release), uncoated, chewable	16.67	mg
Eudragit RS 30 D	Oral; tablet	33.33	mg
Eudragit RS 30 D	Oral; tablet, sustained action	81.6	mg
Eudragit S 100	Oral; tablet	0.82	mg
FD&C blue no. 1	Oral; tablet, coated	0.0085	mg
FD&C blue no. 1	Oral; tablet, sustained action	0.03	mg
FD&C blue no. 1	Sublingual; tablet	0.03	mg
FD&C blue no. 1	Oral; tablet, film coated	0.0324	mg
FD&C blue no. 1	Oral-21; tablet	0.05	mg
FD&C blue no. 1	Oral-28; tablet	0.15	mg
FD&C blue no. 1	Oral; bar, chewable	2	mg
FD&C blue no. 1	Oral; tablet	3	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, delayed action, enteric coated	0.03	mg
FD&C blue no. 1–aluminum lake	Oral-28; tablet	0.1	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, coated	0.1375	mg
FD&C blue no. 1–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	0.18	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, extended release	0.85	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, controlled release	1.665	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, sustained action	2	mg
FD&C blue no. 1–aluminum lake	Oral; tablet, film coated	8	mg
FD&C blue no. 1–aluminum lake	Oral; tablet	360	mg
FD&C blue no. 2	Buccal; tablet	0.008	mg
FD&C blue no. 2	Oral; tablet, delayed action, enteric coated	0.2018	mg
FD&C blue no. 2	Oral; tablet, sustained action	0.6	mg
FD&C blue no. 2	Oral; tablet, film coated	0.7	mg

Ingredient	Dosage form	Quantity	Unit
FD&C blue no. 2	Oral; tablet	21	mg
FD&C blue no. 2	Oral; tablet, coated	24.12	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, orally disintegrating	0.005	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, delayed action, enteric coated	0.05	mg
FD&C blue no. 2–aluminum lake	Oral-21; tablet	0.208	mg
FD&C blue no. 2–aluminum lake	Oral-28; tablet	0.25	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, extended release	0.3	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, controlled release	0.546	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, coated	0.75	mg
FD&C blue no. 2–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	1.25	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, film coated	1.25	mg
FD&C blue no. 2–aluminum lake	Oral; tablet	6.5	mg
FD&C blue no. 2–aluminum lake	Oral; tablet, sustained action	7	mg
FD&C green no. 1	Oral; tablet	0.124	mg
FD&C green no. 1–aluminum lake	Sublingual; tablet	0.25	mg
FD&C green no. 1–aluminum lake	Oral; tablet	4	mg
FD&C green no. 3	Oral; tablet, coated	0.005	mg
FD&C green no. 3	Oral; tablet	10	mg
FD&C orange no. 2	Oral; tablet, coated	0.07	mg
FD&C red no. 1	Oral; tablet	0.092	mg
FD&C red no. 1	Oral; tablet, coated	0.1944	mg
FD&C red no. 19	Oral; tablet	0.0032	mg
FD&C red no. 2	Oral; tablet	0.025	mg
FD&C red no. 3	Oral-21; tablet	0.0025	mg
FD&C red no. 3	Oral; tablet, film coated	0.0042	mg
FD&C red no. 3	Oral; tablet, delayed action, enteric coated	0.0048	mg
FD&C red no. 3	Oral; tablet, extended release	0.03	mg
FD&C red no. 3	Oral; tablet (immed./comp. release), uncoated, chewable	0.05	mg
FD&C red no. 3	Oral; tablet, coated	0.06	mg
FD&C red no. 3	Oral; tablet	2.2	mg
FD&C red no. 3–aluminum lake	Sublingual; tablet	0.01	mg
FD&C red no. 3–aluminum lake	Oral; tablet, sustained action	0.161	mg
FD&C red no. 3–aluminum lake	Oral; tablet, coated	0.541	mg
FD&C red no. 3–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	4.25	mg
FD&C red no. 3–aluminum lake	Oral; tablet	8	mg
FD&C red no. 4	Oral; tablet	0.091	mg
FD&C red no. 4	Oral; tablet, coated	0.35	mg
FD&C red no. 40	Sublingual; tablet	0.0036	mg
FD&C red no. 40	Buccal; tablet	0.006	mg
FD&C red no. 40	Oral-21; tablet	0.007	mg
FD&C red no. 40	Oral-28; tablet	0.007	mg
FD&C red no. 40	Oral; tablet, film coated	0.028	mg
FD&C red no. 40	Oral; tablet, delayed action, enteric coated	0.043	mg

Ingredient	Dosage form	Quantity	Unit
FD&C red no. 40	Oral; tablet	2	mg
FD&C red no. 40	Oral; bar, chewable	10	mg
FD&C red no. 40	Oral; tablet (immed./comp. release), uncoated, chewable	40	mg
FD&C red no. 40–aluminum lake	Sublingual; tablet	0.0005	mg
FD&C red no. 40–aluminum lake	Oral-28; tablet	0.12	mg
FD&C red no. 40–aluminum lake	Oral; tablet, extended release	0.4	mg
FD&C red no. 40–aluminum lake	Oral; tablet, sustained action	0.4	mg
FD&C red no. 40–aluminum lake	Oral; tablet, film coated	2.5	mg
FD&C red no. 40–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	3.5	mg
FD&C red no. 40–aluminum lake	Oral; tablet	21.25	mg
FD&C violet no. 1	Oral; tablet, coated	0.001	mg
FD&C violet no. 1	Oral; tablet	0.2	mg
FD&C yellow no. 1	Oral; tablet	0.025	mg
FD&C yellow no. 10	Oral; tablet, sustained action	0.015	mg
FD&C yellow no. 10	Oral; tablet	3.15	mg
FD&C yellow no. 3	Oral; tablet	0.2	mg
FD&C yellow no. 5	Oral-20; tablet	0.0056	mg
FD&C yellow no. 5	Oral; tablet, sustained action	0.032	mg
FD&C yellow no. 5	Buccal/sublingual; tablet	0.11	mg
FD&C yellow no. 5	Oral; tablet, sustained action, coated	0.7564	mg
FD&C yellow no. 5	Oral; tablet, film coated	1.68	mg
FD&C yellow no. 5	Oral; tablet, coated	7.93	mg
FD&C yellow no. 5	Oral; tablet	500	mg
FD&C yellow no. 5–aluminum lake	Sublingual; tablet	0.03	mg
FD&C yellow no. 5–aluminum lake	Oral; tablet, coated	0.135	mg
FD&C yellow no. 5–aluminum lake	Oral; tablet, film coated	0.6	mg
FD&C yellow no. 5–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	1	mg
FD&C yellow no. 5–aluminum lake	Oral; tablet	2.423	mg
FD&C yellow no. 6	Oral; tablet, delayed action, enteric coated	0.0192	mg
FD&C yellow no. 6	Oral; tablet, repeat action	0.02	mg
FD&C yellow no. 6	Oral-28; tablet	0.03	mg
FD&C yellow no. 6	Oral-21; tablet	0.14	mg
FD&C yellow no. 6	Oral; tablet (immed./comp. release), uncoated, chewable	0.3	mg
FD&C yellow no. 6	Sublingual; tablet	0.4	mg
FD&C yellow no. 6	Oral; tablet, film coated	0.9	mg
FD&C yellow no. 6	Oral; tablet, sustained action	1.06	mg
FD&C yellow no. 6	Oral; tablet, coated	3.17	mg
FD&C yellow no. 6	Oral; tablet	555	mg
FD&C yellow no. 6–aluminum lake	Oral-21; tablet	0.1	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet, film coated	0.254	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet, coated	0.343	mg
FD&C yellow no. 6–aluminum lake	Sublingual; tablet	0.4	mg
FD&C yellow no. 6–aluminum lake	Oral-28; tablet	0.75	mg

Ingredient	Dosage form	Quantity	Unit
FD&C yellow no. 6–aluminum lake	Buccal/sublingual; tablet	1	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet, delayed action, enteric coated	1.4	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet (immed./comp. release), uncoated, chewable	1.76	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet, sustained action	2.8	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet, extended release	3.3	mg
FD&C yellow no. 6–aluminum lake	Oral; tablet	6.97	mg
Ferric oxide	Oral; tablet, orally disintegrating	0.0125	mg
Ferric oxide	Oral; tablet (immed./comp. release), uncoated, chewable	0.1	mg
Ferric oxide	Oral; tablet, sustained action, film coated	0.112	mg
Ferric oxide	Oral; tablet, orally disintegrating, delayed release	0.15	mg
Ferric oxide	Oral; tablet, film coated	0.25	mg
Ferric oxide	Oral; tablet (immed./comp. release), film coated	0.961	mg
Ferric oxide	Oral; tablet, sustained action	1	mg
Ferric oxide	Oral; tablet	50	mg
Ferric oxide green	Oral; tablet, controlled release	1.8	mg
Ferric oxide pink	Oral; tablet, film coated	0.039	mg
Ferric oxide red	Oral-21; tablet	0.0019	mg
Ferric oxide red	Oral-21; tablet, coated	0.014	mg
Ferric oxide red	Oral-28; tablet, coated	0.014	mg
Ferric oxide red	Oral-28; tablet	0.0212	mg
Ferric oxide red	Oral; tablet, multilayer, extended release	0.11	mg
Ferric oxide red	Oral; tablet, controlled release	0.199	mg
Ferric oxide red	Buccal; tablet	0.4	mg
Ferric oxide red	Oral; tablet (immed./comp. release), film coated	0.86	mg
Ferric oxide red	Oral; tablet, extended release	1.01	mg
Ferric oxide red	Oral; tablet (immed./comp. release), uncoated, chewable	1.19	mg
Ferric oxide red	Oral; tablet, sustained action, film coated	1.8	mg
Ferric oxide red	Oral; tablet, delayed action, enteric coated	2.3	mg
Ferric oxide red	Oral; tablet, film coated	3	mg
Ferric oxide red	Oral; tablet, sustained action	3	mg
Ferric oxide red	Oral; tablet, sustained action, coated	3.6	mg
Ferric oxide red	Oral; tablet	13	mg
Ferric oxide red 30	Oral; tablet	0.4	mg
Ferric oxide red-brown	Oral; tablet, sustained action	0.04	mg
Ferric oxide red-brown	Oral; tablet	0.05	mg
Ferric oxide yellow	Oral-21; tablet, coated	0.008	mg
Ferric oxide yellow	Oral-28; tablet, coated	0.008	mg
Ferric oxide yellow	Oral-21; tablet	0.013	mg
Ferric oxide yellow	Oral-28; tablet	0.0275	mg
Ferric oxide yellow	Oral; tablet, extended release	0.03	mg
Ferric oxide yellow	Oral; tablet (immed./comp. release), film coated	0.18	mg
Ferric oxide yellow	Oral; tablet, controlled release	0.36	mg
Ferric oxide yellow	Oral; tablet, coated	0.38	mg

Ingredient	Dosage form	Quantity	Unit
Ferric oxide yellow	Oral; tablet, delayed action, enteric coated	0.43	mg
Ferric oxide yellow	Oral; tablet, orally disintegrating	0.93	mg
Ferric oxide yellow	Buccal; tablet	1	mg
Ferric oxide yellow	Oral; tablet, film coated	1.06	mg
Ferric oxide yellow	Oral; tablet, multilayer, extended release	1.96	mg
Ferric oxide yellow	Oral; tablet	2	mg
Ferric oxide yellow	Oral; tablet, sustained action	3	mg
Ferric oxide, brown	Oral; tablet	1.125	mg
Ferric oxide, hydrated	Oral; tablet, sustained action, film coated	0.0002	mg
Ferric oxide, hydrated	Oral; tablet (immed./comp. release), film coated	0.0653	mg
Ferrosoferric oxide	Oral; tablet (immed./comp. release), film coated	0.0003	mg
Ferrosoferric oxide	Oral; tablet, sustained action, film coated	0.002	mg
Ferrosoferric oxide	Oral; tablet, extended release	0.01	mg
Ferrosoferric oxide	Oral; tablet, film coated	0.2	mg
Ferrosoferric oxide	Oral; tablet, sustained action	1.23	mg
Ferrosoferric oxide	Oral; tablet	149	mg
Ferrous fumarate	Oral; tablet	75	mg
Ferrous fumarate	Oral-21; tablet	75	mg
Ferrous fumarate	Oral-28; tablet	75	mg
Film coating solution, aqueous im-163	Oral; tablet, film coated	6.3	mg
Film coating solution, aqueous im-163	Oral; tablet	20	mg
Flavor banana durarome 860.095 TD09.91	Oral; tablet (immed./comp. release), uncoated, chewable	10	mg
Flavor banana SA84	Oral; tablet	2.5	mg
Flavor butterscotch 61005-U	Oral; tablet (immed./comp. release), uncoated, chewable	12	mg
Flavor cherry 594 S.D.	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
Flavor cherry durarome 860.097 TD10.91	Oral; tablet (immed./comp. release), uncoated, chewable	45	mg
Flavor cherry FI-8568	Oral; tablet, orally disintegrating	1.63	mg
Flavor cherry NV-1489	Oral; tablet	9	mg
Flavor creme 46971	Oral; tablet (immed./comp. release), uncoated, chewable	2.5	mg
Flavor fruit 84.6422	Buccal; gum, chewing	11	mg
Flavor fruit gum 912	Oral; tablet (immed./comp. release), uncoated, chewable	25	mg
Flavor grape 054158	Oral; tablet, orally disintegrating	11.4	mg
Flavor grape 486939	Oral; tablet, film coated	1.35	mg
Flavor grape 59.145/APO5.51	Oral; tablet (immed./comp. release), uncoated, chewable	1.25	mg
Flavor haverstroo ZD 49284	Buccal; gum, chewing	11	mg
Flavor MCP lemon duramone 4409A	Oral; tablet (immed./comp. release), uncoated, chewable	44	mg
Flavor MCP lime duramone 6419	Oral; tablet (immed./comp. release), uncoated, chewable	2	mg
Flavor menthol mint PFC-9926	Oral; troche	1.2	mg
Flavor menthol veralock	Buccal; gum, chewing	3.84	mg
Flavor mint 287	Buccal; gum, chewing	25.92	mg
Flavor mint 51296 TP0551	Oral; tablet, orally disintegrating	0.15	mg
Flavor mint SN027513	Oral; tablet	1.5	mg

Ingredient	Dosage form	Quantity	Unit
Flavor mint SN027513	Oral; tablet, orally disintegrating	9.31	mg
Flavor peppermint seelock 34907	Oral; tablet (immed./comp. release), uncoated, chewable	11	mg
Flavor peppermint WL-6167	Oral; tablet	5	mg
Flavor peppermint, natural spraylene	Oral; tablet	4	mg
Flavor pharmasweet	Oral; tablet, film coated	0.225	mg
Flavor raspberry 954	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
Flavor strawberry 17.36.8509	Oral; tablet, orally disintegrating	12	mg
Flavor strawberry 17C56217	Oral; tablet, orally disintegrating	0.25	mg
Flavor strawberry guarana 586.997/AP05.51	Oral; tablet (immed./comp. release), uncoated, chewable	14.415	mg
Flavor strawberry guarana 586.997/AP05.51	Oral; tablet	20	mg
Flavor sweet 24052	Oral; tablet (immed./comp. release), uncoated, chewable	2.7	mg
Flavor sweet 604978	Oral; tablet, film coated	0.45	mg
Flavor tutti frutti 51.880/AP05.51	Oral; tablet	10	mg
Flour	Oral; tablet	1.16	mg
Flour	Oral; tablet, coated	11.25	mg
Fructose	Oral; bar, chewable	438	mg
Fumaric acid	Oral; tablet (immed./comp. release), uncoated, chewable	10	mg
Fumaric acid	Oral; tablet, extended release	10	mg
Fumaric acid	Oral; tablet	26	mg
Fumaric acid	Oral; tablet, controlled release	36.5	mg
Fumaric acid	Oral; tablet, sustained action	55.56	mg
Galactose	Oral; tablet	0.665	mg
Gelatin	Oral-21; tablet	1	mg
Gelatin	Oral-28; tablet	1	mg
Gelatin	Sublingual; tablet	1.485	mg
Gelatin	Oral; tablet, repeat action	1.608	mg
Gelatin	Oral; tablet (immed./comp. release), uncoated, chewable	2	mg
Gelatin	Oral; tablet, delayed action, enteric coated	15	mg
Gelatin	Oral; tablet, orally disintegrating	23.75	mg
Gelatin	Oral; tablet, film coated	28.35	mg
Gelatin	Oral; tablet, sustained action	40	mg
Gelatin	Oral; tablet, coated	42.12	mg
Gelatin	Oral; tablet	45.36	mg
Gelatin	Oral; pastille	143	mg
Gelatin	Oral; bar, chewable	1000	mg
Gelatin 200 bloom	Oral; tablet	18	mg
Gelatin, crosslinked	Dental; tablet	3.44	mg
Glucose, liquid	Oral; tablet, sustained action	2	mg
Glucose, liquid	Oral; tablet	10.37	mg
Glutamic acid hydrochloride	Oral; tablet	30	mg
Glycerin	Oral-21; tablet, coated	0.137	mg

Ingredient	Dosage form	Quantity	Unit
Glycerin	Oral-28; tablet, coated	0.137	mg
Glycerin	Oral-28; tablet	0.28	mg
Glycerin	Dental; tablet	0.53	mg
Glycerin	Oral; tablet, film coated	0.91	mg
Glycerin	Oral; tablet (immed./comp. release), uncoated, chewable	1	mg
Glycerin	Oral; tablet, sustained action	3.45	mg
Glycerin	Oral; tablet	16	mg
Glycerin	Buccal; gum, chewing	28.8	mg
Glycerin	Oral; bar, chewable	48	mg
Glycerin	Buccal; patch, controlled release	66	mg
Glycerin polymer solution I-137	Oral; tablet	0.5	mg
Glyceryl behenate	Oral; tablet	14	mg
Glyceryl behenate	Oral; tablet, controlled release	15.04	mg
Glyceryl behenate	Oral; tablet, extended release	33	mg
Glyceryl behenate	Oral; tablet, sustained action	50.6	mg
Glyceryl distearate	Oral; tablet, orally disintegrating	4	mg
Glyceryl oleate	Oral; tablet	0.15	mg
Glyceryl oleate	Oral-28; tablet	0.15	mg
Glyceryl palmitostearate	Oral; tablet	18	mg
Glyceryl stearate	Oral; tablet, delayed action, enteric coated	0.005	mg
Glyceryl stearate	Oral; tablet (immed./comp. release), uncoated, chewable	0.253	mg
Glyceryl stearate	Sublingual; tablet	1.231	mg
Glyceryl stearate	Oral; tablet	6	mg
Glyceryl stearate	Oral; tablet, orally disintegrating, delayed release	7.5	mg
Glyceryl stearate	Oral; tablet, sustained action	154	mg
Glyceryl stearate	Oral; tablet, sustained action, film coated	264.3	mg
Glyceryl stearate/PEG stearate	Oral; tablet	1.8	mg
Glyceryl stearate/PEG stearate	Oral; tablet, coated	1.8	mg
Glycine	Oral; tablet, orally disintegrating	12	mg
Glycine	Oral; tablet	163.31	mg
Glycine	Oral; tablet (immed./comp. release), uncoated, chewable	200	mg
Glycine hydrochloride	Oral; tablet	6	mg
Glycyrrhizin, ammoniated	Oral; tablet (immed./comp. release), uncoated, chewable	0.5	mg
Green starch blend	Oral; tablet	2	mg
Guar gum	Buccal/sublingual; tablet	1.1	mg
Guar gum	Vaginal; tablet	2.76	mg
Guar gum	Oral; tablet, sustained action	5.04	mg
Guar gum	Oral; tablet	12.9597	mg
Guar gum	Oral; tablet, film coated	35.4	mg
Guar gum	Oral; bar, chewable	40	mg
Gum base, chewing	Buccal; gum, chewing	729.6	mg
Gum rosin	Oral; tablet, repeat action	8.987	mg
Gum rosin	Oral; tablet, sustained action	9	mg

Ingredient	Dosage form	Quantity	Unit
Hydrogel polymer	Vaginal; insert, extended release	236	mg
Hydroxyethyl cellulose	Oral; tablet, extended release	10.45	mg
Hydroxyethyl cellulose	Oral; tablet (immed./comp. release), uncoated, chewable	11.8	mg
Hydroxyethyl cellulose	Oral; tablet	12	mg
Hydroxyethyl cellulose	Oral; tablet, delayed action, enteric coated	45	mg
Hydroxyethyl cellulose	Oral; tablet, sustained action, film coated	47.99	mg
Hydroxyethyl cellulose	Oral; tablet, sustained action, coated	140	mg
Hydroxyethyl cellulose	Oral; tablet, sustained action	150	mg
Hydroxyethyl cellulose 250L	Oral; tablet	2	mg
Hydroxymethyl cellulose	Oral; tablet, film coated	30	mg
Hydroxypropyl cellulose	Sublingual; tablet	1	mg
Hydroxypropyl cellulose	Oral; tablet (immed./comp. release), uncoated, chewable	2.85	mg
Hydroxypropyl cellulose	Oral; tablet, coated	8.36	mg
Hydroxypropyl cellulose	Oral; tablet, enteric coated particles	9	mg
Hydroxypropyl cellulose	Oral; tablet, orally disintegrating, delayed release	10	mg
Hydroxypropyl cellulose	Oral; tablet (immed./comp. release), film coated	12	mg
Hydroxypropyl cellulose	Oral; tablet, delayed action, enteric coated	15	mg
Hydroxypropyl cellulose	Oral; tablet, sustained action, coated	15	mg
Hydroxypropyl cellulose	Oral; tablet, extended release	16.92	mg
Hydroxypropyl cellulose	Oral; tablet, controlled release	43.8	mg
Hydroxypropyl cellulose	Oral; tablet	46	mg
Hydroxypropyl cellulose	Oral; tablet, multilayer, extended release	107	mg
Hydroxypropyl cellulose	Oral; tablet, film coated	131.67	mg
Hydroxypropyl cellulose	Oral; tablet, sustained action, film coated	187.6	mg
Hydroxypropyl cellulose	Oral; tablet, sustained action	240	mg
Hydroxypropyl cellulose LF	Oral; tablet	16	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet, sustained action	11.66	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet (immed./comp. release), uncoated, chewable	25	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet, delayed action, enteric coated	26.3	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet, film coated	40	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet, orally disintegrating, delayed release	40	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet, multilayer, extended release	63	mg
Hydroxypropyl cellulose, low substituted	Oral; tablet	80	mg
Hydroxypropyl ethylcellulose 250L	Oral; tablet, film coated	1	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, coated	33	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet	86	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, sustained action, coated	94	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, controlled release	105	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, sustained action, film coated	200	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, extended release	320	mg
Hydroxypropyl methylcellulose 2208	Oral; tablet, sustained action	480	mg
Hydroxypropyl methylcellulose 2906	Buccal; tablet	2.25	mg
Hydroxypropyl methylcellulose 2906	Oral; tablet, extended release	17	mg

Ingredient	Dosage form	Quantity	Unit
Hydroxypropyl methylcellulose 2906	Oral; tablet	50	mg
Hydroxypropyl methylcellulose 2910	Oral-21; tablet	0.75	mg
Hydroxypropyl methylcellulose 2910	Oral-28; tablet	0.75	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, sustained action, coated	6	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, orally disintegrating, delayed release	7	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet (immed./comp. release), uncoated, chewable	11.8	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet (immed./comp. release), film coated	16.76	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, delayed action, enteric coated	19	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, controlled release	20	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, multilayer, coated	22	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, coated	29.25	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet	54	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, sustained action, film coated	54	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, film coated	60	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, extended release	150	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, sustained action	250	mg
Hydroxypropyl methylcellulose 2910	Oral; tablet, enteric coated particles	445	mg
Hydroxypropyl methylcellulose 4000	Oral; tablet, controlled release	31.25	mg
Hydroxypropyl methylcellulose phthalate	Oral; tablet, delayed action, enteric coated	44.57	mg
Hydroxypropyl methylcellulose phthalate	Oral; tablet	65	mg
Hydroxypropyl methylcellulose phthalate	Oral; tablet, enteric coated particles	119.4	mg
Illicium anisatum	Oral; tablet	50	mg
Ink black A-10527	Oral; tablet, repeat action	0.185	mg
Ink black SW-9007	Oral; tablet	0.09	mg
Ink black SW-9007	Oral; tablet, film coated	0.09	mg
Ink blue TEK print SB-6029	Oral; tablet, sustained action	0.2	mg
Ink edible black	Oral; tablet, coated	0.1	mg
Ink edible black	Oral-28; tablet	0.2	mg
Ink edible black	Oral; tablet, sustained action	1	mg
Ink edible white	Oral; tablet, repeat action	0.185	mg
Ink fine black 2202C	Oral; tablet	0.0011	ml
Ink green A-10454	Oral; tablet, sustained action	0.125	mg
Ink thinner	Oral; tablet, sustained action	0.018	mg
Iron subcarbonate	Oral; tablet, film coated	0.2	mg
Iron subcarbonate	Oral; tablet	0.7875	mg
Isooctyl acrylate/acrylamide/vinyl acetate copolymer, kollidon VA 64 polymer	Oral; tablet, film coated	53	mg
Isopropyl alcohol	Oral; tablet, delayed action, enteric coated	0.2	mg
Isopropyl alcohol	Oral; tablet, sustained action	0.5	ml
Isopropyl alcohol	Oral-21; tablet	2	mg
Isopropyl alcohol	Oral; tablet	5.21	mg
Kaolin	Oral; tablet, coated	8	mg
Kaolin	Oral; tablet, delayed action, enteric coated	18.5	mg

Ingredient	Dosage form	Quantity	Unit
Kaolin	Oral; tablet	30.4	mg
Kaolin	Oral; tablet, sustained action	66	mg
Karaya gum	Buccal; patch, controlled release	68.1	mg
Lactic acid	Vaginal; tablet	70	mg
Lactoferrin, bovine	Oral; tablet	28.6	mg
Lactose	Oral; tablet, sustained release, film coated	38.75	mg
Lactose	Oral; tablet, sustained action, film coated	51.1	mg
Lactose	Rectal; tablet	65.3816	mg
Lactose	Oral; tablet, controlled release	69.25	mg
Lactose	Oral-20; tablet	70.7	mg
Lactose	Oral-21; tablet	89.275	mg
Lactose	Oral; tablet, delayed action	92.02	mg
Lactose	Oral; tablet (immed./comp. release), uncoated, chewable	117.7	mg
Lactose	Oral; tablet, multilayer, extended release	122	mg
Lactose	Oral; tablet, repeat action	153.2	mg
Lactose	Oral-28; tablet	179.2	mg
Lactose	Buccal; tablet	183.3	mg
Lactose	Sublingual; tablet	191.76	mg
Lactose	Oral; tablet, delayed action, enteric coated	209	mg
Lactose	Buccal/sublingual; tablet	296.7	mg
Lactose	Oral; tablet, coated	332.05	mg
Lactose	Oral; tablet, sustained action	400	mg
Lactose	Oral; tablet, film coated	590	mg
Lactose	Vaginal; tablet	1013	mg
Lactose	Oral; tablet	1020	mg
Lactose monohydrate	Vaginal; tablet, film coated	17.9	mg
Lactose monohydrate	Buccal; tablet	21.375	mg
Lactose monohydrate	Oral; tablet, multilayer, coated	22.7	mg
Lactose monohydrate	Oral; tablet, repeat action	25	mg
Lactose monohydrate	Oral; tablet, orally disintegrating	29.75	mg
Lactose monohydrate	Sublingual; tablet	33.874	mg
Lactose monohydrate	Oral-21; tablet, coated	35.19	mg
Lactose monohydrate	Oral; tablet, delayed action	50	mg
Lactose monohydrate	Oral; tablet (immed./comp. release), uncoated, chewable	62.3	mg
Lactose monohydrate	Oral; tablet, sustained release, film coated	81.9	mg
Lactose monohydrate	Oral-28; tablet, coated	82.89	mg
Lactose monohydrate	Oral-21; tablet	83.645	mg
Lactose monohydrate	Oral-28; tablet	93.865	mg
Lactose monohydrate	Oral; tablet, controlled release	138.913	mg
Lactose monohydrate	Oral; tablet, enteric coated particles	150	mg
Lactose monohydrate	Oral; tablet, delayed action, enteric coated	157.95	mg
Lactose monohydrate	Oral; tablet (immed./comp. release), film coated	182.6	mg
Lactose monohydrate	Oral; tablet, sustained action, coated	215	mg

Ingredient	Dosage form	Quantity	Unit
Lactose monohydrate	Oral; tablet, extended release	258.25	mg
Lactose monohydrate	Oral; tablet, sustained action, film coated	260	mg
Lactose monohydrate	Oral; tablet, sustained action	299.2	mg
Lactose monohydrate	Oral; tablet, coated	346.5	mg
Lactose monohydrate	Oral; tablet, sustained action, multilayer, film coated	374.5	mg
Lactose monohydrate	Oral; tablet, film coated	587.44	mg
Lactose monohydrate	Vaginal; insert	760.5	mg
Lactose monohydrate	Oral; tablet	889.42	mg
Lactose monohydrate - cellulose, microcrystalline	Oral; tablet	211.26	mg
Lactose, anhydrous	Buccal; tablet	23.75	mg
Lactose, anhydrous	Oral; tablet, controlled release	29.99	mg
Lactose, anhydrous	Oral-21; tablet, coated	58	mg
Lactose, anhydrous	Oral-28; tablet, coated	58	mg
Lactose, anhydrous	Oral; tablet, coated	69.94	mg
Lactose, anhydrous	Oral-21; tablet	75.687	mg
Lactose, anhydrous	Oral-28; tablet	79.335	mg
Lactose, anhydrous	Oral; tablet, delayed action, enteric coated	90	mg
Lactose, anhydrous	Oral; tablet (immed./comp. release), uncoated, chewable	108	mg
Lactose, anhydrous	Sublingual; tablet	128	mg
Lactose, anhydrous	Oral; tablet, sustained action, coated	130.7	mg
Lactose, anhydrous	Oral; tablet, sustained action, film coated	157.95	mg
Lactose, anhydrous	Oral; tablet, sustained action	180.9	mg
Lactose, anhydrous	Oral; tablet, film coated	453.6	mg
Lactose, anhydrous	Vaginal; tablet	605	mg
Lactose, anhydrous	Oral; tablet	613.6	mg
Lactose, hydrous	Oral-28; tablet	39.62	mg
Lactose, hydrous	Oral; tablet, extended release	43.23	mg
Lactose, hydrous	Oral-21; tablet	48	mg
Lactose, hydrous	Oral; tablet, sustained action, coated	83.3	mg
Lactose, hydrous	Oral; tablet, delayed action, enteric coated	88.5	mg
Lactose, hydrous	Oral; tablet (immed./comp. release), uncoated, chewable	100	mg
Lactose, hydrous	Oral; tablet, repeat action	155.28	mg
Lactose, hydrous	Oral; tablet, sustained action	156.8	mg
Lactose, hydrous	Sublingual; tablet	164.38	mg
Lactose, hydrous	Oral; tablet, coated	186	mg
Lactose, hydrous	Oral; tablet, film coated	556	mg
Lactose, hydrous	Vaginal; tablet	596	mg
Lactose, hydrous	Oral; tablet	708.9	mg
Landalgene	Oral; tablet, coated	5	mg
Landalgine P	Oral; tablet, coated	5	mg
Lecithin	Oral; bar, chewable	54	mg
Lecithin, egg	Oral; tablet	48	mg
Lemon oil	Oral; tablet	0.0007	ml

Ingredient	Dosage form	Quantity	Unit
Leucine	Oral; tablet	3.6	mg
Levomenthol	Buccal; inhalation	0.1	%
Levomenthol	Buccal; gum, chewing	3.84	mg
Light mineral oil	Oral; tablet, sustained action	0.2	mg
Light mineral oil	Oral; tablet, film coated	2.494	mg
Light mineral oil	Oral; pastille	3.6	mg
Light mineral oil	Oral; tablet, coated	4.8	mg
Light mineral oil	Oral; tablet	1474	mg
Locust bean gum	Oral; bar, chewable	40	mg
Locust bean gum	Oral; tablet, sustained action, coated	74.25	mg
Lubritab	Oral; tablet	10	mg
Lubritab	Oral; tablet, sustained action	35	mg
Magnasweet 100	Oral; tablet	0.75	mg
Magnasweet 135	Oral; tablet (immed./comp. release), uncoated, chewable	11.5	mg
Magnesium aluminum silicate	Oral; tablet (immed./comp. release), uncoated, chewable	8	mg
Magnesium aluminum silicate	Oral; tablet	24	mg
Magnesium aluminum silicate hydrate	Oral; tablet (immed./comp. release), uncoated, chewable	12	mg
Magnesium aluminum silicate hydrate	Oral; tablet	60	mg
Magnesium aspartate	Oral; tablet	1.5	mg
Magnesium carbonate	Oral; tablet, coated	1.157	mg
Magnesium carbonate	Oral; tablet, orally disintegrating, delayed release	10	mg
Magnesium carbonate	Oral; tablet (immed./comp. release), uncoated, chewable	100	mg
Magnesium carbonate	Oral; tablet	175	mg
Magnesium carbonate	Oral; tablet, delayed action, enteric coated	250	mg
Magnesium carbonate	Oral; tablet, film coated	250	mg
Magnesium hydroxide	Oral; tablet	40	mg
Magnesium hydroxide	Oral; tablet, film coated	43.4	mg
Magnesium hydroxide	Oral; tablet, delayed action, enteric coated	60	mg
Magnesium hydroxide	Oral; tablet (immed./comp. release), uncoated, chewable	450	mg
Magnesium oxide	Buccal; gum, chewing	7.2	mg
Magnesium oxide	Oral; tablet, sustained action	25.74	mg
Magnesium oxide	Oral; tablet	26.4	mg
Magnesium oxide	Oral; tablet, film coated	40	mg
Magnesium oxide	Oral; tablet, delayed action, enteric coated	63	mg
Magnesium phosphate	Oral; tablet	0.85	mg
Magnesium silicate	Oral; tablet	10	mg
Magnesium silicate	Oral; tablet, film coated	14.3	mg
Magnesium silicate	Oral; tablet, coated	29.03	mg
Magnesium silicate	Oral; tablet, enteric coated particles	30	mg
Magnesium stearate	Vaginal; tablet, film coated	0.4	mg
Magnesium stearate	Oral-21; tablet, coated	0.88	mg
Magnesium stearate	Oral-28; tablet, coated	0.88	mg
Magnesium stearate	Oral; tablet, multilayer, extended release	1.2	mg

Ingredient	Dosage form	Quantity	Unit
Magnesium stearate	Oral; tablet, repeat action	1.5	mg
Magnesium stearate	Oral-20; tablet	1.5	mg
Magnesium stearate	Oral-21; tablet	1.5	mg
Magnesium stearate	Oral; tablet, delayed action	3	mg
Magnesium stearate	Oral; tablet, multilayer, coated	3	mg
Magnesium stearate	Sublingual; tablet	3	mg
Magnesium stearate	Buccal; tablet	4	mg
Magnesium stearate	Oral; tablet, orally disintegrating, delayed release	6	mg
Magnesium stearate	Oral; tablet, enteric coated particles	7	mg
Magnesium stearate	Oral; tablet, controlled release	7.2	mg
Magnesium stearate	Oral; tablet, uncoated, troche	9	mg
Magnesium stearate	Oral; tablet (immed./comp. release), film coated	10	mg
Magnesium stearate	Oral; tablet, sustained action, coated	10	mg
Magnesium stearate	Oral; tablet, extended release	15	mg
Magnesium stearate	Oral; tablet, sustained action, film coated	15.8	mg
Magnesium stearate	Vaginal; tablet	17	mg
Magnesium stearate	Buccal/sublingual; tablet	17.5	mg
Magnesium stearate	Oral; troche	21	mg
Magnesium stearate	Vaginal; insert	23	mg
Magnesium stearate	Oral; tablet, film coated	28.31	mg
Magnesium stearate	Oral; tablet, coated	40	mg
Magnesium stearate	Oral; tablet (immed./comp. release), uncoated, chewable	50	mg
Magnesium stearate	Oral; tablet, delayed action, enteric coated	53.8	mg
Magnesium stearate	Oral; tablet, orally disintegrating	71.43	mg
Magnesium stearate	Oral-28; tablet	75	mg
Magnesium stearate	Oral; tablet, sustained action	150	mg
Magnesium stearate	Oral; tablet	400.748	mg
Magnesium sulfate	Oral; tablet	2.9	mg
Magnesium sulfate	Oral; tablet, extended release	4	mg
Magnesium sulfate	Oral; tablet, film coated	14	mg
Magnesium tartrate	Oral; tablet	3.24	mg
Magnesium trisilicate	Oral; tablet (immed./comp. release), uncoated, chewable	15	mg
Magnesium trisilicate	Oral; tablet, coated	20	mg
Magnesium trisilicate	Oral; tablet	76.89	mg
Maleic acid	Oral; tablet	4	mg
Maltodextrin	Oral-28; tablet	0.158	mg
Maltodextrin	Oral; tablet, coated	5.6	mg
Maltodextrin	Oral; tablet, sustained action	72.5	mg
Maltodextrin	Oral; tablet	80	mg
Maltodextrin	Oral; tablet, extended release	150	mg
Maltodextrin	Oral; tablet (immed./comp. release), uncoated, chewable	292	mg
Maltose	Oral; tablet	473	mg
Mannitol	Oral; tablet, delayed action, enteric coated	42.7	mg

Ingredient	Dosage form	Quantity	Unit
Mannitol	Oral; tablet (immed./comp. release), film coated	48.88	mg
Mannitol	Buccal/sublingual; tablet	52.5	mg
Mannitol	Oral; tablet, dispersible	90	mg
Mannitol	Buccal; tablet	97.685	mg
Mannitol	Sublingual; tablet	158.45	mg
Mannitol	Oral; tablet, coated	177.7	mg
Mannitol	Oral; tablet, orally disintegrating, delayed release	221	mg
Mannitol	Oral; tablet, film coated	241.21	mg
Mannitol	Oral; tablet, sustained action, film coated	274.972	mg
Mannitol	Oral; tablet, sustained action	392.2	mg
Mannitol	Oral; tablet	454.2	mg
Mannitol	Oral; tablet (immed./comp. release), uncoated, chewable	600	mg
Mannitol	Oral; tablet, orally disintegrating	606.72	mg
Mannitol	Oral; troche	1035.175	mg
Mannitol 2080	Oral; tablet (immed./comp. release), film coated	32.58	mg
Mannitol 60	Oral; tablet, orally disintegrating	174.78	mg
Mannitol M300	Oral; tablet, orally disintegrating	174.76	mg
Mannose, D-	Oral; tablet	1.197	mg
Medical antifoam emulsion C	Oral; tablet	1	mg
Meglumine	Oral; tablet	24	mg
Melojel	Oral; tablet	35	mg
Menthol	Oral; tablet	0.58	mg
Menthol	Buccal; gum, chewing	10	mg
Methacrylic acid copolymer	Oral; tablet	5.8	mg
Methacrylic acid copolymer	Oral; tablet, sustained action, coated	24.6	mg
Methacrylic acid copolymer	Oral; tablet, sustained action	35	mg
Methacrylic acid copolymer	Oral; tablet, delayed action, enteric coated	54	mg
Methacrylic acid copolymer	Oral; tablet, delayed action	58.362	mg
Methacrylic acid copolymer	Oral; tablet, orally disintegrating, delayed release	106.89	mg
Methacrylic acid copolymer type A	Oral; tablet, sustained action	6	mg
Methacrylic acid copolymer type A	Oral; tablet, sustained action, coated	10.5	mg
Methacrylic acid copolymer type A	Oral; tablet, film coated	16	mg
Methacrylic acid copolymer type B	Oral; tablet	0.83	mg
Methacrylic acid copolymer type B	Oral; tablet, sustained action	5.6	mg
Methacrylic acid copolymer type B	Oral; tablet, sustained action, coated	10.5	mg
Methacrylic acid copolymer type B	Oral; tablet, film coated	16	mg
Methacrylic acid copolymer type C	Oral; tablet, sustained action	7.2	mg
Methacrylic acid copolymer type C	Oral; tablet	7.8	mg
Methacrylic acid copolymer type C	Oral; tablet, extended release	66.7	mg
Methyl alcohol	Oral; tablet, film coated	10.36	mg
Methyl alcohol	Oral; tablet, coated	15.7	mg
Methyl alcohol	Oral; tablet	210	mg
Methyl chloride	Oral; tablet	69.82	mg

Ingredient	Dosage form	Quantity	Unit
Methyl ethyl ketone	Oral; tablet, delayed action, enteric coated	61	mg
Methyl hydroxyethyl cellulose	Oral; tablet	24	mg
Methylcellulose	Buccal/sublingual; tablet	4	mg
Methylcellulose	Oral-28; tablet	15	mg
Methylcellulose	Oral; tablet, film coated	21	mg
Methylcellulose	Oral; tablet (immed./comp. release), uncoated, chewable	50	mg
Methylcellulose	Oral; tablet, sustained action	96	mg
Methylcellulose	Oral; tablet, coated	138.3	mg
Methylcellulose	Oral; tablet	183.6	mg
Methylcellulose 1500	Oral; tablet	2.75	mg
Methylcellulose 400	Oral; tablet	33	mg
Methylene chloride	Oral; tablet, film coated	103.6	mg
Methylene chloride	Oral; tablet, coated	157	mg
Methylene chloride	Oral; tablet	209	mg
Methylparaben	Oral; tablet, coated	0.016	mg
Methylparaben	Oral; tablet, controlled release	0.0814	mg
Methylparaben	Oral; tablet, sustained action, multilayer, film coated	0.09	mg
Methylparaben	Oral; tablet, sustained action	0.17	mg
Methylparaben	Oral; tablet, film coated	0.23	mg
Methylparaben	Oral; tablet (immed./comp. release), uncoated, chewable	1.27	mg
Methylparaben	Oral; tablet	1.8	mg
Methylparaben sodium	Oral; tablet	0.1875	mg
Methylparaben sodium	Oral; tablet, orally disintegrating	0.3	mg
Mineral oil	Oral; tablet, coated	1.3	mg
Mineral oil	Oral; tablet, delayed action, enteric coated	5.67	mg
Mineral oil	Oral; tablet	50	mg
Monoglycerides	Oral; tablet	33.33	mg
Monosodium citrate	Oral; tablet	50	mg
Montan wax	Oral; tablet, film coated	0.03	mg
Montan wax	Oral-21; tablet	0.03	mg
Montan wax	Oral-21; tablet, coated	0.05	mg
Montan wax	Oral-28; tablet	0.05	mg
Montan wax	Oral-28; tablet, coated	0.05	mg
Montan wax	Oral; tablet	0.06	mg
Myristyl alcohol	Oral; tablet, sustained action	2	mg
Naphtha	Oral; tablet	0.9934	mg
Nonpareil seeds	Oral; tablet, sustained action	157.5	mg
Nonpareil seeds	Oral; tablet	166.36	mg
N-propyl orthosilicate	Vaginal; intrauterine device	0.7	mg
Oleic acid	Oral; tablet, coated	0.72	mg
Oleic acid	Oral; tablet, repeat action	1.854	mg
Oleic acid	Oral; tablet, sustained action	2	mg
Opacoat NA7013 clear	Oral; tablet, sustained action	4	mg

Ingredient	Dosage form	Quantity	Unit
Opacode NS-78-10013-N	Oral; tablet	0.03	mg
Opacode NS-78-8000 black	Oral; tablet, coated	0.1	mg
Opacode NS-78-8000 black	Oral; tablet, film coated	0.1	mg
Opacode NS-78-8000 black	Oral; tablet, sustained action	0.2	mg
Opacode NS-78-8000 black	Oral; tablet	0.3	mg
Opacode S-1-13001 orange	Oral; tablet	0.03	mg
Opacode S-1-15038 red	Oral; tablet	0.2	mg
Opacode S-1-26514 brown	Oral; tablet, delayed action, enteric coated	0.06	mg
Opacode S-1-4172 blue	Oral; tablet, film coated	1	mg
Opacode S-1-4172M blue	Oral; tablet, film coated	1	mg
Opacode S-1-8090 black	Oral; tablet	0.6	mg
Opacode S-1-8090 black	Oral; tablet, film coated	0.7	mg
Opacode S-1-8090 black	Oral; tablet, coated	2.4	mg
Opacode S-1-8095	Oral; tablet, film coated	0.7	mg
Opacode S-1-8100-HV black	Oral; tablet, sugar coated	0.09	mg
Opacode S-1-8100-HV black	Oral; tablet	0.5	mg
Opacode WB NS-78-10521 blue	Oral; tablet	0.09	mg
Opacode WB NS-78-17715 black	Oral; tablet	0.09	mg
Opacode WB NS-78-18001 white	Oral; tablet, coated	0.2	mg
Opadry 00A28646	Oral; tablet, film coated	3.4	mg
Opadry 02B14941 pink	Oral; tablet	6	mg
Opadry 02B22429 yellow	Oral; tablet	30	mg
Opadry 02B94016 pink	Oral; tablet	1.75	mg
Opadry 02G22555 yellow	Oral; tablet, film coated	5	mg
Opadry 02G24523 pink	Oral; tablet, film coated	8	mg
Opadry 02G26637 brown	Oral; tablet, film coated	8	mg
Opadry 02G28619 white	Oral; tablet, film coated	2.5	mg
Opadry 02-H-22703 yellow	Oral; tablet, sustained action	9	mg
Opadry 03A 58900 white	Oral; tablet	4.46	mg
Opadry 03A14309 pink	Oral; tablet	11.9	mg
Opadry 03B11434 green	Oral; tablet	32.38	mg
Opadry 03B12878 yellow	Oral; tablet, extended release	12	mg
Opadry 03B12896 yellow	Oral; tablet	24	mg
Opadry 03B12914 yellow	Oral; tablet, film coated	2.38	mg
Opadry 03B14424 pink	Oral; tablet, extended release	15	mg
Opadry 03B14436 pink	Oral; tablet	8	mg
Opadry 03B16083 maroon	Oral; tablet, coated	5	mg
Opadry 03B17426 beige	Oral; tablet, extended release	18	mg
Opadry 03B17495 beige	Oral; tablet	8	mg
Opadry 03B22426 yellow	Oral; tablet	15	mg
Opadry 03B24562 peach	Oral; tablet, film coated	18	mg
Opadry 03B50899 blue	Oral; tablet, film coated	5.97	mg
Opadry 03B54504 pink	Oral; tablet, film coated	27	mg

Ingredient	Dosage form	Quantity	Unit
Opadry 03B54573 pink	Oral; tablet	4	mg
Opadry 03B54588 pink	Oral; tablet	2	mg
Opadry 03B54955 pink	Oral; tablet	18.5	mg
Opadry 03B56518 brown	Oral; tablet	3	mg
Opadry 03B57631 grey	Oral; tablet, film coated	2.99	mg
Opadry 03B58902 white	Oral; tablet	10.5	mg
Opadry 03B58930 white	Oral; tablet	13.4	mg
Opadry 03B58965 white	Oral; tablet	24.05	mg
Opadry 03B86636 brown	Oral; tablet, delayed action	9	mg
Opadry 03F12967 yellow	Oral; tablet, film coated	4	mg
Opadry 03F13325 orange	Oral; tablet	12	mg
Opadry 03F14895 pink	Oral; tablet, film coated	4	mg
Opadry 03F54568 pink	Oral; tablet	7	mg
Opadry 03J18312 white	Oral; tablet	30	mg
Opadry 03K14881 pink	Oral; tablet	34.2	mg
Opadry 03K50891 blue	Oral; tablet	3.75	mg
Opadry 03K51211 green	Oral; tablet	2.25	mg
Opadry 03K52543 yellow	Oral; tablet	5	mg
Opadry 03K54121 pink	Oral; tablet	10	mg
Opadry 04F50702 blue	Oral; tablet	5	mg
Opadry 04F58804 white	Oral; tablet	10	mg
Opadry 05B10446 purple	Oral; tablet	16	mg
Opadry 05B10446 purple	Oral; tablet, coated	23	mg
Opadry 05B10457 purple	Oral; tablet	16	mg
Opadry 05B11552 green	Oral; tablet, sustained action	3.642	mg
Opadry 05B11781 green	Oral; tablet	7	mg
Opadry 05B12337 yellow	Oral; tablet	8.5	mg
Opadry 05B15325 red	Oral; tablet	5	mg
Opadry 05B17055 tan	Oral; tablet	4	mg
Opadry 05B17055 tan	Oral; tablet, film coated	5	mg
Opadry 12B58900 white	Oral; tablet	20	mg
Opadry 12F20984 blue	Oral; tablet, film coated	4	mg
Opadry 12F21129 green	Oral; tablet, film coated	2	mg
Opadry 12F22609 yellow	Oral; tablet, film coated	8	mg
Opadry 13B50780 blue	Oral; tablet	4.5	mg
Opadry 13B51260 green	Oral; tablet	2.25	mg
Opadry 13B52329 yellow	Oral; tablet	9	mg
Opadry 13B58802 white	Oral; tablet	9.6	mg
Opadry 15B11947 green	Oral; tablet	2.5	mg
Opadry 15B13335 orange	Oral; tablet, extended release	20	mg
Opadry 15B20780 blue	Oral; tablet	9	mg
Opadry 15B21340 green	Oral; tablet	12	mg
Opadry 15B22275 yellow	Oral; tablet	3	mg

Ingredient	Dosage form	Quantity	Unit
Opadry 15B24473 pink	Oral; tablet	6	mg
Opadry 15B24879 pink	Oral; tablet, film coated	4	mg
Opadry 15B28665 white	Oral; tablet, film coated	8	mg
Opadry 15B53449 orange	Oral; tablet	12.5	mg
Opadry 16B38982 white	Oral; tablet	2	mg
Opadry 16B5900 yellow	Oral; tablet, film coated	7.5	mg
Opadry 20014832 pink	Oral; tablet, film coated	3.745	mg
Opadry 20A52229 yellow	Oral; tablet	5.6	mg
Opadry 20A52560 yellow	Oral; tablet, film coated	4.5	mg
Opadry 20A52900 yellow	Oral; tablet	2.5	mg
Opadry 20A54211 pink	Oral; tablet	22.4	mg
Opadry 20A54239 pink	Oral; tablet	2.8	mg
Opadry 20A54614 pink	Oral; tablet, film coated	16	mg
Opadry 20A54616 pink	Oral; tablet, film coated	2	mg
Opadry 20A54900 pink	Oral; tablet	2.5	mg
Opadry 20A54901 pink	Oral; tablet	20	mg
Opadry 20A56500 brown	Oral; tablet	5	mg
Opadry 20A56694 brown	Oral; tablet, film coated	4	mg
Opadry 20A56788 brown	Oral; tablet, film coated	9	mg
Opadry 20A58806 white	Oral; tablet, film coated	13.5	mg
Opadry 20A58916 white	Oral; tablet, film coated	13.5	mg
Opadry 20A59015 clear	Oral; tablet, film coated	30	mg
Opadry 20B11521 green	Oral; tablet, film coated	28	mg
Opadry 20B17583 gray	Oral; tablet, film coated	21	mg
Opadry 20B97160 beige	Oral; tablet, film coated	12	mg
Opadry 20C15347 red	Oral; tablet, film coated	22	mg
Opadry 20H58983 white	Oral; tablet	8.7	mg
Opadry 31F20963 blue	Oral; tablet, sustained action	23	mg
Opadry 31F32870 yellow	Oral; tablet, sustained action, film coated	21	mg
Opadry 32K14834 pink	Oral; tablet, film coated	16.8	mg
Opadry 32K23123 orange	Oral; tablet, sustained action	7	mg
Opadry 33G12976 yellow	Oral; tablet, film coated	4.5	mg
Opadry 33G25171 brick red	Oral; tablet, film coated	28	mg
Opadry 40L14278 pink	Oral; tablet, film coated	33.6	mg
Opadry 80W 12319 yellow	Oral; tablet	9.7	mg
Opadry 80W22657 AMB yellow	Oral; tablet	7.5	mg
Opadry 80W-93032 AMB orange	Oral; tablet, film coated	9.967	mg
Opadry 85F14999 pink	Oral; tablet	8	mg
Opadry 85G93096 orange	Oral; tablet	4.53	mg
Opadry AMB 80W52110 yellow	Oral; tablet	16	mg
Opadry I 03B22409 yellow	Oral; tablet, multilayer, coated	17	mg
Opadry I 03B23197 orange	Oral; tablet, multilayer, coated	18	mg
Opadry I 03B24658 pink	Oral; tablet, multilayer, coated	17	mg

Ingredient	Dosage form	Quantity	Unit
Opadry II 03B10903 blue	Oral; tablet, sustained action	20.82	mg
Opadry II 31F22071 yellow	Oral; tablet, delayed action, enteric coated	2	mg
Opadry II 31F22088 yellow	Oral; tablet	6	mg
Opadry II 31F23111 orange	Oral; tablet, sustained action	16	mg
Opadry II 31F24239 pink	Oral; tablet	20	mg
Opadry II 31F27625 gray	Oral; tablet, sustained action	19	mg
Opadry II 31F32090 yellow	Oral; tablet	1	mg
Opadry II 31F58914 white	Oral; tablet	3	mg
Opadry II 31K52633 yellow	Oral; tablet	6	mg
Opadry II 32B10817 blue	Oral; tablet	6	mg
Opadry II 32K10054 purple	Oral; tablet	13.1	mg
Opadry II 32K12160 yellow	Oral; tablet, film coated	32.28	mg
Opadry II 32K12884 yellow	Oral; tablet	14	mg
Opadry II 32K12942 yellow	Oral; tablet	38.85	mg
Opadry II 32K12968 yellow	Oral; tablet, controlled release	8.88	mg
Opadry II 32K13357 orange	Oral-21; tablet	5	mg
Opadry II 32K13357 orange	Oral-28; tablet	5	mg
Opadry II 32K13699 orange	Oral; tablet, film coated	9	mg
Opadry II 32K14826 pink	Oral; tablet	7.2	mg
Opadry II 32K14833 pink	Oral; tablet, film coated	5	mg
Opadry II 32K14833 pink	Oral; tablet	21	mg
Opadry II 32K16706 brown	Oral; tablet, film coated	14	mg
Opadry II 32K17089 tan	Oral; tablet	3.75	mg
Opadry II 32K17573 gray	Oral; tablet	7.5	mg
Opadry II 33G10907 blue	Oral; tablet	4.5	mg
Opadry II 33G11635 green	Oral; tablet, sustained action	11.2	mg
Opadry II 33G28707 white	Oral; tablet	31.25	mg
Opadry II 40 L14235 pink	Oral; tablet, sustained action, film coated	22	mg
Opadry II 40 L17589 gray	Oral; tablet, sustained action	26	mg
Opadry II 40014876 pink	Oral; tablet, film coated	4.93	mg
Opadry II 40B12994 beige	Oral; tablet	10	mg
Opadry II 40B97172 yellow	Oral; tablet	5	mg
Opadry II 40C10881 blue	Oral; tablet, film coated	6	mg
Opadry II 40C13396 orange	Oral; tablet, film coated	6	mg
Opadry II 40C18303 white	Oral; tablet, film coated	6	mg
Opadry II 40L10412 purple	Oral; tablet, sustained action	5.25	mg
Opadry II 40L10884 blue	Oral; tablet, film coated	18	mg
Opadry II 40L11438 green	Oral; tablet, sustained action	-40	mg
Opadry II 40L11588 green	Oral; tablet, sustained action, film coated	22	mg
Opadry II 40L11588 green	Oral; tablet	26.25	mg
Opadry II 40L12917 yellow	Oral; tablet, film coated	18	mg
Opadry II 40L12979 yellow	Oral; tablet, sustained action, coated	30	mg
Opadry II 40L13950 orange	Oral; tablet	9	mg

Ingredient	Dosage form	Quantity	Unit
Opadry II 40L14190 pink	Oral; tablet	24.5	mg
Opadry II 40L14336 pink	Oral; tablet	9	mg
Opadry II 40L14836 pink	Oral; tablet, film coated	4.75	mg
Opadry II 40L17427 beige	Oral; tablet	9	mg
Opadry II 40L17587 gray	Oral; tablet	6.2	mg
Opadry II 40L92058 yellow	Oral; tablet, sustained action, film coated	12.9	mg
Opadry II 40093122 orange	Oral; tablet	9	mg
Opadry II 49B10882 blue	Oral; tablet	26.9	mg
Opadry II 49B13460 orange	Oral; tablet	19	mg
Opadry II 49B16716 brown	Oral; tablet	9.57	mg
Opadry II 85F10919 blue	Oral; tablet	24	mg
Opadry II 85F12345 yellow	Oral; tablet	6	mg
Opadry II 85F12372 yellow	Oral; tablet	4.5	mg
Opadry II 85F13980 orange	Oral; tablet	4.5	mg
Opadry II 85F16876 brown	Oral; tablet	24	mg
Opadry II 85F18378 white	Oral; tablet	40	mg
Opadry II 85F18422 white	Oral; tablet	35.4	mg
Opadry II 85F22055 yellow	Oral; tablet	10	mg
Opadry II 85F23470 pink	Oral; tablet	7.5	mg
Opadry II 85F24033 pink	Oral; tablet	7.5	mg
Opadry II 85F24307 pink	Oral; tablet	35	mg
Opadry II 85F28751 white	Oral; tablet	24	mg
Opadry II 85F288751 white	Oral; tablet	30	mg
Opadry II 85F94172 pink	Oral; tablet	46.5	mg
Opadry II 85G20583 blue	Oral; tablet	48	mg
Opadry II OY-L-22903	Oral; tablet, film coated	6	mg
Opadry II OY-L-23028 orange	Oral; tablet, film coated	4.5	mg
Opadry II OY-L-24802 pink	Oral; tablet, film coated	4.5	mg
Opadry II OY-L-24803 pink	Oral; tablet, film coated	9	mg
Opadry II OY-L-24808	Oral; tablet, film coated	12	mg
Opadry II OY-L-32920	Oral; tablet, film coated	12	mg
Opadry II pink 85G94027	Oral; tablet	16.2	mg
Opadry II pink 85G94065	Oral; tablet (immed./comp. release), film coated	7	mg
Opadry II red 85G94101	Oral; tablet (immed./comp. release), film coated	7	mg
Opadry II Y-19-7483 clear	Oral; tablet	5.6	mg
Opadry II Y-19-7483 clear	Oral; tablet, sustained action, coated	9.8	mg
Opadry II Y-19-7483 clear	Oral; tablet, film coated	34	mg
Opadry II Y-19-7483 clear	Oral; tablet, sustained action	35	mg
Opadry II Y-22-10274 lavender	Oral; tablet, film coated	8	mg
Opadry II Y-22-10274 lavender	Oral; tablet, sustained action	14.95	mg
Opadry II Y-22-10508 blue	Oral; tablet	14.83	mg
Opadry II Y-22-10519 blue	Oral; tablet	29.66	mg
Opadry II Y-22-10538 blue	Oral; tablet	90	mg

Ingredient	Dosage form	Quantity	Unit
Opadry II Y-22-10702 blue	Oral; tablet, sustained action	5.25	mg
Opadry II Y-22-10702 blue	Oral; tablet	6.2	mg
Opadry II Y-22-10764 blue	Oral; tablet	15	mg
Opadry II Y-22-11184 green	Oral; tablet	8	mg
Opadry II Y-22-11210 green	Oral; tablet	3	mg
Opadry II Y-22-11251 green	Oral; tablet	2	mg
Opadry II Y-22-12098 yellow	Oral; tablet	9	mg
Opadry II Y-22-12664 yellow	Oral; tablet, delayed action, enteric coated	12	mg
Opadry II Y-22-12664 yellow	Oral; tablet	86.4	mg
Opadry II Y-22-12718 yellow	Oral; tablet, sustained action	15	mg
Opadry II Y2212720 pale yellow	Oral; tablet, film coated	2.375	mg
Opadry II Y-22-12780 yellow	Oral; tablet, film coated	10.85	mg
Opadry II Y-22-13034 orange	Oral; tablet	4.2	mg
Opadry II Y-22-13061 orange	Oral; tablet, sustained action	-40	mg
Opadry II Y-22-13061 orange	Oral; tablet, film coated	6.5	mg
Opadry II Y-22-13061 orange	Oral; tablet, coated	13	mg
Opadry II Y-22-13061 orange	Oral; tablet	24	mg
Opadry II Y-22-13083 orange	Oral; tablet	15	mg
Opadry II Y-22-13089 orange	Oral; tablet	4.9	mg
Opadry II Y-22-13167 orange	Oral; tablet, controlled release	6	mg
Opadry II Y-22-13167 orange	Oral; tablet, sustained action, film coated	17.19	mg
Opadry II Y-22-13167 orange	Oral; tablet	25	mg
Opadry II Y-22-13577 flesh	Oral; tablet	4	mg
Opadry II Y-22-13577 flesh	Oral; tablet, film coated	9.3	mg
Opadry II Y-22-13577 flesh	Oral; tablet, sustained action	15	mg
Opadry II Y-22-13603 orange	Oral; tablet	67.5	mg
Opadry II Y-22-13663 orange	Oral; tablet, sustained action	5.25	mg
Opadry II Y-22-14001 pink	Oral; tablet	6	mg
Opadry II Y2214701 pink	Oral; tablet, film coated	19	mg
Opadry II Y-22-15061	Oral; tablet, sustained action, coated	17.1	mg
Opadry II Y-22-16562 brown	Oral; tablet	15	mg
Opadry II Y-22-16577 brown	Oral; tablet, sustained action, coated	12	mg
Opadry II Y-22-17025 beige	Oral; tablet, film coated	15	mg
Opadry II Y-22-17165 beige	Oral; tablet	20	mg
Opadry II Y-22-17221 beige	Oral; tablet, film coated	12	mg
Opadry II Y2217279 beige	Oral; tablet, film coated	9.5	mg
Opadry II Y-22-17515 gray	Oral; tablet, sustained release, film coated	40	mg
Opadry II Y-22-18238 white	Oral; tablet	3	mg
Opadry II Y-22-18238 white	Oral; tablet, controlled release	5.85	mg
Opadry II Y-22-7719 white	Oral; tablet, sustained action	9	mg
Opadry II Y-22-7719 white	Oral; tablet, sustained action, multilayer, film coated	17.91	mg
Opadry II Y-22-7719 white	Oral; tablet, sustained action, coated	18.15	mg
Opadry II Y-22-7719 white	Oral; tablet, film coated	40	mg

Ingredient	Dosage form	Quantity	Unit
Opadry II Y-22-7719 white	Oral; tablet	42.42	mg
Opadry II Y-30-10701 blue	Oral; tablet	40	mg
Opadry II Y-30-12705 yellow	Oral; tablet, sustained action	20	mg
Opadry II Y-30-12736A yellow	Oral; tablet, sustained action, film coated	7	mg
Opadry II Y-30-12736A yellow	Oral; tablet, film coated	18	mg
Opadry II Y-30-12737A yellow	Oral; tablet, film coated	5	mg
Opadry II Y-30-12737A yellow	Oral; tablet	6	mg
Opadry II Y-30-12842A yellow	Oral; tablet	2	mg
Opadry II Y-30-12863A yellow	Oral; tablet, film coated	4.5	mg
Opadry II Y-30-13091 orange	Oral-21; tablet	3	mg
Opadry II Y-30-13091 orange	Oral-28; tablet	3	mg
Opadry II Y-30-13616 orange	Oral; tablet	6	mg
Opadry II Y-30-13642A orange	Oral; tablet, sustained action	24.5	mg
Opadry II Y-30-14700A pink	Oral; tablet, film coated	7	mg
Opadry II Y-30-14758 pink	Oral; tablet, sustained action, film coated	7.99	mg
Opadry II Y-30-17295A tan	Oral; tablet	6	mg
Opadry II Y-30-17296A beige	Oral; tablet	6	mg
Opadry II Y-30-17340A beige	Oral; tablet, film coated	6	mg
Opadry II Y-30-17528 gray	Oral; tablet, sustained action	5.6	mg
Opadry II Y-30-17528 gray	Oral; tablet	25	mg
Opadry II Y-30-18037 white	Oral; tablet	16	mg
Opadry II Y-30-18037 white	Oral; tablet, sustained release, film coated	26	mg
Opadry II Y-30-18037 white	Oral; tablet, extended release	33	mg
Opadry II Y-30-18037 white	Oral; tablet, controlled release	38	mg
Opadry II Y-30-18037 white	Oral; tablet, film coated	43.2	mg
Opadry II YS-1-12524A	Oral; tablet, film coated	16	mg
Opadry II YS-1-19025A clear	Oral; tablet, coated	9.9	mg
Opadry II YS-1-7006 clear	Oral; tablet	4.8	mg
Opadry II YS-1-7006 clear	Oral; tablet, coated	4.8	mg
Opadry II YS-1-7006 clear	Oral; tablet, sustained action	13	mg
Opadry II YS-22-13571 orange	Oral; tablet, film coated	7.5	mg
Opadry II YS-22-17227A beige	Oral; tablet, film coated	5.25	mg
Opadry II YS-22-18096 white	Oral; tablet	28.5	mg
Opadry II YS-30-12788A yellow	Oral; tablet, controlled release	18	mg
Opadry II YS-30-13641A orange	Oral; tablet	15	mg
Opadry II YS-30-14743A pink	Oral; tablet, film coated	5.1	mg
Opadry II YS-30-14777A pink	Oral; tablet, film coated	5	mg
Opadry II YS-30-17265A beige	Oral; tablet	6	mg
Opadry II YS-30-17265A beige	Oral; tablet, sustained action	9	mg
Opadry II YS-30-17271A beige	Oral; tablet, film coated	15.46	mg
Opadry II YS-30-18105 white	Oral; tablet, sustained action	9	mg
Opadry II YS-30-18105 white	Oral; tablet, film coated	13.2	mg
Opadry OS-F-32867 yellow	Oral; tablet	20	mg

Ingredient	Dosage form	Quantity	Unit
opadry OY-27301 butterscotch	Oral; tablet, delayed action, enteric coated	6	mg
Opadry OY-3736 butterscotch	Oral; tablet	29.2	mg
Opadry OY-38924 white	Oral; tablet	39	mg
Opadry OY-52945 yellow	Oral; tablet, film coated	11.95	mg
Opadry OY-52945 yellow	Oral; tablet	23.16	mg
Opadry OY-54937 pink	Oral; tablet, film coated	3	mg
Opadry OY-58900 white	Oral; tablet	31.8	mg
Opadry OY-7240 clear	Oral; tablet	24	mg
Opadry OY-7300 white	Oral; tablet	35	mg
Opadry OY-8764H orange	Oral; tablet, film coated	25.2	mg
Opadry OY-B-28920 white	Oral; tablet, film coated	14	mg
Opadry OY-B-28920 white	Oral; tablet	28	mg
Opadry OY-B-32830	Oral; tablet	28	mg
Opadry OY-GM-28900	Oral; tablet, film coated	26	mg
Opadry OY-L-27204 tan	Oral; tablet	4	mg
Opadry OY-L-27205 beige	Oral; tablet	4	mg
Opadry OY-L-28906	Oral; tablet	4.5	mg
Opadry OY-L-34836 pink	Oral; tablet	4	mg
Opadry OY-LS-20921 blue	Oral; tablet	15	mg
Opadry OY-LS-23016 orange	Oral; tablet, film coated	6	mg
Opadry OY-LS-23018 orange	Oral; tablet, delayed action, enteric coated	6	mg
Opadry OY-LS-28908 white	Oral; tablet	7.5	mg
Opadry OY-LS-28908 white	Oral; tablet, film coated	13.5	mg
Opadry OY-LS-28914 white	Oral; tablet, sustained action	7	mg
Opadry OY-LS-28914 white	Oral; tablet, film coated	15	mg
Opadry OY-LS-33111 orange	Oral; tablet	7	mg
Opadry OY-LS-37200 buff	Oral; tablet, film coated	9	mg
Opadry OY-S-1387 pink	Oral; tablet, sustained action, film coated	0.25	mg
Opadry OY-S-20007 purple	Oral; tablet, sustained action, coated	13	mg
Opadry OY-S-20900 blue	Oral; tablet, film coated	4.5	mg
Opadry OY-S-20901 blue	Oral; tablet	8	mg
Opadry OY-S-21001 green	Oral; tablet, film coated	4.5	mg
Opadry OY-S-21027 green	Oral; tablet	9	mg
Opadry OY-S-22802 yellow	Oral; tablet	5	mg
Opadry OY-S-22815 yellow	Oral-28; tablet	1.22	mg
Opadry OY-S-22907 yellow	Oral; tablet, film coated	4.5	mg
Opadry OY-S-23049 orange	Oral-28; tablet	1.21	mg
Opadry OY-S-24900 pink	Oral; tablet, film coated	4.5	mg
Opadry OY-S-24972 pink	Oral; tablet	8.6	mg
Opadry OY-S-26530 red	Oral-28; tablet	1.21	mg
Opadry OY-S-28849 white	Oral; tablet	5	mg
Opadry OY-S-28924 white	Oral; tablet	13	mg
Opadry OY-S-28924 white	Oral; tablet, film coated	16.52	mg

Ingredient	Dosage form	Quantity	Unit
Opadry OY-S-29019 clear	Oral; tablet, sustained action	30	mg
Opadry OY-S-30013 purple	Oral; tablet	17	mg
Opadry OY-S-30913 blue	Oral; tablet	10	mg
Opadry OY-S-30953 blue	Oral; tablet	6	mg
Opadry OY-S-32921 yellow	Oral; tablet	4	mg
Opadry OY-S-32921 yellow	Oral; tablet, film coated	4	mg
Opadry OY-S-32986 yellow	Oral; tablet	10.35	mg
Opadry OY-S-33016	Oral; tablet	30	mg
Opadry OY-S-34800 pink	Oral; tablet	6	mg
Opadry OY-S-34817 pink	Oral; tablet, film coated	18	mg
Opadry OY-S-34923 pink	Oral; tablet	8	mg
Opadry OY-S-34995 pink	Oral; tablet	13.8	mg
Opadry OY-S-38928	Oral; tablet, film coated	20	mg
Opadry OY-S-38944 white	Oral; tablet	11	mg
Opadry OY-S-52902 yellow	Oral; tablet	16.656	mg
Opadry OY-S-53010 orange	Oral; tablet	8.328	mg
Opadry OY-S-54902 pink	Oral; tablet, film coated	5.24	mg
Opadry OY-S-54904 pink	Oral; tablet, film coated	3.6	mg
Opadry OY-S-6937 pink	Oral; tablet, film coated	6	mg
Opadry OY-S-7322 white	Oral; tablet, film coated	9	mg
Opadry OY-S-7399 white	Oral; tablet, film coated	10	mg
Opadry OY-S-7399 white	Oral; tablet	19	mg
Opadry OY-S-9476 brown	Oral; tablet, sustained action	28.26	mg
Opadry OY-S-9603 white	Oral; tablet	24	mg
Opadry OY-S-9603 white	Oral; tablet, film coated	38.5	mg
Opadry OY-SR-34907	Oral; tablet	12.25	mg
Opadry Y-1-17272A beige	Oral; tablet	12	mg
Opadry Y-1-2102 yellow	Oral; tablet, coated	10.87	mg
Opadry Y-1-2132 yellow	Oral; tablet	28	mg
Opadry Y-1-2516 orange	Oral; tablet, sustained action	5	mg
Opadry Y-1-2553 orange	Oral; tablet	10.5	mg
Opadry Y-1-4205 blue	Oral; tablet, film coated	12.2	mg
Opadry Y-1-4206 blue	Oral; tablet, sustained action	5.7	mg
Opadry Y-1-4234 blue	Oral; tablet	3.055	mg
Opadry Y-1-7000 white	Oral; tablet, coated	3	mg
Opadry Y-1-7000 white	Oral; tablet, extended release	11.1	mg
Opadry Y-1-7000 white	Oral; tablet, film coated	27	mg
Opadry Y-1-7000 white	Oral; tablet	30	mg
Opadry Y-1-7000B white	Oral; tablet	10	mg
Opadry Y-1-7000H white	Oral; tablet	15	mg
Opadry Y-1-7000H white	Oral; tablet, film coated	28	mg
Opadry Y-1-7006 blue	Oral; tablet	3.232	mg
Opadry Y-1-7503 gray	Oral; tablet, sustained action	5	mg

Ingredient	Dosage form	Quantity	Unit
Opadry Y-22-12720 pale yellow	Oral; tablet, film coated	4.2	mg
Opadry Y-22-12751 yellow	Oral; tablet	25.8	mg
Opadry Y-22-13558 orange	Oral; tablet	12.8	mg
Opadry Y-22-14525 pink	Oral; tablet	4.8	mg
Opadry Y-22-15008 red	Oral; tablet, film coated	3.83	mg
Opadry Y-22-15119 red	Oral; tablet, sustained action, coated	18	mg
Opadry Y-22-18238 white	Oral; tablet, film coated	6	mg
Opadry Y-30-13168A orange	Oral; tablet	7	mg
Opadry Y-30-14565 pink	Oral; tablet (immed./comp. release), film coated	18	mg
Opadry Y-30-14565 pink	Oral; tablet, film coated	36	mg
Opadry Y-5-10300 lavender	Oral; tablet, film coated	2	mg
Opadry Y-5-10670 blue	Oral; tablet	18	mg
Opadry Y-5-1244 pink	Oral; tablet	2	mg
Opadry Y-5-12539 yellow	Oral; tablet	12.6	mg
Opadry Y-5-12544A yellow	Oral; tablet, film coated	6	mg
Opadry Y-5-12584 yellow	Oral; tablet, delayed action, enteric coated	11.55	mg
Opadry Y-5-13512 orange	Oral; tablet	25.2	mg
Opadry Y-5-13513 orange	Oral; tablet, sustained action	5	mg
Opadry Y-5-14530A pink	Oral; tablet, delayed action, enteric coated	11.55	mg
Opadry Y-5-1727 red	Oral; tablet	7	mg
Opadry Y-5-2042 yellow	Oral; tablet, sustained action	18.3	mg
Opadry Y-5-2086 yellow	Oral; tablet	26	mg
Opadry Y-5-2328 orange	Oral; tablet	24.6	mg
Opadry Y-5-2371 orange	Oral; tablet	28.875	mg
Opadry Y-5-2394 orange	Oral; tablet	31.5	mg
Opadry Y-5-2450 orange	Oral; tablet, film coated	7.875	mg
Opadry Y-5-2450 orange	Oral; tablet	20.895	mg
Opadry Y-5-2451 orange	Oral; tablet	6	mg
Opadry Y-5-2646 beige	Oral; tablet	14	mg
Opadry Y-5-3171 green	Oral; tablet, sustained action	10	mg
Opadry Y-5-3296 green	Oral; tablet	36.4	mg
Opadry Y-5-4129 blue	Oral; tablet	7	mg
Opadry Y-5-4270 blue	Oral; tablet	14	mg
Opadry Y-5-4295 blue	Oral; tablet, sustained action, coated	17.11	mg
Opadry Y-5-6233 light orange	Oral; tablet, film coated	6	mg
Opadry Y-5-6301 yellow	Oral; tablet, film coated	5.25	mg
Opadry Y-5-7058 white	Oral; tablet, coated	3	mg
Opadry Y-5-7058 white	Oral; tablet	6	mg
Opadry Y-5-7068 white	Oral; tablet, controlled release	5	mg
Opadry Y-5-7068 white	Oral; tablet, sustained action	6	mg
Opadry Y-5-7068 white	Oral; tablet, coated	21	mg
Opadry Y-5-7068 white	Oral; tablet, film coated	22.5	mg
Opadry Y-5-7068 white	Oral; tablet	120	mg

Ingredient	Dosage form	Quantity	Unit
Opadry Y-5-7411 purple	Oral; tablet	12	mg
Opadry Y-5-7524 grey	Oral; tablet, sustained action, film coated	31.5	mg
Opadry Y-5-8050 black	Oral; tablet	7	mg
Opadry Y-5-9006 brown	Oral; tablet	8	mg
Opadry Y-5-9006 brown	Oral; tablet, extended release	15	mg
Opadry Y-5-9006 brown	Oral; tablet, sustained action	15	mg
Opadry Y-5-9020 brown	Oral; tablet, film coated	12	mg
Opadry yellow	Oral; tablet, film coated	1.89	mg
Opadry yellow	Oral; tablet	12.75	mg
Opadry YPS-7-2127	Oral; tablet, delayed action, enteric coated	54	mg
Opadry YS-1-003 white	Oral; tablet	7	mg
Opadry YS-1-10010 purple	Oral; tablet	18	mg
Opadry YS-1-10291 lavender	Oral; tablet, sustained action	5	mg
Opadry YS-1-10523A blue	Oral; tablet, film coated	12	mg
Opadry YS-1-10525 blue	Oral; tablet	23	mg
Opadry YS-1-10533A	Oral; tablet	8.16	mg
Opadry YS-1-10542A blue	Oral; tablet, sustained action	5	mg
Opadry YS-1-10547A blue	Oral; tablet, film coated	35	mg
Opadry YS-1-10563 blue	Oral; tablet	4.2	mg
Opadry YS-1-10618	Oral; tablet, film coated	3.75	mg
Opadry YS-1-10629	Oral; tablet	9.12	mg
Opadry YS-1-10654A blue	Oral; tablet	2.17	mg
Opadry YS-1-10682 blue	Oral; tablet, film coated	24	mg
Opadry YS-1-10699 blue	Oral; tablet, extended release	19.59	mg
Opadry YS-1-10748A light blue	Oral; tablet	4.5	mg
Opadry YS-1-10755 blue	Oral; tablet	8.4	mg
Opadry YS-1-10783A blue	Oral; tablet	2.17	mg
Opadry YS-1-11000 pink	Oral; tablet, film coated	3.75	mg
Opadry YS-1-11051 green	Oral; tablet, coated	16	mg
Opadry YS-1-11051 green	Oral; tablet	17.56	mg
Opadry YS-1-11060 green	Oral; tablet, film coated	10	mg
Opadry YS-1-1107 green	Oral; tablet, film coated	12	mg
Opadry YS-1-11075A green	Oral; tablet, sustained action	8	mg
Opadry YS-1-11113 green	Oral; tablet, sustained action	30	mg
Opadry YS-1-11171 green	Oral; tablet	6.3	mg
Opadry YS-1-11234 green	Oral; tablet	5.89	mg
Opadry YS-1-11305 green	Oral; tablet	7.2	mg
Opadry YS-1-11369 green	Oral; tablet, sustained action	21	mg
Opadry YS-1-1246 pink	Oral; tablet	4.3	mg
Opadry YS-1-1252 pink	Oral; tablet, film coated	4.5	mg
Opadry YS-1-12524A yellow	Oral; tablet	9	mg
Opadry YS-1-12525A yellow	Oral; tablet, controlled release	5	mg
Opadry YS-1-12525A yellow	Oral; tablet, film coated	5	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-12525A yellow	Oral; tablet	7	mg
Opadry YS-1-12526A yellow	Oral; tablet, film coated	5	mg
Opadry YS-1-12526A yellow	Oral; tablet	15	mg
Opadry YS-1-12529 yellow	Oral; tablet, film coated	3.75	mg
Opadry YS-1-12541 yellow	Oral; tablet, coated	12	mg
Opadry YS-1-12541 yellow	Oral; tablet	22	mg
Opadry YS-1-1256-A yellow	Oral; tablet	7.5	mg
Opadry YS-1-12573 yellow	Oral; tablet, film coated	20	mg
Opadry YS-1-12581 yellow	Oral; tablet	8.4	mg
Opadry YS-1-1262 pink	Oral; tablet, film coated	10.5	mg
Opadry YS-1-12625 yellow	Oral; tablet	10	mg
Opadry YS-1-12702A yellow	Oral; tablet (immed./comp. release), film coated	12.5	mg
Opadry YS-1-12732 yellow	Oral; tablet, film coated	20.96	mg
Opadry YS-1-1277 pink	Oral; tablet	2.4	mg
Opadry YS-1-12826 yellow	Oral; tablet	8.1	mg
Opadry YS-1-12844 yellow	Oral; tablet, film coated	10	mg
Opadry YS-1-12847 yellow	Oral; tablet, sustained action	9.66	mg
Opadry YS-1-1298 pink	Oral; tablet	4.4	mg
Opadry YS-1-13013 peach	Oral; tablet	10.3	mg
Opadry YS-1-13065A orange	Oral; tablet	41	mg
Opadry YS-1-13119 orange	Oral; tablet	4.2	mg
Opadry YS-1-13121 yellow	Oral; tablet, film coated	11.25	mg
Opadry YS-1-13148A orange	Oral; tablet, film coated	5	mg
Opadry YS-1-13148A orange	Oral; tablet	10	mg
Opadry YS-1-13214 orange	Oral; tablet, controlled release	7.68	mg
Opadry YS-1-13269 orange	Oral; tablet, film coated	5	mg
Opadry YS-1-13271 orange	Oral; tablet, film coated	20	mg
Opadry YS-1-13555 orange	Oral; tablet	6	mg
Opadry YS-1-13591A orange	Oral; tablet, film coated	9	mg
Opadry YS-1-13664A orange	Oral; tablet	10.11	mg
Opadry YS-1-13673A orange	Oral; tablet	5.09	mg
Opadry YS-1-13675A orange	Oral; tablet	5.09	mg
Opadry YS-1-14012 pink	Oral; tablet	5	mg
Opadry YS-1-14129 pink	Oral; tablet, film coated	19	mg
Opadry YS-1-14130 pink	Oral-21; tablet, coated	5	mg
Opadry YS-1-14130 pink	Oral-28; tablet, coated	5	mg
Opadry YS-1-14130 pink	Oral; tablet	12	mg
Opadry YS-1-1418 pink	Oral; tablet	2.4	mg
Opadry YS-1-1441G	Oral; tablet, film coated	8	mg
Opadry YS-1-1448G pink	Oral; tablet, sustained action	11	mg
Opadry YS-1-14518A pink	Oral; tablet	4.5	mg
Opadry YS-1-14518A pink	Oral; tablet, controlled release	5	mg
Opadry YS-1-14518A pink	Oral; tablet, film coated	8	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-14518A pink	Oral; tablet, sustained action	12	mg
Opadry YS-1-14519A pink	Oral; tablet	18	mg
Opadry YS-1-14532 pink	Oral; tablet, sustained action	15	mg
Opadry YS-1-1454 pink	Oral; tablet, film coated	15	mg
Opadry YS-1-14555A pink	Oral; tablet, film coated	4	mg
Opadry YS-1-1456G pink	Oral; tablet, coated	10.9	mg
Opadry YS-1-14587A pink	Oral-21; tablet	2.38	mg
Opadry YS-1-14587A pink	Oral-28; tablet	2.38	mg
Opadry YS-1-14593A pink	Oral; tablet, film coated	12	mg
Opadry YS-1-14595 pink	Oral; tablet	10	mg
Opadry YS-1-14608A	Oral; tablet	10.18	mg
Opadry YS-1-14643A pink	Oral; tablet	32	mg
Opadry YS-1-14725 pink	Oral; tablet	39	mg
Opadry YS-1-14756A pink	Oral; tablet	8	mg
Opadry YS-1-14779A pink	Oral; tablet, controlled release	7.48	mg
Opadry YS-1-15050 red	Oral; tablet	6	mg
Opadry YS-1-1510 pink	Oral; tablet	4.2	mg
Opadry YS-1-1528 pink	Oral; tablet	15	mg
Opadry YS-1-1543 pink	Oral; tablet, film coated	4.8	mg
Opadry YS-1-1543 pink	Oral; tablet	6	mg
Opadry YS-1-15585A red	Oral; tablet	15	mg
Opadry YS-1-16002 maroon	Oral-21; tablet	4	mg
Opadry YS-1-16002 maroon	Oral-28; tablet	4	mg
Opadry YS-1-16518A brown	Oral; tablet	16.2	mg
Opadry YS-1-17180A beige	Oral; tablet	15	mg
Opadry YS-1-17181A beige	Oral; tablet	34.5	mg
Opadry YS-1-17192A	Oral; tablet	20.36	mg
Opadry YS-1-17209 beige	Oral; tablet	30	mg
Opadry YS-1-17220	Oral; tablet, film coated	7.5	mg
Opadry YS-1-17222A tan	Oral; tablet (immed./comp. release), film coated	20	mg
Opadry YS-1-17235A peach	Oral; tablet	18	mg
Opadry YS-1-1724 red	Oral; tablet	18.566	mg
Opadry YS-1-17277A beige	Oral; tablet	3.75	mg
Opadry YS-1-17307A butterscotch	Oral; tablet, film coated	5	mg
Opadry YS-1-17307A butterscotch	Oral; tablet	5.6	mg
Opadry YS-1-17505A gray	Oral; tablet, sustained action	20	mg
Opadry YS-1-17506A gray	Oral; tablet, film coated	15	mg
Opadry YS-1-17506A gray	Oral; tablet	15.75	mg
Opadry YS-1-1751G red	Oral; tablet, coated	13.6	mg
Opadry YS-1-1755 gray	Oral; tablet	4.5	mg
Opadry YS-1-18005 white	Oral; tablet	5.89	mg
Opadry YS-1-18022 white	Oral; tablet	30.54	mg
Opadry YS-1-18027 white	Oral; tablet	12.6	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-18027 white	Oral; tablet, film coated	16.32	mg
Opadry YS-1-18027A white	Oral; tablet, film coated	5.5	mg
Opadry YS-1-18027A white	Oral; tablet	21	mg
Opadry YS-1-18028 white	Oral; tablet	18.8	mg
Opadry YS-1-1811 red	Oral; tablet, sustained action	43.35	mg
Opadry YS-1-18111 white	Oral; tablet, film coated	32	mg
Opadry YS-1-18130A white	Oral; tablet	2.17	mg
Opadry YS-1-18177A white	Oral; tablet, film coated	8.4	mg
Opadry YS-1-18177A white	Oral; tablet	18	mg
Opadry YS-1-18202A white	Oral; tablet	21	mg
Opadry YS-1-18229 white	Oral; tablet, sustained action	18.09	mg
Opadry YS-1-1847 red	Oral; tablet	25	mg
Opadry YS-1-19025-A clear	Oral; tablet, sustained action, film coated	0.8	mg
Opadry YS-1-19025-A clear	Oral; tablet, film coated	1.1	mg
Opadry YS-1-19025-A clear	Oral; tablet, coated	4.45	mg
Opadry YS-1-19025-A clear	Oral; tablet	6	mg
Opadry YS-1-19025-A clear	Oral; tablet, controlled release	6	mg
Opadry YS-1-19025-A clear	Oral; tablet, sustained release, film coated	10	mg
Opadry YS-1-2007 yellow	Oral; tablet, film coated	5.25	mg
Opadry YS-1-2013 yellow	Oral; tablet	8	mg
Opadry YS-1-2063 yellow	Oral; tablet, film coated	30	mg
Opadry YS-1-2074 yellow	Oral; tablet, film coated	4.8	mg
Opadry YS-1-2074 yellow	Oral; tablet	19.25	mg
Opadry YS-1-2083 yellow	Oral; tablet, sustained action	27.1	mg
Opadry YS-1-2115 yellow	Oral; tablet	14.144	mg
Opadry YS-1-2134 yellow	Oral; tablet	147.8	mg
Opadry YS-1-2136 yellow	Oral; tablet	3.75	mg
Opadry YS-1-2167 yellow	Oral; tablet, sustained action	25.32	mg
Opadry YS-1-2181 yellow	Oral; tablet	15	mg
Opadry YS-1-2184 gold	Oral; tablet	15.52	mg
Opadry YS-1-2192 yellow	Oral-21; tablet	1.9	mg
Opadry YS-1-2305 orange	Oral; tablet, film coated	1.2	mg
Opadry YS-1-2308 dark orange	Oral; tablet, film coated	3	mg
Opadry YS-1-2383 orange	Oral; tablet	12.755	mg
Opadry YS-1-2398 orange	Oral; tablet	25.3	mg
Opadry YS-1-2449 orange	Oral; tablet, extended release	15	mg
Opadry YS-1-2522 orange	Oral; tablet	22.5	mg
Opadry YS-1-2527 orange	Oral; tablet	20	mg
Opadry YS-1-2534	Oral; tablet, film coated	20	mg
Opadry YS-1-2534	Oral; tablet	147.8	mg
Opadry YS-1-2546 orange	Oral; tablet	11.7	mg
Opadry YS-1-2546 orange	Oral; tablet, film coated	14	mg
Opadry YS-1-2548 orange	Oral; tablet	6.9	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-2548 orange	Oral; tablet, film coated	13	mg
Opadry YS-1-2549 orange	Oral; tablet	120	mg
Opadry YS-1-2558 orange	Oral; tablet, film coated	14	mg
Opadry YS-1-2558 orange	Oral; tablet	25	mg
Opadry YS-1-2563 orange	Oral; tablet	11.25	mg
Opadry YS-1-2564	Oral; tablet	7.5	mg
Opadry YS-1-2578 orange	Oral; tablet, sustained action	21	mg
Opadry YS-1-2596 orange	Oral; tablet, film coated	20	mg
Opadry YS-1-2604 beige	Oral; tablet	7.5	mg
Opadry YS-1-2612 beige	Oral; tablet, sustained action	34.5	mg
Opadry YS-1-2619	Oral; tablet	23	mg
Opadry YS-1-2621 rust	Oral; tablet, film coated	17	mg
Opadry YS-1-2621 rust	Oral; tablet	20	mg
Opadry YS-1-2623 brown	Oral; tablet, film coated	34	mg
Opadry YS-12630 yellow	Oral; tablet	4	mg
Opadry YS-1-2635 tan	Oral; tablet, sustained action	13	mg
Opadry YS-1-2660 salmon	Oral; tablet	7.5	mg
Opadry YS-1-2665 beige	Oral; tablet	9	mg
Opadry YS-1-2669 rust	Oral; tablet	24	mg
Opadry YS-1-2671 beige	Oral; tablet	16	mg
Opadry YS-1-3105 green	Oral; tablet	15	mg
Opadry YS-1-3130 green	Oral; tablet, controlled release	8.08	mg
Opadry YS-1-3130 green	Oral; tablet, coated	20	mg
Opadry YS-1-3130 green	Oral; tablet	36	mg
Opadry YS-1-3134 green	Oral; tablet, film coated	16	mg
Opadry YS-1-3146 green	Oral; tablet	10	mg
Opadry YS-1-3147	Oral; tablet	0.8	mg
Opadry YS-1-3166 green	Oral; tablet	12	mg
Opadry YS-1-3256 green	Oral; tablet	12	mg
Opadry YS-1-3288 green	Oral; tablet	4.05	mg
Opadry YS-1-4014 blue	Oral; tablet	7.8	mg
Opadry YS-1-4018 blue	Oral; tablet	28	mg
Opadry YS-1-4112 blue	Oral; tablet	147.8	mg
Opadry YS-1-4137 blue	Oral; tablet	11.5	mg
Opadry YS-1-4228 blue	Oral; tablet	19.94	mg
Opadry YS-1-4229 blue	Oral; tablet	22.5	mg
Opadry YS-1-4234 blue	Oral; tablet, sustained action	2.5	mg
Opadry YS-1-4235 blue	Oral; tablet	20.25	mg
Opadry YS-1-4236 blue	Oral; tablet	4.4	mg
Opadry YS-1-4236 blue	Oral; tablet, sustained action	5	mg
Opadry YS-1-4236 blue	Oral; tablet, film coated	12.5	mg
Opadry YS-1-4240 blue	Oral; tablet	11.34	mg
Opadry YS-1-4241 blue	Oral; tablet, film coated	6	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-4245 blue	Oral; tablet	6	mg
Opadry YS-1-4249 blue	Oral; tablet	22.68	mg
Opadry YS-1-4251 blue	Oral; tablet, film coated	2.52	mg
Opadry YS-1-4255	Oral; tablet, film coated	22.5	mg
Opadry YS-1-4256 blue	Oral; tablet, film coated	15.7	mg
Opadry YS-1-4256 blue	Oral; tablet, sustained action, coated	35.4	mg
Opadry YS-1-4282 blue	Oral; tablet, sustained action, film coated	10	mg
Opadry YS-1-4298 blue	Oral; tablet, film coated	20	mg
Opadry YS-14644 pink	Oral; tablet, sustained action	7.95	mg
Opadry YS-1-4700 purple	Oral; tablet	0.0064	mg
Opadry YS-1-4710	Oral; tablet	4	mg
Opadry YS-1-4739 lavender	Oral; tablet, sustained action	25	mg
Opadry YS-1-4812 lavender	Oral; tablet, sustained action	5	mg
Opadry YS-1-4845 purple	Oral; tablet, sustained action, film coated	16	mg
Opadry YS-1-6275 orange	Oral; tablet	3	mg
Opadry YS-1-6300	Oral; tablet, film coated	20	mg
Opadry YS-1-6312 yellow	Oral; tablet, film coated	17.45	mg
Opadry YS-1-6318 yellow	Oral; tablet	6	mg
Opadry YS-1-6320 yellow	Oral; tablet	4.8	mg
Opadry YS-1-6357 yellow	Oral; tablet	6	mg
Opadry YS-1-6370G yellow	Oral; tablet, coated	10	mg
Opadry YS-1-6378G yellow	Oral; tablet	13.4	mg
Opadry YS-1-6381 yellow	Oral; tablet, coated	3	mg
Opadry YS-1-6382G yellow	Oral; tablet, coated	6	mg
Opadry YS-1-6382G yellow	Oral; tablet	11	mg
Opadry YS-1-7000E white	Oral; tablet, film coated	40	mg
Opadry YS-1-7002 white	Oral; tablet, film coated	11.7	mg
Opadry YS-1-7003 white	Oral; tablet, sustained action, coated	6.24	mg
Opadry YS-1-7003 white	Oral; tablet, delayed action, enteric coated	9	mg
Opadry YS-1-7003 white	Oral; tablet, coated	14	mg
opadry YS-1-7003 white	Oral; tablet, controlled release	23.7	mg
Opadry YS-1-7003 white	Oral; tablet, extended release	24.39	mg
Opadry YS-1-7003 white	Oral; tablet, film coated	36	mg
Opadry YS-1-7003 white	Oral; tablet, sustained action	42.97	mg
Opadry YS-1-7003 white	Oral; tablet	147.8	mg
Opadry YS-1-7003H white	Oral; tablet, film coated	4	mg
Opadry YS-1-7006 clear	Oral-28; tablet	1.5	mg
Opadry YS-1-7006 clear	Oral; tablet, sustained action, film coated	2.625	mg
Opadry YS-1-7006 clear	Oral; tablet, delayed action, enteric coated	9	mg
Opadry YS-1-7006 clear	Oral; tablet, film coated	11	mg
Opadry YS-1-7006 clear	Oral; tablet, coated	11.16	mg
Opadry YS-1-7006 clear	Oral; tablet, controlled release	14.9	mg
Opadry YS-1-7006 clear	Oral; tablet, sustained action	38.4	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-1-7006 clear	Oral; tablet, extended release	47.05	mg
Opadry YS-1-7006 clear	Oral; tablet	50	mg
Opadry YS-1-7022 off-white	Oral; tablet	4	mg
Opadry YS-1-7027 white	Oral; tablet, sustained action, coated	16	mg
Opadry YS-1-7027 white	Oral; tablet	37	mg
Opadry YS-1-7040 white	Oral; tablet (immed./comp. release), film coated	17.88	mg
Opadry YS-1-7040 white	Oral; tablet	35.76	mg
Opadry YS-1-7059 white	Oral; tablet, sustained action, film coated	5	mg
Opadry YS-1-7059 white	Oral; tablet, sustained action	30	mg
Opadry YS-1-7060 white	Oral-21; tablet	1.9	mg
Opadry YS-1-7086 white	Oral; tablet, sustained action, coated	10	mg
Opadry YS-1-7086 white	Oral; tablet	12	mg
Opadry Y-S-17191 brown	Oral; tablet, delayed action, enteric coated	11.55	mg
Opadry YS-1-7444G white	Oral; tablet, coated	22	mg
Opadry YS-1-7449 white	Oral; tablet, film coated	12	mg
Opadry YS-1-7472 clear	Oral-21; tablet	1.5	mg
Opadry YS-1-7472 clear	Oral-28; tablet	1.5	mg
Opadry YS-1-7472 clear	Oral; tablet	2.18	mg
Opadry YS-1-7472 clear	Oral; tablet, sustained action, coated	2.9	mg
Opadry YS-1-7507 grey	Oral; tablet, film coated	6	mg
Opadry YS-1-7507 grey	Oral; tablet	19.057	mg
Opadry YS-1-7507 grey	Oral; tablet, sustained action, coated	34.23	mg
Opadry YS-1-7552 grey	Oral; tablet	7.5	mg
Opadry YS-1-7700 white	Oral; tablet	35.2	mg
Opadry YS-1-7706G white	Oral; tablet, coated	18.1	mg
Opadry YS-1-8325 beige	Oral; tablet	15	mg
Opadry YS-1-8343G beige	Oral; tablet, sustained action	19	mg
Opadry YS-1-8345G beige	Oral; tablet, film coated	6	mg
Opadry YS-1-8608 orange	Oral; tablet, film coated	10	mg
Opadry YS-1-8619 orange	Oral; tablet, film coated	11	mg
Opadry YS-1-89193 clear	Oral; tablet	13	mg
Opadry YS-1-9011 brown	Oral-21; tablet	1.9	mg
Opadry YS-1-9012 brown	Oral; tablet	13.4	mg
Opadry YS-1-9012 brown	Oral; tablet, sustained action, film coated	15.5	mg
Opadry YS1R1418 pink	Oral; tablet, film coated	8	mg
Opadry YS-1R-7006 clear	Oral; tablet	26.25	mg
Opadry YS-2-10657 blue	Oral; tablet	9.75	mg
Opadry YS-2-19071A clear	Oral; tablet, film coated	4.4	mg
Opadry YS-2-19114A clear	Oral; tablet, controlled release	1.11	mg
Opadry YS-2-19114A clear	Oral; tablet, sustained action	1.5	mg
Opadry YS-2-19114A clear	Oral; tablet	4.5	mg
Opadry YS-2-19114A clear	Oral; tablet, film coated	23.5	mg
Opadry YS-22-16576 brown	Oral; tablet	10	mg

Ingredient	Dosage form	Quantity	Unit
Opadry YS-22-18119 white	Oral; tablet	10	mg
Opadry YS-2-7013 clear	Oral; tablet, film coated	1.2	mg
Opadry YS-2-7013 clear	Oral; tablet, coated	2.7	mg
Opadry YS-2-7013 clear	Oral; tablet	4.44	mg
Opadry YS-2-7063 white	Oral; tablet, film coated	2.5	mg
Opadry YS-2-7063 white	Oral; tablet, sustained action	24	mg
Opadry YS-3-7011 clear	Oral; tablet, film coated	1	mg
Opadry YS-3-7011 clear	Oral; tablet	17.2	mg
Opadry YS-3-7031 clear	Oral; tablet	8	mg
Opadry YS-3-7413 clear	Oral; tablet, film coated	1.5	mg
Opadry YS-3-7413 clear	Oral; tablet, coated	2.4	mg
Opadry YS-3-7413 clear	Oral; tablet	4	mg
Opadry YS-3-7413 clear	Oral; tablet, extended release	4	mg
Opadry YS-5-12575 yellow	Oral; tablet, film coated	7.5	mg
Opadry YS-5-12576 yellow	Oral; tablet, film coated	15	mg
Opadry YS-5-1260 pink	Oral; tablet, sustained action	150	mg
Opadry YS-5-1296 pink	Oral; tablet	7.455	mg
Opadry YS-5-17266 tan	Oral; tablet, film coated	3.91	mg
Opadry YS-5-18068 white	Oral; tablet	12.25	mg
Opadry YS-5-18074 white	Oral; tablet	24	mg
Opadry YS-5-4277 blue	Oral; tablet, film coated	0.9	mg
Opadry YS-5-4278 blue	Oral; tablet, film coated	2.16	mg
Opadry YS-5-7017	Oral; tablet, sustained action, coated	32.3	mg
Opadry YS-5-7042 clear	Oral; tablet	22	mg
Opadry YS-5-7068	Oral; tablet	1.5	mg
Opadry YS-5-7099 white	Oral; tablet, extended release	11	mg
Opaglos GS 2-0310	Oral; tablet, sugar coated	0.76	mg
Opaglos GS 2-0310	Oral; tablet	3.5	mg
Opaglos S 0750	Oral; tablet	0.028	mg
Opalux AS 1406 pink	Oral; tablet	1	mg
Opalux AS 1537 pink	Oral; tablet, coated	9.1	mg
Opalux AS 1589 pink	Oral; tablet, coated	0.07	mg
Opalux AS 2006 yellow	Oral; tablet	0.6	mg
Opalux AS 2007 yellow	Oral; tablet	0.02	mg
Opalux AS 2052 yellow	Oral-28; tablet	2.7	mg
Opalux AS 2062 yellow	Oral; tablet	1.4	mg
Opalux AS 2086 chartreuse	Oral; tablet	3.6	mg
Opalux AS 2094	Oral; tablet, delayed action, enteric coated	2.4	mg
Opalux AS 2167 yellow	Oral; tablet, coated	4	mg
Opalux AS 2236	Oral; tablet	10.2	mg
Opalux AS 2236	Oral; tablet, sustained action	11.8	mg
Opalux AS 2236	Oral; tablet, coated	22.125	mg
Opalux AS 2269 yellow	Oral; tablet	1.424	mg

Ingredient	Dosage form	Quantity	Unit
Opalux AS 2324 orange	Oral; tablet, coated	10.6	mg
Opalux AS 2336 orange	Oral; tablet	0.972	mg
Opalux AS 2395 peach	Oral; tablet	0.6	mg
Opalux AS 2433 orange	Oral; tablet	0.8	mg
Opalux AS 2498 orange	Oral; tablet	0.2	mg
Opalux AS 2498 orange	Oral; tablet, coated	3	mg
Opalux AS 2613 tan	Oral; tablet, sugar coated	2.18	mg
Opalux AS 2620-B tan	Oral; tablet	2.62	mg
Opalux AS 2676 salmon jasper red	Oral; tablet	1.4	mg
Opalux AS 2768	Oral; tablet	0.082	mg
Opalux AS 2787 butterscotch	Oral; tablet	4.47	mg
Opalux AS 3288 green	Oral; tablet, repeat action	8.605	mg
Opalux AS 3308 green	Oral; tablet, coated	6	mg
Opalux AS 3348-C green	Oral; tablet, sustained action	6	mg
Opalux AS 3381	Oral; tablet	0.01	mg
Opalux AS 3391 green	Oral; tablet	0.2	mg
Opalux AS 3391 green	Oral; tablet, coated	1.184	mg
Opalux AS 3942 maroon	Oral; tablet	17.6	mg
Opalux AS 4025	Oral; tablet	0.0082	mg
Opalux AS 4151 blue	Oral; tablet, repeat action	8.429	mg
Opalux AS 4188 blue	Oral; tablet, sustained action	0.2	mg
Opalux AS 4258 blue	Oral; tablet	0.0047	ml
Opalux AS 4270 blue	Oral; tablet, coated	12.632	mg
Opalux AS 4855 purple	Oral; tablet	0.02	mg
Opalux AS 5034 red	Oral; tablet, coated	0.02	mg
Opalux AS 5107	Oral; tablet, sustained action	17.6	mg
Opalux AS 5162 green	Oral; tablet	4.4	mg
Opalux AS 5178 green	Oral; tablet	20	mg
Opalux AS 5203 green	Oral; tablet	9.6	mg
Opalux AS 7000-B	Oral; tablet, coated	4.95	mg
Opalux AS 7000-P white	Oral; tablet	3.81	mg
Opalux AS 7001	Oral; tablet	0.0082	mg
Opalux AS 9010 brown	Oral; tablet, coated	0.45	mg
Opalux AS 9050 brown	Oral-28; tablet	2.76	mg
Opalux AS-9030 brown	Oral; tablet	2.5	mg
Opalux blue	Oral; tablet	0.0021	ml
Opalux green	Oral; tablet	0.8	mg
Opaspray 3-1700	Oral; tablet	2.17	mg
Opaspray 3-1810	Oral; tablet	2.43	mg
Opaspray IM-176	Oral; tablet	23.5	mg
Opaspray K-1-1243	Oral; tablet, sustained action	7.6	mg
Opaspray K-1-1254	Oral; tablet, film coated	4.5	mg
Opaspray K-1-1279	Oral; tablet	21.13	mg

Ingredient	Dosage form	Quantity	Unit
Opaspray K-1-1289 pink	Oral; tablet	21.13	mg
Opaspray K-1-14016 pink	Oral; tablet, film coated	3.75	mg
Opaspray K-1-1413 pink	Oral; tablet	1.818	mg
Opaspray K-1-1414 pink	Oral; tablet	11.4	mg
Opaspray K-1-1455 pink	Oral; tablet	0.56	mg
Opaspray K-1-1526 pink	Oral; tablet	2	mg
Opaspray K-1-1563 pink	Oral; tablet, film coated	3.1	mg
Opaspray K-1-1573 lavender	Oral; tablet	12	mg
Opaspray K-1-1574	Oral; tablet, coated	2.5	mg
Opaspray K-1-1719 red	Oral; tablet, film coated	1.67	mg
Opaspray K-1-2004 yellow	Oral; tablet	1.06	mg
Opaspray K-1-2013 yellow	Oral; tablet	8	mg
Opaspray K-1-2043 yellow	Oral; tablet	0.263	mg
Opaspray K-1-2182 yellow	Oral; tablet, film coated	1	mg
Opaspray K-1-2182 yellow	Oral; tablet	3	mg
Opaspray K-1-2186 yellow	Oral; tablet	6.4	mg
Opaspray K-1-2216-A yellow	Oral; tablet, coated	0.5	mg
Opaspray K-1-2216-A yellow	Oral; tablet	3	mg
Opaspray K-1-2216-A yellow	Oral; tablet, film coated	3	mg
Opaspray K-1-2216-A yellow	Oral; tablet, sustained action	6.8	mg
Opaspray K-1-2227 yellow	Oral; tablet, film coated	1.69	mg
Opaspray K-1-2227 yellow	Oral; tablet	6	mg
Opaspray K-1-2228 yellow	Oral; tablet, sustained action	17.8	mg
Opaspray K-1-2239	Oral; tablet	10	mg
Opaspray K-1-2240 yellow	Oral; tablet	2.2	mg
Opaspray K-1-2256 yellow	Oral; tablet	6.586	mg
Opaspray K-1-2300 peach	Oral; tablet	3.001	mg
Opaspray K-1-2301 peach	Oral; tablet	4.7	mg
Opaspray K-1-2303 orange	Oral; tablet	0.35	mg
Opaspray K-1-2304 orange	Oral; tablet	1.8	mg
Opaspray K-1-2314 orange	Oral; tablet	3.74	mg
Opaspray K-1-2327 orange	Oral; tablet, sustained action	6	mg
Opaspray K-1-2330 orange	Oral; tablet	11.1	mg
Opaspray K-1-2335 orange	Oral; tablet, film coated	0.525	mg
Opaspray K-1-2406 orange	Oral; tablet, film coated	2.1	mg
Opaspray K-1-2406 orange	Oral; tablet	4.42	mg
Opaspray K-1-2417 orange	Oral; tablet, coated	9	mg
Opaspray K-1-2430	Oral; tablet	13.5	mg
Opaspray K-1-2441 orange	Oral; tablet	4.48	mg
Opaspray K-1-2471 orange	Oral; tablet	6.02	mg
Opaspray K-1-2473	Oral; tablet, film coated	2.5	mg
Opaspray K-1-2473	Oral; tablet	22.5	mg
Opaspray K-1-2492	Oral; tablet	36	mg

Ingredient	Dosage form	Quantity	Unit
Opaspray K-1-2531	Oral; tablet, coated	2.25	mg
Opaspray K-1-2554	Oral; tablet, coated	1.8	mg
Opaspray K-1-2568 orange	Oral; tablet	1.2	mg
Opaspray K-1-2570 orange	Oral; tablet	5.25	mg
Opaspray K-1-2588 orange	Oral; tablet	5.44	mg
Opaspray K-1-2614 beige	Oral; tablet	6	mg
Opaspray K-1-2614 beige	Oral; tablet, film coated	6	mg
Opaspray K-1-2621 brown	Oral; tablet, film coated	1.49	mg
Opaspray K-1-2626 orange	Oral; tablet	4	mg
Opaspray K-1-2656 beige	Oral; tablet, film coated	9.08	mg
Opaspray K-1-2674 beige	Oral; tablet	0.35	mg
Opaspray K-1-2685	Oral; tablet	3	mg
Opaspray K-1-2711	Oral; tablet	12.6	mg
Opaspray K-1-2723 butterscotch	Oral; tablet	7.5	mg
Opaspray K-1-2837	Oral; tablet, film coated	5.8	mg
Opaspray K-1-3000	Oral; tablet	0.6	mg
Opaspray K-1-3000	Oral; tablet, coated	0.6	mg
Opaspray K-1-3142 green	Oral; tablet, sustained action	5.1	mg
Opaspray K-1-3144 green	Oral; tablet	5.214	mg
Opaspray K-1-3147	Oral; tablet, film coated	0.6	mg
Opaspray K-1-3147	Oral; tablet, sustained action	2	mg
Opaspray K-1-3147	Oral; tablet	3	mg
Opaspray K-1-3148 green	Oral; tablet, film coated	0.737	mg
Opaspray K-1-3148 green	Oral; tablet	1.35	mg
Opaspray K-1-3156	Oral; tablet	1.683	mg
Opaspray K-1-3173 green	Oral; tablet	1.188	mg
Opaspray K-1-3178 green	Oral; tablet	1.6	mg
Opaspray K-1-3197 green	Oral; tablet	1.12	mg
Opaspray K-1-3209 green	Oral; tablet	3.476	mg
Opaspray K-1-3220 green	Oral; tablet	1.798	mg
Opaspray K-1-3227	Oral; tablet, coated	3.2	mg
Opaspray K-1-3227	Oral; tablet	4	mg
Opaspray K-1-3300-A green	Oral; tablet	1.188	mg
Opaspray K-1-3300-C green	Oral; tablet	2.1	mg
Opaspray K-1-4108 blue	Oral; tablet	1.5	mg
Opaspray K-1-4108 blue	Oral; tablet, film coated	1.5	mg
Opaspray K-1-4119	Oral; tablet	0.6	mg
Opaspray K-1-4119	Oral; tablet, coated	0.6	mg
Opaspray K-1-4122 blue	Oral; tablet	2.2	mg
Opaspray K-1-4122 blue	Oral; tablet, film coated	4.5	mg
Opaspray K-1-4136 blue	Oral; tablet, coated	0.6	mg
Opaspray K-1-4136 blue	Oral; tablet, film coated	3	mg
Opaspray K-1-4205 blue	Oral; tablet, coated	3	mg

Ingredient	Dosage form	Quantity	Unit
Opaspray K-1-4210-A	Oral; tablet	3.26	mg
Opaspray K-1-4213 blue	Oral; tablet, film coated	1.75	mg
Opaspray K-1-4214	Oral; tablet	2.7	mg
Opaspray K-1-4214	Oral; tablet, coated	2.7	mg
Opaspray K-1-4234 blue	Oral; tablet	1.528	mg
Opaspray K-1-4235 blue	Oral; tablet	15.567	mg
Opaspray K-1-4728	Oral; tablet	4.677	mg
Opaspray K-1-4731 purple	Oral; tablet	0.5	ml
Opaspray K-1-4743 lavender	Oral; tablet	2.2	mg
Opaspray K-1-4786	Oral; tablet	2.1	mg
Opaspray K-1-4786	Oral; tablet, coated	2.1	mg
Opaspray K-1-7000 white	Oral; tablet, coated	0.9	mg
Opaspray K-1-7000 white	Oral; tablet, sustained action	6.25	mg
Opaspray K-1-7000 white	Oral; tablet, film coated	7.5	mg
Opaspray K-1-7000 white	Oral; tablet	22.5	mg
Opaspray K-1-70008 white	Oral; tablet	22.4	mg
Opaspray K-1-7000B	Oral; tablet	15	mg
Opaspray K-1-7076	Oral; tablet, film coated	1.5	mg
Opaspray K-1-9027 brown	Oral; tablet	1.2	mg
Opaspray K-1-9039-L brown	Oral; tablet, film coated	4.65	mg
Opaspray K-1-9039-L brown	Oral; tablet	12.2	mg
Opaspray K-1-9060 red	Oral; tablet	2.9	mg
Opaspray K-1-9080 brown	Oral; tablet	3.275	mg
Opaspray K-1-9112 brown	Oral; tablet	2.7	mg
Opaspray L-2113	Oral; tablet	2.92	mg
Opaspray L-3305 green	Oral; tablet	6.34	mg
Opaspray L-3306 green	Oral; tablet	4.12	mg
Opaspray L-7000 white	Oral; tablet	3.69	mg
Opaspray M-1-2042	Oral; tablet, film coated	1.11	mg
Opaspray M-1-3459 B orange	Oral; tablet	4	mg
Opaspray M-1-4395B blue	Oral; tablet	2.63	mg
Opaspray M-1-7111-B	Oral; tablet, film coated	2.9	mg
Opaspray M-1-7111-B	Oral; tablet	40	mg
Opaspray M-1-711B white	Oral; tablet	27.78	mg
Opaspray M-1-7120 white	Oral; tablet, film coated	1.52	mg
Opaspray M-1-7120 white	Oral; tablet	4.57	mg
Opaspray WD-1270 pink	Oral; tablet, delayed action, enteric coated	6.7	mg
Opatint AD-25000 red	Oral; tablet, orally disintegrating	2.5	mg
Opatint DD-13009 orange	Oral; tablet	1.52	mg
Opatint DD-14000 pink	Oral; tablet, film coated	0.94	mg
Opatint DD-1800 white	Oral; tablet	84	mg
Opatint DD-18000 white	Oral; tablet, film coated	0.68	mg
Orange oil	Oral; tablet (immed./comp. release), uncoated, chewable	0.002	mg

Ingredient	Dosage form	Quantity	Unit
Palmitic acid	Oral; tablet	6	mg
Paraffin	Oral; tablet, extended release	0.06	mg
Paraffin	Oral; tablet, coated	0.07	mg
Paraffin	Oral; tablet, sustained action	150.2	mg
Pectin	Oral; bar, chewable	1400	mg
Pentasodium triphosphate	Oral; tablet	4	mg
Peppermint	Oral; tablet, orally disintegrating	2	mg
Peppermint	Oral; tablet, film coated	5	mg
Peppermint OIL	Sublingual; tablet	0.15	mg
Peppermint oil	Oral; tablet, orally disintegrating	0.6	mg
Peppermint oil	Oral; tablet	3.5	mg
Pharmaburst B1	Oral; tablet, orally disintegrating	671.13	mg
Pharmaburst B2	Oral; tablet, orally disintegrating	91.187	mg
Pharmaceutical glaze	Oral; tablet, film coated	0.74	mg
Pharmaceutical glaze	Oral; tablet, coated	3.4	mg
Pharmaceutical glaze	Oral; tablet	18	mg
Pharmaceutical glaze	Oral; tablet, delayed action, enteric coated	21.44	mg
Pharmaceutical glaze	Oral; tablet, sustained action	213.24	mg
Pharmacoat 606	Oral; tablet, delayed action, enteric coated	5.25	mg
Pharmacoat 606	Oral; tablet	6.25	mg
Pharmatose DCL II	Oral; tablet	455	mg
Phosphoric acid	Oral; tablet, sustained action, film coated	2.975	mg
Piperazine	Oral; tablet	0.4	mg
Placebo	Oral; tablet	305.04	mg
Plusweet	Sublingual; tablet	0.25	mg
Polacrilin	Oral-21; tablet	3	mg
Polacrilin	Oral-28; tablet	3	mg
Polacrilin potassium	Oral-21; tablet	3	mg
Polacrilin potassium	Oral; tablet, coated	5	mg
Polacrilin potassium	Oral-28; tablet	8	mg
Polacrilin potassium	Oral; tablet, sustained action	10	mg
Polacrilin potassium	Oral; tablet (immed./comp. release), uncoated, chewable	21	mg
Polacrilin potassium	Oral; tablet, film coated	40	mg
Polacrilin potassium	Oral; tablet	45.8	mg
Polish wax 7625 P 100	Oral; tablet	0.05	mg
Polishing solution IM-182	Oral; tablet	0.7	mg
Poloxamer 188	Oral; tablet, controlled release	5.61	mg
Poloxamer 188	Oral; tablet	66.9	mg
Poloxamer 407	Oral; tablet	100	mg
Poloxamer 407	Oral; tablet, film coated	106.7	mg
Polycarbophil	buccal; tablet	3.125	mg
Polycarbophil, calcium	Oral; troche	32.039	mg
Polydextrose	Oral; tablet, film coated	3.83	mg

Ingredient	Dosage form	Quantity	Unit
Polydextrose	Oral; tablet	3.84	mg
Polydextrose	Oral; tablet, coated	7.67	mg
Polydextrose K	Oral; tablet, film coated	8.125	mg
Polyethylene	Oral; tablet, sustained action	0.64	mg
Polyethylene	Buccal/sublingual; tablet	70	mg
Polyethylene glycol 1000	Oral; tablet, film coated	1.5197	mg
Polyethylene glycol 1450	Oral; tablet, film coated	0.125	mg
Polyethylene glycol 1450	Oral-28; tablet	0.125	mg
Polyethylene glycol 1450	Oral-21; tablet	0.6	mg
Polyethylene glycol 1450	Oral; tablet, extended release	4.24	mg
Polyethylene glycol 1500	Oral; tablet	1.2	mg
Polyethylene glycol 20000	Oral; tablet, delayed action, enteric coated	0.008	mg
Polyethylene glycol 20000	Oral; tablet	0.3	mg
Polyethylene glycol 20000	Oral-28; tablet	0.3	mg
Polyethylene glycol 300	Oral; tablet	1	mg
Polyethylene glycol 300	Oral; tablet, film coated	1.5	mg
Polyethylene glycol 3350	Oral; tablet, coated	0.5	mg
Polyethylene glycol 3350	Oral; tablet, controlled release	0.72	mg
Polyethylene glycol 3350	Oral; tablet, extended release	1	mg
Polyethylene glycol 3350	Oral; tablet, sustained action, coated	4.2	mg
Polyethylene glycol 3350	Oral; tablet, sustained action	8.5	mg
Polyethylene glycol 3350	Oral; tablet, film coated	13	mg
Polyethylene glycol 3350	Oral; tablet (immed./comp. release), uncoated, chewable	15	mg
Polyethylene glycol 3350	Oral; tablet	25	mg
Polyethylene glycol 3500	Oral; tablet	3.048	mg
Polyethylene glycol 400	Oral-21; tablet	0.15	mg
Polyethylene glycol 400	Oral-28; tablet	0.15	mg
Polyethylene glycol 400	Oral; tablet, sustained action, film coated	1.8	mg
Polyethylene glycol 400	Oral; tablet, coated	3.15	mg
Polyethylene glycol 400	Oral; tablet, film coated	5.91	mg
Polyethylene glycol 400	Oral; tablet, enteric coated particles	12.5	mg
Polyethylene glycol 400	Oral; tablet (immed./comp. release), film coated	20	mg
Polyethylene glycol 400	Oral; tablet, extended release	45	mg
Polyethylene glycol 400	Oral; tablet, sustained action	45	mg
Polyethylene glycol 400	Oral; tablet	105.065	mg
Polyethylene glycol 4000	Oral; tablet, delayed action, enteric coated	0.96	mg
Polyethylene glycol 4000	Oral; tablet, sustained action, film coated	1.8	mg
Polyethylene glycol 4000	Oral; tablet, film coated	1.859	mg
Polyethylene glycol 4000	Oral; tablet, coated	2	mg
Polyethylene glycol 4000	Sublingual; tablet	2.5	mg
Polyethylene glycol 4000	Oral; tablet, multilayer, extended release	2.8	mg
Polyethylene glycol 4000	Oral; tablet	15	mg
Polyethylene glycol 4000	Oral; tablet, extended release	45	mg

Ingredient	Dosage form	Quantity	Unit
Polyethylene glycol 4000	Oral; tablet, sustained action	454	mg
Polyethylene glycol 4500	Oral; tablet, film coated	0.386	mg
Polyethylene glycol 600	Oral; tablet, sustained action	1.2	mg
Polyethylene glycol 600	Oral; tablet	6	mg
Polyethylene glycol 6000	Vaginal; tablet, film coated	0.064	mg
Polyethylene glycol 6000	Oral-28; tablet	0.2024	mg
Polyethylene glycol 6000	Oral; tablet (immed./comp. release), film coated	0.322	mg
Polyethylene glycol 6000	Oral; tablet, sustained action, film coated	0.322	mg
Polyethylene glycol 6000	Oral; tablet, sustained action, coated	0.5	mg
Polyethylene glycol 6000	Oral; tablet, delayed action, enteric coated	0.6	mg
Polyethylene glycol 6000	Oral; tablet, extended release	1.4	mg
Polyethylene glycol 6000	Oral; tablet, delayed action	1.713	mg
Polyethylene glycol 6000	Oral-21; tablet, coated	2.148	mg
Polyethylene glycol 6000	Oral-28; tablet, coated	2.148	mg
Polyethylene glycol 6000	Vaginal; tablet	3	mg
Polyethylene glycol 6000	Oral; tablet, sustained action	12.5	mg
Polyethylene glycol 6000	Oral; tablet, film coated	30	mg
Polyethylene glycol 6000	Oral; tablet, coated	40	mg
Polyethylene glycol 6000	Oral; tablet	375	mg
Polyethylene glycol 7000K	Oral; tablet, controlled release	132.66	mg
Polyethylene glycol 800	Oral; tablet	0.9	mg
Polyethylene glycol 8000	Oral; tablet, sustained action, film coated	0.18	mg
Polyethylene glycol 8000	Oral; tablet, coated	0.21	mg
Polyethylene glycol 8000	Oral; tablet, delayed action, enteric coated	0.75	mg
Polyethylene glycol 8000	Oral-28; tablet	2.05	mg
Polyethylene glycol 8000	Oral; tablet, extended release	2.52	mg
Polyethylene glycol 8000	Oral; tablet, orally disintegrating, delayed release	2.55	mg
Polyethylene glycol 8000	Vaginal; tablet	3	mg
Polyethylene glycol 8000	Oral; tablet (immed./comp. release), uncoated, chewable	6.5	mg
Polyethylene glycol 8000	Oral; tablet, sustained action, coated	14	mg
Polyethylene glycol 8000	Oral; tablet, film coated	49	mg
Polyethylene glycol 8000	Oral; tablet, sustained action	100	mg
Polyethylene glycol 8000	Oral; tablet	167.6	mg
Polyethylene oxide	Oral; tablet	57.86	mg
Polyethylene oxide	Oral; tablet, sustained action, film coated	180	mg
Polyethylene oxide	Oral; tablet, controlled release	252.14	mg
Polyethylene oxide	Oral; tablet, extended release	335.79	mg
Polyethylene oxide	Oral; tablet, sustained action	543.9	mg
Polyethylene oxide 200K	Oral; tablet, extended release	81.43	mg
Polyethylene oxide 7000K	Oral; tablet, extended release	73.7	mg
Polyoxyl 20 stearate	Oral; tablet, sustained action	0.08	mg
Polyoxyl 40 hydrogenated castor oil	Oral; tablet, sustained action	25	mg
Polyoxyl 40 stearate	Oral; tablet, film coated	2	mg

Ingredient	Dosage form	Quantity	Unit
Polyoxyl 40 stearate	Oral; tablet	8.48	mg
Polyoxyl glyceryl stearate	Oral; tablet	23.33	mg
Polyoxylethylene isononylphenyl ester	Oral; tablet, sustained action, coated	1.54	mg
Polypropylene glycol	Oral; tablet	1.26	mg
Polysaccharides	Oral; tablet, delayed action, enteric coated	80.4	mg
Polysaccharides soy	Oral; tablet, delayed action, enteric coated	53.5	mg
Polysorbate 20	Oral; tablet, extended release	2.8	mg
Polysorbate 20	Oral; tablet	6	mg
Polysorbate 20	Vaginal; tampon	64.8	mg
Polysorbate 80	Sublingual; tablet	0.075	mg
Polysorbate 80	Oral; tablet, extended release	0.12	mg
Polysorbate 80	Oral; tablet, sustained action	0.12	mg
Polysorbate 80	Oral; tablet, sustained action, film coated	0.2	mg
Polysorbate 80	Oral; tablet, coated	2.2	mg
Polysorbate 80	Oral; tablet, orally disintegrating, delayed release	2.25	mg
Polysorbate 80	Oral; tablet, sustained action, coated	8	mg
Polysorbate 80	Oral; tablet, film coated	14.8	mg
Polysorbate 80	Oral; tablet	21.25	mg
Polysorbate 80	Oral; tablet (immed./comp. release), film coated	24	mg
Polyvinyl acetate	Oral; tablet	7	mg
Polyvinyl acetate	Oral; tablet, sustained action	46	mg
Polyvinyl alcohol	Oral; tablet, coated	0.697	mg
Polyvinyl alcohol	Oral; tablet, orally disintegrating	2	mg
Polyvinyl alcohol	Oral; tablet	14.4	mg
Polyvinyl alcohol	Oral; tablet, film coated	20	mg
Polyvinyl alcohol	Oral; tablet, extended release	34.1	mg
Polyvinylacetal	Oral; tablet	41.85	mg
Polyvinylpyrrolidone ethylcellulose	Oral; tablet	1.71	mg
Potassium bicarbonate	Oral; troche	4	mg
Potassium bicarbonate	Oral; tablet	12.2	mg
Potassium bitartrate	Oral; tablet, controlled release	10	mg
Potassium carbonate	Oral; tablet	25	mg
Potassium chloride	Oral; tablet	40	mg
Potassium phosphate, monobasic	Oral; tablet, sustained action	4	mg
Potassium phosphate, monobasic	Oral; tablet	25	mg
Potassium sorbate	Oral; tablet, sustained release, film coated	0.2	mg
Potassium sorbate	Oral; tablet	0.8	mg
Povidone K25	Oral; tablet, multilayer, extended release	1.8	mg
Povidone K25	Oral; tablet, delayed action, enteric coated	20	mg
Povidone K25	Oral; tablet, film coated	22.5	mg
Povidone K25	Oral; tablet	52	mg
Povidone K26/28	Oral; tablet	26.6	mg
Povidone K29-32	Oral-21; tablet	4.5	mg

Ingredient	Dosage form	Quantity	Unit
Povidone K29-32	Oral-28; tablet	4.51	mg
Povidone K29-32	Oral-28; tablet, coated	4.51	mg
Povidone K29-32	Sublingual; tablet	6	mg
Povidone K29-32	Oral; tablet (immed./comp. release), uncoated, chewable	10	mg
Povidone K29-32	Oral; tablet, delayed action, enteric coated	13	mg
Povidone K29-32	Oral; tablet, multilayer, coated	15	mg
Povidone K29-32	Oral; tablet, enteric coated particles	18.6	mg
Povidone K29-32	Oral; tablet, coated	21	mg
Povidone K29-32	Oral; tablet, extended release	40	mg
Povidone K29-32	Oral; tablet, sustained action	45	mg
Povidone K29-32	Oral; tablet	49.55	mg
Povidone K29-32	Vaginal; tablet	50	mg
Povidone K29-32	Oral; tablet, film coated	75	mg
Povidone K30	Oral-21; tablet	5	mg
Povidone K30	Oral-28; tablet	5	mg
Povidone K30	sublingual; tablet	8	mg
Povidone K30	Oral; tablet (immed./comp. release), uncoated, chewable	18	mg
Povidone K30	Oral; tablet, delayed action, enteric coated	27.2	mg
Povidone K30	Oral; tablet, orally disintegrating	35.71	mg
Povidone K30	Oral; tablet (immed./comp. release), uncoated, effervescent	40	mg
Povidone K30	Oral; tablet, film coated	42	mg
Povidone K30	Oral; tablet, extended release	50	mg
Povidone K30	Oral; tablet, sustained action	55	mg
Povidone K30	Oral; tablet	75	mg
Povidone K90	Oral-28; tablet	0.174	mg
Povidone K90	Oral; tablet, delayed action, enteric coated	4	mg
Povidone K90	Oral; tablet, coated	9.767	mg
Povidone K90	Oral; tablet, enteric coated particles	27.6	mg
Povidone K90	Oral; tablet, controlled release	35	mg
Povidone K90	Oral; tablet, sustained action	40.8	mg
Povidone K90	Oral; tablet, film coated	44	mg
Povidone K90	Oral; tablet	55	mg
Povidone K90	Oral; tablet, extended release	78	mg
Povidone K90F	Oral; tablet, sustained action	60	mg
Primajel	Oral; tablet	33.75	mg
Propyl gallate	Oral; tablet	0.04	mg
Propyl gallate	Oral; tablet, sustained action, coated	0.04	mg
Propyl gallate	Oral; tablet, sustained action	0.06	mg
Propylene glycol	Oral; tablet, coated	1.5	mg
Propylene glycol	Oral; tablet, enteric coated particles	4.3	mg
Propylene glycol	Oral; tablet, delayed action, enteric coated	6.95	mg
Propylene glycol	Oral; tablet, sustained action	9	mg
Propylene glycol	Oral; tablet, sustained action, film coated	12.8	mg

Ingredient	Dosage form	Quantity	Unit
Propylene glycol	Oral; tablet, film coated	14.4	mg
Propylene glycol	Oral; tablet	14.7	mg
Propylene glycol	Vaginal; tampon	62.1	mg
Propylene glycol–lecithin	Buccal; patch, controlled release	49.4	mg
Propylparaben	Oral; tablet, coated	0.002	mg
Propylparaben	Oral; tablet, film coated	0.04	mg
Propylparaben	Oral; tablet, sustained action	0.12	mg
Propylparaben	Oral; tablet (immed./comp. release), uncoated, chewable	0.142	mg
Propylparaben	Oral; tablet	0.2	mg
Propylparaben sodium	Oral; tablet	0.0625	mg
Propylparaben sodium	Oral; tablet, orally disintegrating	0.1	mg
Prosolv 50	Oral; tablet	11.4286	mg
Prosolv 50	Oral; tablet, controlled release	24	mg
Prosolv 50	Oral; tablet, sustained action	217.5	mg
Prosolv 50	Oral; tablet, extended release	315	mg
Prosolv 90	Oral; tablet, controlled release	-22.07	mg
Prosolv 90	Oral; tablet	104.307	mg
Prosolv SMCC 50	Oral; tablet	194	mg
Prosolv SMCC 90	Oral; tablet, controlled release	20	mg
Prosolv SMCC 90	Oral; tablet	199	mg
Prosweet	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
QUSO F-22	Oral; tablet	0.6	mg
Rosin	Oral; tablet, coated	3.44	mg
Saccharin	Sublingual; tablet	0.2	mg
Saccharin sodium	Buccal/sublingual; tablet	0.4	mg
Saccharin sodium	Rectal; tablet	0.6	mg
Saccharin sodium	Oral; tablet, film coated	1	mg
Saccharin sodium	Sublingual; tablet	1	mg
Saccharin sodium	Oral; tablet (immed./comp. release), uncoated, chewable	9	mg
Saccharin sodium	Oral; tablet	20	mg
Saccharin sodium, anhydrous	Oral; tablet	2.08	mg
Saccharin sodium, anhydrous	Oral; tablet (immed./comp. release), uncoated, chewable	7.5	mg
Satialgine H	Oral; tablet	20	mg
SD alcohol 3A	Oral; tablet	0.11	ml
SEPIFILM LP-761 blanc	Oral; tablet	5	mg
SEPIFILM LP-761 blanc	Oral; tablet, delayed action, enteric coated	10	mg
Shellac	Oral; tablet, delayed action, enteric coated	3.314	mg
Shellac	Oral; tablet, film coated	4.4	mg
Shellac	Oral; tablet, coated	5	mg
Shellac	Oral; tablet, sustained action	7.3	mg
Shellac	Oral; tablet	24.04	mg
Shellac P.V.P. solution no. 4	Oral-28; tablet	5.62	mg
Silica, diatomaceous	Oral; tablet (immed./comp. release), uncoated, chewable	2	mg

Ingredient	Dosage form	Quantity	Unit
Silica, diatomaceous	Oral; tablet	5	mg
Silica, diatomaceous	Oral; tablet, coated	7.2	mg
Silicon dioxide	Sublingual; tablet	1.2	mg
Silicon dioxide	Oral; tablet, coated	5	mg
Silicon dioxide	Oral; tablet, sustained action, coated	7	mg
Silicon dioxide	Oral; tablet, orally disintegrating	7.1	mg
Silicon dioxide	Oral; tablet, film coated	8	mg
Silicon dioxide	Oral; tablet, extended release	15	mg
Silicon dioxide	Oral; tablet	19.8	mg
Silicon dioxide	Oral; tablet, sustained release, film coated	26	mg
Silicon dioxide	Oral; tablet (immed./comp. release), uncoated, chewable	33	mg
Silicon dioxide	Oral; tablet, sustained action	40	mg
Silicon dioxide	Oral; tablet, sustained action, film coated	60	mg
Silicon dioxide	Oral; tablet, delayed action, enteric coated	85	mg
Silicon dioxide	Oral; tablet, delayed action	170	mg
Silicon dioxide, colloidal	Oral; tablet, repeat action	0.5	mg
Silicon dioxide, colloidal	Oral-21; tablet	0.65	mg
Silicon dioxide, colloidal	Oral-28; tablet	0.65	mg
Silicon dioxide, colloidal	Oral; tablet, for solution	0.75	mg
Silicon dioxide, colloidal	Oral; tablet, sugar coated	0.8	mg
Silicon dioxide, colloidal	Sublingual; tablet	1	mg
Silicon dioxide, colloidal	Buccal; tablet	1.25	mg
Silicon dioxide, colloidal	Oral; tablet, sustained action, multilayer, film coated	1.55	mg
Silicon dioxide, colloidal	Vaginal; insert	2.5	mg
Silicon dioxide, colloidal	Oral; tablet, enteric coated particles	3	mg
Silicon dioxide, colloidal	Oral; tablet, sustained action, coated	5	mg
Silicon dioxide, colloidal	Oral; tablet, controlled release	5.6	mg
Silicon dioxide, colloidal	Oral; tablet, delayed action, enteric coated	6	mg
Silicon dioxide, colloidal	Oral; tablet, dispersible	6	mg
Silicon dioxide, colloidal	Oral; tablet, sustained action, film coated	6.1	mg
Silicon dioxide, colloidal	Oral; tablet, orally disintegrating	7.8	mg
Silicon dioxide, colloidal	Vaginal; tablet	8	mg
Silicon dioxide, colloidal	Oral; tablet (immed./comp. release), film coated	8.5	mg
Silicon dioxide, colloidal	Oral; tablet, coated	16	mg
Silicon dioxide, colloidal	Oral; tablet, extended release	24.8	mg
Silicon dioxide, colloidal	Oral; tablet, sustained release, film coated	30	mg
Silicon dioxide, colloidal	Oral; tablet, film coated	33	mg
Silicon dioxide, colloidal	Oral; tablet, sustained action	48	mg
Silicon dioxide, colloidal	Oral; tablet (immed./comp. release), uncoated, chewable	84.8	mg
Silicon dioxide, colloidal	Oral; tablet	99	mg
Silicone	Vaginal; intrauterine device	27.48	mg
Simethicone	Oral; tablet, coated	0.0004	mg
Simethicone	Oral; tablet, orally disintegrating	0.04	mg

Ingredient	Dosage form	Quantity	Unit
Simethicone	Oral; tablet, film coated	0.18	mg
Simethicone	Oral; pastille	0.4	mg
Simethicone	Oral; tablet, delayed action, enteric coated	0.56	mg
Simethicone	Oral; tablet, extended release	0.61	mg
Simethicone	Oral; tablet	1.5	mg
Simethicone	Oral; tablet, sustained action	7.5	mg
Simethicone C	Oral; tablet, extended release	0.08	mg
Simethicone emulsion	Oral; tablet, coated	0.009	mg
Simethicone emulsion	Oral; tablet, delayed action, enteric coated	0.04	mg
Simethicone emulsion	Oral; tablet, sustained action	0.07	mg
Simethicone emulsion	Oral; tablet (immed./comp. release), film coated	0.12	mg
Simethicone emulsion	Oral; tablet	0.35	mg
Simethicone emulsion	Oral; tablet, sustained action, coated	1.41	mg
Simethicone MDX4-4036	Oral; tablet, sustained action	1.14	mg
Soap	Oral; tablet, sustained action	0.4	mg
Sodium alginate	Oral; tablet	20	mg
Sodium alginate	Oral; troche	64.309	mg
Sodium alginate	Oral; tablet, sustained action, film coated	240	mg
Sodium alginate	Oral; tablet, controlled release	262	mg
Sodium alginate	Oral; tablet (immed./comp. release), film coated	320	mg
Sodium alginate	Oral; tablet, sustained action	350	mg
Sodium aminobenzoate	Oral; tablet	0.001	mg
Sodium ascorbate	Oral; tablet	5	mg
Sodium benzoate	Oral; tablet, film coated	0.02	mg
Sodium benzoate	Oral; tablet, delayed action, enteric coated	0.34	mg
Sodium benzoate	Oral; tablet	0.75	mg
Sodium benzoate	Oral; tablet, for solution	5	mg
Sodium benzoate	Oral; tablet, coated	9	mg
Sodium benzoate	Oral; tablet (immed./comp. release), uncoated, effervescent	60	mg
Sodium bicarbonate	Oral; tablet, sustained action	2.56	mg
Sodium bicarbonate	Oral; tablet, sustained action, coated	2.56	mg
Sodium bicarbonate	Oral; tablet (immed./comp. release), film coated	4.24	mg
Sodium bicarbonate	Oral; tablet, coated	9	mg
Sodium bicarbonate	Buccal; gum, chewing	10	mg
Sodium bicarbonate	Oral; tablet, delayed action, enteric coated	15	mg
Sodium bicarbonate	Oral; tablet, orally disintegrating	26.97	mg
Sodium bicarbonate	Oral; tablet, film coated	40	mg
Sodium bicarbonate	Buccal; tablet	42	mg
Sodium bicarbonate	Vaginal; insert	43	mg
Sodium bicarbonate	Oral; tablet	125	mg
Sodium bicarbonate	Oral; tablet (immed./comp. release), uncoated, chewable	140	mg
Sodium bicarbonate	Oral; tablet (immed./comp. release), uncoated, effervescent	267	mg
Sodium bisulfite	Sublingual; tablet	0.5	mg

Ingredient	Dosage form	Quantity	Unit
Sodium bisulfite	Oral; tablet	0.65	mg
Sodium bitartrate	Oral; tablet, sustained action	306	mg
Sodium carbonate	Oral; tablet, delayed action, enteric coated	10	mg
Sodium carbonate	Oral; tablet	10.4	mg
Sodium carbonate	Buccal; tablet	20	mg
Sodium carbonate	Oral; tablet, film coated	25	mg
Sodium carbonate	Oral; troche	25	mg
Sodium carbonate	Buccal; gum, chewing	30	mg
Sodium carbonate	Oral; tablet, extended release	30	mg
Sodium carbonate hydrate	Oral; tablet	4.92	mg
Sodium carboxymethyl betaglucan	Oral-21; tablet	4	mg
Sodium caseinate	Oral; tablet	100	mg
Sodium chloride	Oral; tablet (immed./comp. release), uncoated, chewable	7.5	mg
Sodium chloride	Oral; tablet, controlled release	36	mg
Sodium chloride	Oral; tablet, sustained action	143.26	mg
Sodium chloride	Oral; tablet	148	mg
Sodium chloride	Oral; tablet, extended release	223.4	mg
Sodium citrate	Sublingual; tablet	2.68	mg
Sodium citrate	Oral; tablet, coated	18.34	mg
Sodium citrate	Oral; tablet, delayed action, enteric coated	82	mg
Sodium citrate	Oral; tablet, film coated	200	mg
Sodium citrate	Oral; tablet	275	mg
Sodium citrate	Oral; tablet (immed./comp. release), uncoated, chewable	300	mg
Sodium citrate, anhydrous	Oral; tablet, delayed action, enteric coated	15	mg
Sodium citrate, anhydrous	Oral; tablet	28	mg
Sodium citrate, anhydrous	Oral; tablet (immed./comp. release), uncoated, effervescent	935	mg
Sodium cyclamate	Oral; tablet (immed./comp. release), uncoated, chewable	75	mg
Sodium hydroxide	Oral; tablet, sustained action, coated	0.04	mg
Sodium hydroxide	Oral; tablet, orally disintegrating	0.156	mg
Sodium hydroxide	Oral; tablet, delayed action	0.211	mg
Sodium hydroxide	Oral; tablet, delayed action, enteric coated	0.32	mg
Sodium hydroxide	Oral; tablet, sustained action	0.4	mg
Sodium hydroxide	Oral; tablet, extended release	2.7	mg
Sodium hydroxide	Oral; tablet	6.72	mg
Sodium laureth sulfate	Oral; tablet	0.91	mg
Sodium lauryl sulfate	Sublingual; tablet	0.02	mg
Sodium lauryl sulfate	Oral; tablet, orally disintegrating	0.1	mg
Sodium lauryl sulfate	Oral-28; tablet	0.65	mg
Sodium lauryl sulfate	Oral; tablet (immed./comp. release), film coated	0.7	mg
Sodium lauryl sulfate	Oral; tablet, multilayer, extended release	0.8	mg
Sodium lauryl sulfate	Buccal/sublingual; tablet	1.1	mg
Sodium lauryl sulfate	Oral; tablet (immed./comp. release), uncoated, chewable	5	mg
Sodium lauryl sulfate	Vaginal; insert	5	mg

Ingredient	Dosage form	Quantity	Unit
Sodium lauryl sulfate	Oral; tablet, coated	5.2	mg
Sodium lauryl sulfate	Oral; tablet, delayed action, enteric coated	8.09	mg
Sodium lauryl sulfate	Oral; tablet, sustained action, coated	10.5	mg
Sodium lauryl sulfate	Oral; tablet, film coated	11.25	mg
Sodium lauryl sulfate	Oral; tablet, sustained action	20.62	mg
Sodium lauryl sulfate	Oral; tablet	50	mg
Sodium lauryl sulfate	Oral; tablet, extended release	51.69	mg
Sodium metabisulfite	Rectal; tablet	2	mg
Sodium metabisulfite	Sublingual; tablet	2	mg
Sodium metabisulfite	Oral; tablet	8	mg
Sodium phosphate	Oral-21; tablet	0.75	mg
Sodium phosphate	Oral; tablet	16	mg
Sodium phosphate, dibasic, anhydrous	Oral; tablet	48	mg
Sodium phosphate, dibasic, anhydrous	Oral; tablet, sustained action	110	mg
Sodium phosphate, dibasic, heptahydrate	Oral-20; tablet	0.0008	mg
Sodium phosphate, dibasic, heptahydrate	Oral; tablet, coated	0.22	mg
Sodium phosphate, dibasic, heptahydrate	Oral; tablet, delayed action, enteric coated	4	mg
Sodium phosphate, dibasic, heptahydrate	Oral; tablet, sustained action	70	mg
Sodium phosphate, dibasic, heptahydrate	Oral; tablet	80	mg
Sodium phosphate, dibasic, heptahydrate	Oral; tablet, sustained action, film coated	105	mg
Sodium phosphate, monobasic	Oral; tablet	1.376	mg
Sodium phosphate, monobasic, anhydrous	Oral-20; tablet	0.075	mg
Sodium phosphate, monobasic, anhydrous	Oral-21; tablet	0.075	mg
Sodium phosphate, monobasic, anhydrous	Oral; tablet	4.18	mg
Sodium phosphate, monobasic, anhydrous	Oral; tablet, delayed action, enteric coated	23.4	mg
Sodium phosphate, monobasic, anhydrous	Oral; tablet, sustained action, film coated	30.97	mg
Sodium phosphate, monobasic, monohydrate	Oral; tablet	31.72	mg
Sodium phosphate, monobasic, monohydrate	Oral; tablet, delayed action, enteric coated	35	mg
Sodium phosphate, tribasic, hydrate	Oral; tablet, delayed action, enteric coated	11	mg
Sodium starch glycolate	Oral; tablet, multilayer, coated	2	mg
Sodium starch glycolate	Oral-28; tablet	3.999	mg
Sodium starch glycolate	Oral-21; tablet	4	mg
Sodium starch glycolate	Sublingual; tablet	5.5	mg
Sodium starch glycolate	Buccal; tablet	8.3	mg
Sodium starch glycolate	Oral; tablet, delayed action	9	mg
Sodium starch glycolate	Oral; tablet, sustained action, film coated	10	mg
Sodium starch glycolate	Oral; tablet, enteric coated particles	12	mg
Sodium starch glycolate	Oral; tablet, controlled release	15	mg
Sodium starch glycolate	Oral; tablet, sustained action	15	mg
Sodium starch glycolate	Oral; tablet, delayed action, enteric coated	21	mg
Sodium starch glycolate	Oral; tablet, extended release	30	mg
Sodium starch glycolate	Oral; tablet (immed./comp. release), uncoated, chewable	50	mg

Ingredient	Dosage form	Quantity	Unit
Sodium starch glycolate	Oral; tablet, orally disintegrating	71.43	mg
Sodium starch glycolate	Oral; tablet, coated	73	mg
Sodium starch glycolate	Oral; tablet, film coated	85.5	mg
Sodium starch glycolate	Oral; tablet	876	mg
Sodium stearate	Oral; tablet, orally disintegrating	0.85	mg
Sodium stearate	Oral; tablet	9.48	mg
Sodium stearyl fumarate	Oral; tablet, coated	1.18	mg
Sodium stearyl fumarate	Oral; tablet (immed./comp. release), film coated	2	mg
Sodium stearyl fumarate	Oral; tablet (immed./comp. release), uncoated, chewable	2	mg
Sodium stearyl fumarate	Oral; tablet, controlled release	2	mg
Sodium stearyl fumarate	Oral; tablet, sustained action, coated	4	mg
Sodium stearyl fumarate	Oral; tablet, orally disintegrating	6	mg
Sodium stearyl fumarate	Oral; tablet, sustained action	8.9	mg
Sodium stearyl fumarate	Oral; tablet, sustained action, film coated	16	mg
Sodium stearyl fumarate	Oral; tablet, extended release	20	mg
Sodium stearyl fumarate	Oral; tablet	24.4	mg
Sodium stearyl fumarate	Oral; tablet, film coated	26	mg
Sodium stearyl fumarate	Oral; tablet, delayed action, enteric coated	27	mg
Sodium sulfate	Oral; tablet	7.37	mg
Sodium sulfate	Oral-20; tablet	120	mg
Sodium sulfate, anhydrous	Oral-21; tablet	96	mg
Sodium sulfate, anhydrous	Oral; tablet	105.1	mg
Sodium thiosulfate	Oral; tablet	3	mg
Sodium thiosulfate, anhydrous	Oral; tablet	0.6	mg
Sorbic acid	Oral; tablet, delayed action, enteric coated	0.0285	mg
Sorbic acid	Sublingual; tablet	0.16	mg
Sorbic acid	Oral; tablet, sustained action, film coated	0.4	mg
Sorbic acid	Oral; tablet	0.935	mg
Sorbitan monolaurate	Oral; tablet, film coated	83.9	mg
Sorbitan monooleate	Oral; tablet, coated	0.108	mg
Sorbitan monooleate	Oral; tablet, film coated	0.69	mg
Sorbitan monooleate	Oral; tablet, sustained action, film coated	1	mg
Sorbitan monooleate	Oral; tablet	1.7	mg
Sorbitan monooleate	Oral; tablet, delayed action, enteric coated	1.89	mg
Sorbitan monooleate	Oral; tablet, sustained action	7.8	mg
Sorbitol	Oral; tablet, film coated	5	mg
Sorbitol	Oral; tablet, coated	12.96	mg
Sorbitol	Sublingual; tablet	50.5	mg
Sorbitol	Oral; tablet, sustained action	53.75	mg
Sorbitol	Oral; bar, chewable	144	mg
Sorbitol	Buccal; gum, chewing	212.9	mg
Sorbitol	Oral; tablet (immed./comp. release), uncoated, chewable	300	mg
Sorbitol	Oral; tablet	337.28	mg

Ingredient	Dosage form	Quantity	Unit
Sorbitol solution	Oral; tablet	14	mg
Sorbitol solution	Buccal; gum, chewing	38.1	mg
Soybean oil	Oral; tablet (immed./comp. release), uncoated, chewable	0.14	mg
Soybean oil, hydrogenated	Oral; tablet, coated	3	mg
Soybean oil, hydrogenated	Oral; tablet	13.5	mg
Spearmint	Oral; tablet, orally disintegrating	0.0625	mg
Spectrablend CSL-15764 (blue)	Oral; tablet	5.91	mg
Stannous octoate	Vaginal; intrauterine device	0.14	mg
Starch	Buccal/sublingual; tablet	14.19	mg
Starch	Oral-20; tablet	22.25	mg
Starch	Buccal; tablet	22.5	mg
Starch	Oral; tablet (immed./comp. release), uncoated, chewable	25.75	mg
Starch	Oral; tablet, sustained action, coated	27	mg
Starch	Oral-21; tablet	34.465	mg
Starch	Oral-28; tablet	35.46	mg
Starch	Oral; tablet, sugar coated	43.25	mg
Starch	Oral; tablet, sustained action	48.6	mg
Starch	Rectal; tablet	55	mg
Starch	Sublingual; tablet	55	mg
Starch	Oral; tablet (immed./comp. release), film coated	74.3	mg
Starch	Oral; tablet, delayed action, enteric coated	76	mg
Starch	Oral; tablet, film coated	100	mg
Starch	Oral; tablet, coated	210	mg
Starch	Vaginal; tablet	260	mg
Starch	Oral; tablet	615.6	mg
Starch 1500 pregelatinized	Oral; tablet	50	mg
Starch 1500, pregelatinized	Oral; tablet, coated	22	mg
Starch 1500, pregelatinized	Oral; tablet, sustained action, multilayer, film coated	35	mg
Starch 1500, pregelatinized	Sublingual; tablet	43	mg
Starch 1500, pregelatinized	Oral; tablet (immed./comp. release), uncoated, chewable	50	mg
Starch 1500, pregelatinized	Oral; tablet, delayed action, enteric coated	51.5	mg
Starch 1500, pregelatinized	Vaginal; tablet	165	mg
Starch 1500, pregelatinized	Oral; tablet, film coated	180	mg
Starch 1500, pregelatinized	Oral; tablet	435.8	mg
Starch 1551	Sublingual; tablet	11	mg
Starch 1551	Oral; tablet (immed./comp. release), uncoated, chewable	25	mg
Starch 1551	Oral; tablet, film coated	90	mg
Starch 1551	Oral; tablet	100	mg
Starch 21	Oral; tablet, delayed action, enteric coated	20	mg
Starch 21	Oral; tablet	100	mg
Starch 7150	Oral; tablet	50	mg
Starch 826	Oral; tablet, film coated	10	mg
Starch 826	Sublingual; tablet	12	mg

Ingredient	Dosage form	Quantity	Unit
Starch 826	Oral; tablet	138	mg
Starch, corn	Vaginal; tablet, film coated	8	mg
Starch, corn	Oral-21; tablet, coated	9.9	mg
Starch, corn	Oral-28; tablet, coated	9.9	mg
Starch, corn	Oral; tablet, multilayer, extended release	10	mg
Starch, corn	Buccal; tablet	16.6	mg
Starch, corn	Oral; tablet, extended release	18	mg
Starch, corn	Oral-28; tablet	30.1	mg
Starch, corn	Oral; tablet, repeat action	32	mg
Starch, corn	Oral-21; tablet	33	mg
Starch, corn	Oral; tablet, delayed action, enteric coated	54	mg
Starch, corn	Oral-20; tablet	57	mg
Starch, corn	Sublingual; tablet	60	mg
Starch, corn	Oral; tablet, sustained action, film coated	74.3	mg
Starch, corn	Oral; tablet, sustained action	92	mg
Starch, corn	Vaginal; tablet	150	mg
Starch, corn	Oral; tablet, film coated	158	mg
Starch, corn	Oral; tablet (immed./comp. release), uncoated, chewable	170	mg
Starch, corn	Oral; tablet, coated	285	mg
Starch, corn	Oral; tablet	433.32	mg
Starch, corn 21	Oral; tablet	110.4	mg
Starch, modified	Oral; tablet	50	mg
Starch, potato	Oral; tablet, coated	2.1	mg
Starch, potato	Oral; tablet	80.5895	mg
Starch, pregelatinized	Oral-21; tablet, coated	6.6	mg
Starch, pregelatinized	Oral-28; tablet, coated	6.6	mg
Starch, pregelatinized	Oral; tablet, sugar coated	9.4	mg
Starch, pregelatinized	Oral-21; tablet	22.25	mg
Starch, pregelatinized	Oral-28; tablet	26.35	mg
Starch, pregelatinized	Oral; tablet (immed./comp. release), uncoated, chewable	32	mg
Starch, pregelatinized	Oral; tablet, sustained action, coated	33.75	mg
Starch, pregelatinized	Sublingual; tablet	43	mg
Starch, pregelatinized	Oral; tablet, sustained action	60	mg
Starch, pregelatinized	Oral; tablet, delayed action, enteric coated	64.8	mg
Starch, pregelatinized	Oral; tablet (immed./comp. release), film coated	71.35	mg
Starch, pregelatinized	Oral; tablet, coated	73	mg
Starch, pregelatinized	Oral; tablet, sustained action, film coated	75	mg
Starch, pregelatinized	Oral; tablet, film coated	240	mg
Starch, pregelatinized	Oral; tablet	345.95	mg
Starch, pregelatinized corn	Oral; tablet, coated	26.4	mg
Starch, pregelatinized corn	Oral; tablet, film coated	70	mg
Starch, pregelatinized corn	Vaginal; insert	210	mg
Starch, pregelatinized corn	Oral; tablet	482	mg

Ingredient	Dosage form	Quantity	Unit
Starch, pregelatinized tapioca	Oral; tablet	5	mg
Starch, rice	Oral; tablet, sustained action	301	mg
Starch, wheat	Oral; tablet	65.5895	mg
Stearic acid	Oral; tablet, sugar coated	0.9	mg
Stearic acid	Oral-21; tablet	1	mg
Stearic acid	Oral-28; tablet	1	mg
Stearic acid	Buccal; tablet	5	mg
Stearic acid	Oral; tablet, enteric coated particles	5	mg
Stearic acid	Sublingual; tablet	5.049	mg
Stearic acid	Buccal/sublingual; tablet	6	mg
Stearic acid	Oral; tablet, delayed action, enteric coated	8	mg
Stearic acid	Oral; tablet, sustained release, film coated	9	mg
Stearic acid	Oral; tablet (immed./comp. release), uncoated, chewable	15	mg
Stearic acid	Oral; tablet, film coated	22	mg
Stearic acid	Oral; tablet, sustained action, multilayer, film coated	26.48	mg
Stearic acid	Oral; tablet, coated	42.4	mg
Stearic acid	Vaginal; tablet	60	mg
Stearic acid	Oral; tablet	72	mg
Stearic acid	Oral; tablet, extended release	180	mg
Stearic acid	Oral; tablet, sustained action	187.5	mg
Stear-O-wet C	Oral; tablet, sustained action	10	mg
Stear-O-wet C	Oral; tablet	12	mg
Stear-O-wet M	Oral; tablet, extended release	1.2	mg
Stear-O-wet M	Oral; tablet, delayed action, enteric coated	4	mg
Stear-O-wet M	Oral; tablet, coated	5.5	mg
Stear-O-wet M	Oral; tablet, controlled release	11	mg
Stear-O-wet M	Oral; tablet (immed./comp. release), film coated	13.11	mg
Stear-O-wet M	Oral; tablet, film coated	18	mg
Stear-O-wet M	Oral; tablet	860	mg
Stearyl alcohol	Oral; tablet, controlled release	25	mg
Stearyl alcohol	Oral; tablet, sustained action, film coated	60	mg
Stearyl alcohol	Oral; tablet, sustained action	244	mg
Strawberry	Oral; tablet, orally disintegrating	1	mg
Strawberry	Oral; tablet, orally disintegrating, delayed release	3	mg
Succinic acid	Oral; tablet (immed./comp. release), uncoated, chewable	2.857	mg
Succinic acid	Oral; tablet, controlled release	4	mg
Succinic acid	Oral; tablet	65.1	mg
Sucralose	Oral-28; tablet	0.018	mg
Sucralose	Oral; tablet (immed./comp. release), uncoated, chewable	1.88	mg
Sucralose	Oral; tablet, orally disintegrating	5.75	mg
Sucrose	Sublingual; tablet	8.415	mg
Sucrose	Oral-20; tablet	12	mg
Sucrose	Oral-21; tablet	12	mg

Ingredient	Dosage form	Quantity	Unit
Sucrose	Buccal; tablet	16.6	mg
Sucrose	Oral-21; tablet, coated	19.374	mg
Sucrose	Oral-28; tablet, coated	19.374	mg
Sucrose	Oral; tablet, sugar coated	73.18	mg
Sucrose	Oral; tablet, film coated	84.2	mg
Sucrose	Buccal/sublingual; tablet	91	mg
Sucrose	Oral; tablet, sustained action, film coated	119.12	mg
Sucrose	Oral; tablet, repeat action	152.664	mg
Sucrose	Oral; tablet, sustained action	202	mg
Sucrose	Oral-28; tablet	216.5	mg
Sucrose	Oral; tablet, delayed action, enteric coated	279.495	mg
Sucrose	Oral; tablet, coated	400	mg
Sucrose	Oral; pastille	426	mg
Sucrose	Oral; tablet	900	mg
Sucrose	Oral; tablet (immed./comp. release), uncoated, chewable	1200	mg
Sucrose stearate	Oral; tablet, extended release	44.56	mg
Sucrose syrup	Oral; tablet	182.4	mg
Sugar confectioners	Sublingual; tablet	17	mg
Sugar confectioners	Oral-21; tablet	40	mg
Sugar confectioners	Oral-28; tablet	40	mg
Sugar confectioners	Oral; tablet, delayed action, enteric coated	44.5	mg
Sugar confectioners	Oral; tablet, coated	54	mg
Sugar confectioners	Oral; tablet, sustained action	175	mg
Sugar confectioners	Oral; tablet, film coated	200	mg
Sugar confectioners	Oral; tablet	215.68	mg
Sugar confectioners	Oral; tablet (immed./comp. release), uncoated, chewable	1438	mg
Sugar fruit fine	Oral; tablet	64.924	mg
Synchron oral carrier	Oral; tablet, sustained action	475	mg
Synchron oral carrier base KF	Oral; tablet, sustained action	30	mg
Synchron oral carrier vehicle type EM	Oral; tablet, sustained action	220	mg
Talc	Buccal; tablet	1.5	mg
Talc	Oral; tablet, controlled release	2.5	mg
Talc	Oral; tablet, orally disintegrating, delayed release	3	mg
Talc	Oral-21; tablet	3	mg
Talc	Oral-21; tablet, coated	4.198	mg
Talc	Oral-28; tablet, coated	4.198	mg
Talc	Oral-28; tablet	6.34	mg
Talc	Oral; tablet, enteric coated particles	6.5	mg
Talc	Buccal/sublingual; tablet	15	mg
Talc	Oral; tablet (immed./comp. release), uncoated, chewable	18	mg
Talc	Oral; tablet (immed./comp. release), film coated	22.8	mg
Talc	Oral; tablet, extended release	25	mg
Talc	Oral; tablet, delayed action	27.4	mg

Ingredient	Dosage form	Quantity	Unit
Talc	Oral; tablet, sustained action, coated	29.3	mg
Talc	Oral; tablet, sustained action, film coated	30	mg
Talc	Rectal; tablet	32.4	mg
Talc	Sublingual; tablet	32.4	mg
Talc	Oral; tablet, orally disintegrating	36	mg
Talc	Oral; tablet, film coated	54.72	mg
Talc	Oral; tablet, repeat action	73.933	mg
Talc	Oral; tablet, coated	75	mg
Talc	Oral; tablet, sustained action	91	mg
Talc	Oral; tablet	91.2	mg
Talc	Oral; tablet, delayed action, enteric coated	110	mg
Talcum powder	Oral; tablet, film coated	4.61	mg
Tartaric acid	Oral; tablet, coated	10	mg
Tartaric acid	Oral; tablet	15	mg
Tartaric acid	Oral; tablet, sustained action	29.2	mg
Tartaric acid	Oral; tablet, film coated	30	mg
Tartaric acid	Oral; tablet, orally disintegrating	45	mg
Tartaric acid, DL-	Sublingual; tablet	1.5	mg
Tartaric acid, DL-	Oral; tablet	13.74	mg
Tartaric acid, DL-	Oral; tablet, sustained action	30	mg
Tetrachloroethylene	Oral; tablet, delayed action, enteric coated	702	mg
Titanium dioxide	Oral-21; tablet	0.12	mg
Titanium dioxide	Oral-21; tablet, coated	0.274	mg
Titanium dioxide	Oral-28; tablet, coated	0.274	mg
Titanium dioxide	Oral; tablet, multilayer, extended release	1.1	mg
Titanium dioxide	Oral-28; tablet	1.1748	mg
Titanium dioxide	Oral; tablet (immed./comp. release), film coated	2.11	mg
Titanium dioxide	Oral; tablet, controlled release	2.463	mg
Titanium dioxide	Oral; tablet, orally disintegrating, delayed release	3	mg
Titanium dioxide	Oral; tablet, sustained action, film coated	3	mg
Titanium dioxide	Oral; tablet, sustained action, coated	4.17	mg
Titanium dioxide	Oral; tablet, delayed action	7.8	mg
Titanium dioxide	Oral; tablet, extended release	7.93	mg
Titanium dioxide	Oral; tablet, coated	10.57	mg
Titanium dioxide	Oral; tablet, film coated	12.5	mg
Titanium dioxide	Oral; tablet, enteric coated particles	15	mg
Titanium dioxide	Oral; tablet	27	mg
Titanium dioxide	Oral; tablet, delayed action, enteric coated	358	mg
Titanium dioxide	Oral; tablet, sustained action	358	mg
Tocophersolan	Oral-28; tablet	0.03	mg
Tragacanth	Oral; tablet	4	mg
Tragacanth	Buccal/sublingual; tablet	5	mg
Tragacanth	Oral; tablet, coated	7.5	mg

Ingredient	Dosage form	Quantity	Unit
Triacetin	Oral; tablet (immed./comp. release), film coated	0.72	mg
Triacetin	Oral; tablet, coated	1	mg
Triacetin	Oral; tablet, extended release	1.39	mg
Triacetin	Oral; tablet, sustained action	1.96	mg
Triacetin	Oral; tablet	3.7	mg
Triacetin	Oral; tablet, delayed action, enteric coated	6	mg
Triacetin	Oral; tablet, film coated	15.12	mg
Triacetin	Oral; tablet, controlled release	540	mg
Tribehenin	Oral; tablet	4.8	mg
Triceteareth-4 phosphate	Oral; tablet	180	mg
Triethyl citrate	Oral; tablet, sustained action, film coated	0.5	mg
Triethyl citrate	Oral; tablet, repeat action	0.9	mg
Triethyl citrate	Oral; tablet, sustained action	1.6	mg
Triethyl citrate	Oral; tablet, extended release	1.97	mg
Triethyl citrate	Oral; tablet, sustained action, coated	2.31	mg
Triethyl citrate	Oral; tablet (immed./comp. release), uncoated, chewable	2.8	mg
Triethyl citrate	Oral; tablet, film coated	3.6	mg
Triethyl citrate	Oral; tablet	5.1	mg
Triethyl citrate	Oral; tablet, orally disintegrating, delayed release	18.7	mg
Triethyl citrate	Oral; tablet, delayed action, enteric coated	20.177	mg
Trimyristin	Oral; tablet	16	mg
Trisodium citrate dihydrate	Oral; tablet	110	mg
TY-MED filler, blue	Oral; tablet	80	mg
Urea	Oral; tablet, coated	0.018	mg
Urea	Vaginal; tablet	50	mg
Vanillin	Oral; tablet, enteric coated particles	0.7	mg
Vanillin	Oral; tablet, film coated	0.78	mg
Vanillin	Oral; tablet, delayed action	0.8	mg
Vanillin	Oral; tablet, sustained action, film coated	0.8	mg
Vanillin	Oral; tablet, delayed action, enteric coated	1.16	mg
Vanillin	Oral; tablet	1.5	mg
Vanillin	Oral; tablet (immed./comp. release), uncoated, chewable	2.5	mg
Vanillin	Oral; tablet, sustained action	3.4	mg
Vanillin	Oral; tablet, coated	65.5	mg
Vegetable oil	Buccal; gum, chewing	14.4	mg
Vegetable oil	Oral; tablet	25	mg
Vegetable oil glyceride, hydrogenated	Oral; tablet, sustained action	35	mg
Vegetable oil, hydrogenated	Oral; tablet, coated	2	mg
Vegetable oil, hydrogenated	Oral; tablet (immed./comp. release), uncoated, chewable	8	mg
Vegetable oil, hydrogenated	Oral; tablet, extended release	20	mg
Vegetable oil, hydrogenated	Oral; tablet, film coated	33	mg
Vegetable oil, hydrogenated	Oral; tablet	40	mg
Vegetable oil, hydrogenated	Oral; tablet, sustained action	228.5	mg

Ingredient	Dosage form	Quantity	Unit
Velvetine black powder	Oral; tablet	0.025	mg
Vitamin E	Oral; tablet	0.033	mg
Vitamin E	Oral-21; tablet	0.1	mg
Vitamin E	Oral-28; tablet	0.1	mg
Vitamin E	Oral; tablet, sustained action	1.34	mg
Wax	Oral; tablet	0.02	mg
Wax, vegetable	Oral; tablet, enteric coated particles	2.5	mg
Wax, white	Oral; tablet, repeat action	0.037	mg
Wax, white	Oral; tablet, film coated	0.2	mg
Wax, white	Oral; tablet	0.4	mg
Wax, white	Oral; tablet, coated	3	mg
Wax, white	Oral; tablet, sustained action	14	mg
Wax, yellow	Oral; tablet, coated	0.296	mg
Wax, yellow	Oral; tablet	3.22	mg
Wheat flour	Oral; tablet	1.16	mg
Xanthan gum	Oral; tablet, orally disintegrating	0.15	mg
Xanthan gum	Oral; tablet	14	mg
Xanthan gum	Oral; tablet, sustained action	50	mg
Xanthan gum	Oral; troche	63.2	mg
Xanthan gum	Oral; tablet, sustained action, coated	74.25	mg
Xanthan gum	Oral; tablet, extended release	101.2	mg
Xylitol	Oral; tablet	15.04	mg
Xylitol	Oral; tablet, orally disintegrating	42.3	mg
Xylitol	Buccal; gum, chewing	203.6	mg
Zarzarol	Oral; tablet, coated	8.5	mg
Zein	Oral; tablet, repeat action	4.71	mg
Zein	Oral; tablet, coated	7.1278	mg
Zein	Oral; tablet, sustained action	135	mg
Zeolex	Oral; tablet, sustained action	2	mg
Zinc stearate	Oral; tablet, film coated	4.615	mg
Zinc stearate	Oral; tablet	10.2	mg
Zinc stearate	Oral; tablet, sustained action	36	mg

Part II

Manufacturing Formulations

Pharmaceutical Manufacturing Formulations

Acetaminophen and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophen (fine powder)	500.00
65.00	2	Anhydrous caffeine	65.00
15.00	3	Maize starch	15.00
10.00	4	Povidone (PVP K-30)	10.00
5.00	5	Croscarmellose sodium (Ac-Di-Sol)	5.00
33.00	6	Maize starch	33.00
8.00	7	Povidone (PVP K-90)	8.00
1.00	8	Polysorbate 80 (Tween 80)	1.00
10.00	9	Microcrystalline cellulose (Avicel™ PH102)	10.00
7.00	10	Sodium starch glycolate (Primojel®)	7.00
5.00	11	Croscarmellose sodium (Ac-Di-Sol)	5.00
2.00	12	Stearic acid (fine powder)	2.00
4.00	13	Talc (fine powder)	4.00
–	14	Purified water	155.00

Manufacturing Directions

1. Sift items 1 to 5 through a stainless steel 630-µm sieve. Load into mixer. Mix for 5 minutes at low speed.
2. Dissolve items 7 and 8 in 115 g of purified water (80–90°C) in a vessel.
3. Prepare slurry of item 6 in 40 g of purified water (25–30°C).
4. Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C.
5. Add the binder (item 4) to the paste.
6. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes.
7. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules into stainless steel trays for drying.
8. Dry the wet granules at 55°C for 8 hours. After 2 hours of drying, scrape the semidried granules to break the lumps to promote uniform drying. Check the LOD (limit: 1.5–2.0%). If required, dry further at 55°C for 1 hour.
9. Grind the dried granules through a 1.25-mm sieve, using a granulator at medium speed. Collect in stainless steel drums.
10. Load the granules into blender. Sift items 9 to 11 through a 500-µm sieve, using a suitable sifter, and add it to the blender. Mix for 2 minutes.
11. Sift items 12 and 13 through a 500-µm sieve.
12. Add 5 to 10 g of granules from bulk. Mix in.
13. Check temperature and humidity before compressing (recommended: relative humidity 55–60% at a temperature not exceeding 27°C).
14. Compress the granules using a rotary tabletting machine. Average weight of tablet is 665.00 mg.

Acetaminophen and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophen (crystalline)	500
50.00	2	Caffeine (Knoll)	50
90.00	3	Avicel® PH101	90
10.00	4	Kollidon® 30	10
20.00	5	Kollidon® CL	20
10.00	6	Polyethylene glycol (PEG-6000) (powder)	10

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with high-compression force.
2. Compress into 683-mg tablets, using 12-mm biplanar punches.
3. If the flowability of the powder mixture for tabletting is not high enough, some Aerosil 200 should be added.

Acetaminophen and Codeine Tablets (Tylenol)[a]

Each Tylenol with codeine tablet contains
No. 2 codeine phosphate, 15 mg; acetaminophen, 300 mg
No. 3 codeine phosphate, 30 mg; acetaminophen, 300 mg
No. 4 codeine phosphate, 60 mg; acetaminophen, 300 mg

[a]Tylenol inactive ingredients: Powdered cellulose, magnesium stearate, sodium metabisulfite, pregelatinized starch, starch (corn).

Acetaminophen and Diphenhydramine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Acetaminophen (fine powder)	325.00
26.00	2	Diphenhydramine HCl	26.00
50.00	3	Maize starch	50.00
07.00	4	Povidone (PVP K-30)	7.00
50.00	5	Microcrystalline cellulose (Avicel™ PH101)	50.00
42.00	6	Cornstarch	42.00
10.00	7	Povidone (PVP K-30)	10.00
09.50	8	Cellulose (powdered)	9.50
65.50	9	Cellulose (microcrystalline) (Avicel™ PH102)	65.50
20.00	10	Sodium starch glycolate (Primojel®)	20.00
08.00	11	Stearic acid (fine powder)	8.00
05.00	12	Talc (fine powder)	5.00
02.00	13	Magnesium stearate	2.00
–	14	Purified water	180.00

Manufacturing Directions

1. Sift items 1 to 5 through a 630-μm stainless steel sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 7 in 135 g of purified water (80–90°C) in a vessel.
4. Prepare a slurry of item 6 in 45 g of purified water (25–30°C).
5. Add the slurry to the vessel to make a translucent paste.
6. Cool to 45°C to 50°C.
7. Add the binder (item 4).
8. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.)
9. Unload the wet granules into stainless steel trays for drying.
10. Dry the wet granules in an oven at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break the lumps to promote uniform drying. Check the LOD (limit: 1–2%). If required, dry further at 55°C for 1 hour.
11. Grind the dried granules through a 1.25-mm sieve at medium speed.
12. Collect in stainless steel drums. Load the granules into blender.
13. Sift items 8 to 10 through a 500-μm sieve, using a suitable sifter, and add mixture to blender. Mix for 2 minutes.
14. Sift items 11 to 13 through a 500-μm sieve. Add 5 to 10 g of granules from bulk.
15. Mix in polyethylene bag for 1 minute. Add to blender. Blend for 1 minute.
16. Check the temperature and humidity before compressing (limit: temperature not exceeding 27°C; relative humidity 55–65%).
17. Compress the granules with a rotary tabletting machine. Compress to an average tablet weight of 620 mg.
18. Disintegration time is not more than (NMT) 15 minutes; friability NMT is 1.0%.
19. Coating: Use one of the HPMC aqueous formulations described in the Appendix, such as Yellow Opadry.

Acetaminophen and Orphenadrine Citrate Tablets (450 mg/35 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
450.00	1	Acetaminophen powder	450.00
35.00	2	Orphenadrine citrate, 5% excess	35.00
66.00	3	Starch (maize)	66.00
20.00	4	Microcrystalline cellulose (Avicel PH 102)	5.00
7.50	5	Aerosil 200	7.50
0.25	6	Dye yellow	0.25
16.00	7	PVP K30	16.00
5.00	8	Aerosil 200	5.00
7.50	9	Glycerine	7.50
10.00	10	Gelatin powder	10.00
25.00	11	Premojel	25.00
12.00	12	Avicel PH 102	12.00
2.00	13	Aerosil 200	2.00
2.00	14	Magnesium stearate	2.00
–	15	Water, purified, ca	464 mL

Manufacturing Directions

1. Charge items 7 and 6 into a mixer, add 50% of item 15, and mix for 10 to 15 minutes at medium speed.
2. Add item 5 into step 1 slowly, while stirring at medium speed, and disperse well.
3. Add item 9 and mix for 3 minutes.
4. In a separate vessel, add item 10 and the remaining 50% of item 15; mix for 5 minutes at medium speed.
5. Add step 3 into step 4 and mix for 2 to 3 minutes.
6. In a separate mixer, charge items 1 to 5 and mix and chop for 3 minutes at slow speed.
7. Add the solution from step 5 to step 6 and mix for 2 to 3 minutes.
8. Dry the wet mass in a fluid-bed dryer at 60°C for 60 minutes until a loss on drying rate of 1.5% to 2.5% is reached.
9. Pass the dried granules through a 6-mm sieve followed by a 1.5-mm sieve in a granulator.
10. Add to the granules items 11 to 13, previously sieved through a 500-μm sieve. Mix for 3 minutes.
11. Add item 14, previously sieved through a 250-μm sieve, and blend for 1 minute.
12. Compress using 12.7-mm round flat punches to a fill weight of 660 mg.

Acetaminophen and Phenprobamat Tablets (200 mg/200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Acetaminophen powder $<$ 0.5 mm	200.00
200.00	2	Phenprobamat	200.00
35.00	3	Microcrystalline cellulose (Avicel PH 101)	35.00
20.00	4	Kollidon VA 64	20.00
10.00	5	Kollidon CL	10.00
5.00	6	Magnesium stearate	5.00
6.00	7	Aerosil 200	6.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 475-mg tablets, using 12-mm biplanar punches.

Acetaminophen and Pseudoephedrine Hydrochloride Tablets

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
50.00	3	Cornstarch	50.00
7.00	4	Povidone (PVP K-30)	7.00
50.00	5	Microcrystalline cellulose (Avicel™ PH101)	50.00
42.00	6	Cornstarch	42.00
10.00	7	Povidone (PVP K-30)	10.00
9.50	8	Cellulose (powdered)	9.50
60.00	9	Cellulose (microcrystalline) (Avicel™ PH102)	60.00
20.00	10	Sodium starch glycolate (Primojel®)	20.00
8.00	11	Stearic acid (fine powder)	8.00
5.00	12	Talc (fine powder)	5.00
2.00	13	Magnesium stearate	2.00
–	14	Purified water	180.00

Manufacturing Directions

1. Sift items 1 to 5 through a stainless steel 630-μm sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 7 in 135 g of purified water (80–90°C) in a vessel.
4. Prepare a slurry of item 6 in 45 g of purified water (25–30°C).
5. Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C. Add the binder (item 4).
6. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules into stainless steel trays for drying.
7. Dry the wet granules in oven at 55°C for 10 hours.
8. After 2 hours of drying, scrape the semidried granules to break up the lumps for uniform drying.
9. Check the LOD (limit: 1–2.0%). If required, dry further at 55°C for 1 hour.
10. Transfer the dried granules to stainless steel drums.
11. Grind the dried granules through a 1.25-mm sieve, using granulator at medium speed. Collect in stainless steel drums. Load the granules into blender.
12. Sift items 8 to 10 through a 500-μm sieve, using a suitable sifter, and add to blender. Mix for 2 minutes.
13. Sift items 11 to 13 through a 500-μm sieve.
14. Add 5 to 10 g of granules.
15. Mix in a polyethylene bag for 1 minute. Add to blender. Blend for 1 minute. Unload in stainless steel drums.
16. Compress into 620-mg tablets, using 6-mm capsule-shaped punches.
17. Coat: The formula for the coating solution is determined to obtain a weight gain of 10 mg per caplet, considering evaporation and loss during the coating operation.

Acetaminophen Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Acetaminophen, milled (Hoechst)	300.00
600.00	2	Sucrose, milled	600.00
550.00	3	Kollidon® CL-M	550.00
30.00	4	Orange flavor (FDO)	30.00
30.00	5	Strawberry flavor (FDO)	30.00
60.00	6	Kollidon® 30	60.00
QS	7	Ethanol (96%)	~425.00

Manufacturing Directions

1. Granulate mixture of items 1 to 5 with solution of items 6 and 7, pass through a sieve, and press with medium-compression force.
2. Average weight of tablet is 1620 mg, obtained using a 20-mm biplanar punch.
3. Taste is sweet, fruity, and only very slightly bitter.

Acetaminophen, Chlorpheniramine Maleate, and Pseudoephedrine Caplets

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
2.10	3	Chlorpheniramine maleate	2.10
50.00	4	Cornstarch	50.00
7.00	5	Povidone (PVP K-30)	7.00
50.00	6	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
42.00	7	Cornstarch	42.00
10.00	8	Povidone (PVP K-30)	10.00
9.50	9	Powdered cellulose	9.50
77.90	10	Cellulose (microcrystalline) (Avicel™ PH102)	77.90
20.00	11	Sodium starch glycolate (Primojel®)	20.00
8.00	12	Stearic acid (fine powder)	8.00
5.00	13	Talc (fine powder)	5.00
2.00	14	Magnesium stearate	2.00
–	15	Purified water	180.00

Manufacturing Directions

1. Sift items 1 to 6 through a 630-μm stainless steel sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 8 in 135 g of item 15 (80–90°C) in a vessel.
4. Prepare a slurry of item 7 in 45 g of item 15 (25–30°C). Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C.
5. Add the binder (item 5) to step above.
6. Mix at low speed over a period of 3 minutes. Scrape sides and blades.
7. Mix and chop at low speed for 1 for 2 minutes. Check the end point of granulation. If required, add additional item 15 to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules in stainless steel trays for drying.
8. Dry the wet granules at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying. Check the LOD (limit: 1.0–2.0%). If required, dry further at 55°C for 1 hour.
9. Grind the dried granules through a 1.25-mm sieve at medium speed. Collect in stainless steel drums.
10. Load the granules into blender.
11. Sift items 9 to 11 through a 500-μm sieve, using suitable sifter, and add mixture to blender. Mix for 2 minutes.
12. Sift items 12 to 14 through a 500-μm sieve.
13. Add 5 to 10 g of granules from bulk. Mix in a polyethylene bag for 1 minute.
14. Add to blender. Blend for 1 minute.
15. Check temperature and humidity before start of compression; temperature should not exceed 27°C and recommended relative humidity is 55% to 65%.
16. Compress the granules using rotary tabletting machine. Tablet weight is 640 mg.
17. Coating: Select an appropriate coating such as Opadry HPMC. The formula for the coating solution is determined to obtain a weight gain of 10 mg per caplet, considering evaporation and loss during coating operation.

Acetaminophen, Dextromethorphan, and Pseudoephedrine Caplets

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
15.50	3	Dextromethorphan HBr	15.50
50.00	4	Cornstarch	50.00
7.00	5	Povidone (PVP K-30)	7.00
50.00	6	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
42.00	7	Cornstarch	42.00
10.00	8	Povidone (PVP K-30)	10.00
9.50	9	Cellulose (powdered)	9.50
64.50	10	Cellulose (microcrystalline) (Avicel™ PH102)	64.50
20.00	11	Sodium starch glycolate (Primojel®)	20.00
8.00	12	Stearic acid (fine powder)	8.00
5.00	13	Talc (fine powder)	5.00
2.00	14	Magnesium stearate	2.00
–	15	Purified water	180.00

Manufacturing Directions

Follow the manufacturing directions provided for acetaminophen, chlorpheniramine, and pseudoephedrine caplets.

Acetaminophen, Dextropropoxyphen Hydrochloride Tablets (325 mg/32 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Acetaminophen	325.000
32.00	2	Dextropropoxyphen hydrochloride	32.500
8.00	3	Povidone (K29–32)	8.000
7.50	4	Starch (maize)	7.500
QS	5	Water, purified	80.00 mL
10.00	6	Cellulose microcrystalline (Avicel PH 101)	10.000
5.00	7	Talc purified	5.000
2.00	8	Magnesium stearate	2.000
QS	9	Coating solution white opaque methocel-ethocel	160.000 mL

Manufacturing Directions

1. Granulation
   a. Pass acetaminophen, dextropropoxyphen, and starch through a 595-µm aperture screen, transfer to a suitable mixer, and mix for 10 minutes.
   b. Warm the water and dissolve the povidone.
   c. Slowly add the povidone solution to the mixer and mix until a suitable-consistency mass is obtained. Add extra water if needed.
   d. Pass the mass through a 4-mm aperture screen on an oscillating granulator and dry in a tray dryer at 105°C until the LOD is below 2% (Brabender, 105°C, 1 hour) or the equivalent.
   e. Pass the granules through a 1.59-mm aperture screen on a suitable comminuting mill, at medium speed, with knives forward into tared polyethylene-lined drums.
2. Lubrication
   a. Transfer the dried granulation to a suitable blender.
   b. Screen the cellulose microcrystalline, talc, and povidone through a 595-µm aperture screen, add to the blender, and blend for 5 minutes.
   c. Screen the magnesium stearate through a 400-µm aperture screen and add it to the blender. Blend for 2 minutes.
   d. Discharge the granule into polyethylene-lined drums, seal, and weigh for yield.

3. Compression
   a. Compress using 14.5 × 7.5 mm capsule-shaped punches. Weight of 10 tablets is about 4.05 g, not more than 3% variation; thickness is 5.2 to 5.8 mm (range not more than ±5%); hardness is 8 kPa; and disintegration time not more than 15 minutes in water.
   b. Collect in *clean*, tared polyethylene-lined drums, and weigh for yield.
4. Coating
   a. *Pan spray:* Binks Bullow L450 spray gun or equivalent, fitted with a No. 63B material nozzle, a No. 66SF or 66SD atomizing nozzle, or a No. 39 needle.
      i. Divide tablets and solution.
      ii. Load into pan and preheat for 3 hours to 48°C.
      iii. Apply the solution at 10 to 21 psi, with a liquid pressure of 5 to 10 psi, to give a flow rate of 350 to 500 mL/min at a pan speed of 20 to 25 rpm. Rotate pan and commence spraying with continuous application of hot air at 46°C to 49°C (damper fully open). Ensure that the tablet bed does not become too hot. Tablets should be put only just above room temperature. You must switch off hot air when a coating solution is not being sprayed. Continue applying the solution until the average tablet weight has increased by 8 mg. When this weight gain is achieved, roll the tablets in cool air until dry. When completely dry, remove the tablets from the pan, and transfer to polyethylene-lined drums. Leave the drums open for at least 6 hours in a dust-free area.
   b. *Accela Cota:* Airless high-pressure spray system with two guns. Nozzle type: 0.018-in. (0.45-mm) orifice diameter with a 65° spray angle, pan speed of 5 rpm, inlet temperature of 70°C, inlet airflow set at quarter to half available flow, and exhaust sufficient to maintain coating drum under negative pressure (set water gauge at 7 in.).
      i. Divide tablets and solution.
      ii. Load tablets, rotate pan occasionally, and warm tablets until the exhaust temperature is 38°C to 42°C. Do not rotate longer than is necessary to achieve even warming.
      iii. Adjust the pump pressure to give an application rate of approximately 500 to 600 mL/min. Commence spraying with the coating solution. Adjust the pressure to maintain the exhaust temperature of 38°C to 42°C.
      iv. When the average weight gain of 8 mg is obtained, the tablets are dried: reduce pan speed to 7 rpm and maintain the inlet temperature and exhaust settings for 5 minutes. If the exhaust temperature reaches 45°C, switch off heat and control rotation for another 10 minutes; occasionally rotate the pan to ensure even cooling. Remove tablets when the exhaust temperature is 28°C to 32°C.
      v. Ensure that tablets are thoroughly dry, and unload into polyethylene-lined drums; leave the drum unsealed for 1 hour in a dust-free humidity-controlled area.

Acetaminophen Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophenl (powder < 300 μm)	500.00
500.00	2	Sodium bicarbonate	500.00
430.00	3	Tartaric acid (powder)	430.00
200.00	4	Dextrose	200.00
QS	5	Flavoring	QS
20.00	6	Kollidon® 30	20.00
—	7	Isopropanol	100.00 mL
60.00	8	PEG-6000 (powder)	60.00

Manufacturing Directions

1. Granulate the mixture of items 1 to 5 with solution of items 6 and 7.
2. Pass through an 0.8-mm sieve, add item 8, and then mix.
3. Press to tablets (average weight, 1700 mg; 16-mm-diameter biplanar tablet).

Acetaminophen Fast-Dissolving Tablet

Manufacturing Directions

1. To the vortex of a rapidly stirred vessel containing 2.85 kg of deionized water is added 300 g of croscarmellose sodium, forming slurry. This slurry is mixed for 10 minutes.
2. Concurrently, 5.0 kg of powdered acetaminophen is placed in the bowl of a mixer.
3. At the conclusion of the mixing time for the slurry of croscarmellose sodium, the slurry is added slowly to the acetaminophen in the mixer bowl, forming a granulation, which is then placed in trays and dried at 70°C in an oven for 3 hours.
4. The dry granulation is then passed through a US Standard 14-mesh screen (1410 μm).
5. Dry granulation (4796 g) is then placed in a twin-shell blender, and to this are added 1584 g of Avicel AC-815 (85% microcrystalline cellulose coprocessed with 15% of a calcium sodium alginate complex) and 1584 g of microcrystalline cellulose (Avicel PH-302).
6. This is thoroughly blended for 10 to 15 minutes after which 36.24 g of magnesium stearate is added and mixed for an additional 5 minutes.
7. Prior to being added to the blender, the magnesium stearate had been passed through a US Standard 30-mesh screen.
8. The resulting blend is compressed into caplet-shaped tablets with an average weight of 0.884 g and an average thickness of 7.869 mm (0.3098 in.).
9. The hardness of these tablets averaged 11.98 kPa. Friability of these tablets is measured at 0.433% after 10 minutes and 0.847% after 19 minutes.
10. The average disintegration time is 26 seconds in 10 mL of deionized water, forming a suspension with minimal shaking.

Acetaminophen, Ibuprofen, and Orphenadrine Tablets (250 mg/200 mg/200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetaminophen (powder < 300 μm)	250.00
200.00	2	Ibuprofen	200.00
200.00	3	Orphenadine hydrochloride	200.00
200.00	4	Ludipress	200.00
5.00	5	Magnesium stearate	5.00
5.00	6	Aerosil 200	5.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with high-compression force.
2. Compress into 761-mg tablets, using 12-mm planar punches.

Acetaminophen, Ibuprofen, and Orphenadine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetaminophen (powder < 300 μm)	250.00
200.00	2	Ibuprofen	200.00
100.00	3	Orphenadine hydrochloride	100.00
200.00	4	Ludipress®	200.00
5.00	5	Magnesium stearate	5.00
5.00	6	Aerosil® 200	5.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve and mix.
2. Press with high-compression force.
3. Tablet weight is 761 mg for a 12-mm biplanar tablet.

Acetaminophen Microsphere Tablet

Manufacturing Directions

1. Formulation: Acetaminophen (APAP) powder (melting point 169–170.5°C) 85%, carnauba wax 7.5%, Pluronic F68 7.5%.
2. Pluronic is milled through a FitzMill, using a 40-mesh screen.
3. All of the ingredients are blended at 60 Hz of slow speed, with chopper, for 10 minutes.
4. The blend is then subjected to liquiflash processing at 60 Hz and 37% nominal power, using the 5-in. V-groove heater head.
5. The collected microspheres are sieved.
6. The fraction passing through a 40-mesh sieve and retained on 120-mesh sieve is coated.
7. The microspheres selected are coated in a fluid-bed coater for taste-masking at a 30% coating level with a coating solution containing a 1:1 ethylcellulose/hydroxypropylcellulose blend in acetone:isopropyl alcohol solvent.
8. A preblend of 78.25% sucrose, 11.0% sorbitol, 10.0% xylitol, and 0.75% TWEEN (Polysorbate) 80 is prepared.
9. The floss preblend is processed using the 5 in. crown head at a temperature of 250°C and rotational speed of 60 Hz (3600 rpm).
10. The floss collected is mixed with 2% lactose (w/w) for 2 minutes at 100 rpm and 200 proof ethanol sprayed in a quantity equal to 0.5% (w/w) of the quantity of the floss.
11. The floss is then dried at 45°C for 90 minutes with intermittent mixing.
12. The dried floss is screened through a 20-mesh screen.
13. APAP taste-masked microspheres (step 5) 47.97, floss (step 6) 48.88, grape flavor 0.70, citric acid 1.50, acesulfame potassium 0.20, silicon dioxide 0.25, and sodium stearyl fumarate 0.50 are processed.
14. The coated APAP microspheres are blended with the sieved floss for 5 minutes in a mixer, followed by the addition of flavors, sweeteners, and citric acid for another 3 minutes.
15. Thereafter silicon dioxide is added and the mix blended for another 2 minutes. The final addition, sodium stearyl fumarate, is followed by blending for an additional 2 minutes.
16. The blend is then tabletted using flat-faced bevel edge punches (tablet weights are 255 mg for 9-mm punch tooling, equivalent to 80-mg APAP dose, and 510 mg for 12-mm punch tooling, equivalent to 160-mg APAP dose).
17. The hardness values ranged from 0.5 to 2.0 kPa.

Acetaminophen, Norephedrine, and Phenyltoloxamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Acetaminophen (crystalline) (Merck)	300.00
25.00	2	Norephedrine hydrochloride (Knoll)	25.00
22.00	3	Phenyltoloxamine	22.00
200.00	4	Cornstarch	200.00
25.00	5	Kollidon® 30	25.00
–	6	Ethanol (96%)	QS
25.00	7	Kollidon® CL	25.00
5.00	8	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate mixture of items 1 to 5 with solution of items 5 and 6.
2. Dry, pass through an 0.8-mm sieve, and add items 7 and 8.
3. Press with high-compression force.
4. Tablet weight is 601 mg for 12-mm biplanar tablet.

Acetaminophen, Norephedrine, and Phenyltoloxamine Tablets (300 mg/25 mg/22 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Acetaminophen crystalline	300.00
25.00	2	Norephedrine hydrochloride	25.00
22.00	3	Phenyltoloxamine	22.00
200.00	4	Starch (maize)	200.00
25.00	5	Kollidon 30	25.00
–	6	Alcohol	QS
25.00	7	Kollidon CL	25.00
5.00	8	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate the mixture of items 1 through 4 with a solution of items 5 and 6.
2. Dry, pass through a 0.8-mm sieve, add items 7 and 8, and press with high-compression force.
3. Compress into 601-mg tablets, using 12-mm planar punches.

Acetaminophen, Phenylpropanoloamine, Dextromethorphan, and Chlorpheniramine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Acetaminophen	200.00
12.50	2	Phenylpropanolamine hydrochloride (10% excess)	13.75
10.00	3	Dextromethorphan hydrobromide (10% excess)	11.00
1.00	4	Chlorpheniramine maleate (10% excess)	1.10
64.65	5	Cellulose (microcrystalline) (Avicel™ PH101)	121.72
28.00	6	Sodium starch glycolate (pH 5.5–7.5)	28.00
17.00	7	Povidone (PVP K-29–32)	17.5
–	8	Distilled purified water	~80.0 mL
2.00	9	Magnesium stearate	2.00
125.00	10	Acetaminophen	125.00
50.00	11	Ascorbic acid; use item 12	–
56.25	12	Sodium ascorbate (special grade) (20% excess)	67.50
24.00	13	Sodium starch glycolate (pH 5.5–7.5)	24.00
15.00	14	Povidone (PVP K-29–32)	~15.00
–	15	Alcohol SD 3A (200 proof)	75.0 mL

Manufacturing Directions

1. Dissolve chlorpheniramine and Povidone (item 7) in the purified water.
2. Pass phenylpropanolamine, dextromethorphan, and an equal portion of Avicel (item 5) through a 790-μm screen to break any agglomerates.
3. Blend the screened items in a suitable mixer for 5 minutes.
4. Load acetaminophen (item 1), sodium starch glycolate (item 6), remaining Avicel (item 5), and blended items from the previous step into a suitable planetary mixer.
5. Blend for 10 minutes.
6. Granulate the blend from the solution above.
7. Add the granulating solution in three equal portions, massing for 5 minutes after each addition.
8. Pass the wet mass through a 4.2-mm screen onto paper-lined trays.
9. Dry at 50°C until the granule LOD is 1% to 1.5%.
10. Pass the dried granules through an oscillating granulator fitted with a 790-μm screen.
11. Load the dried granules into a suitable blender.
12. Pass the magnesium stearate through a 600-μm screen and add to the blender.
13. Blend for 5 minutes.
14. Compress to the following specifications: tablet weight of 291.0 mg and tablet thickness of 4.20 to 4.40 mm.

Acetaminophen, Propoxyphenazone, and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetaminophen powder	250.00
150.00	2	Propoxyphenazone (isopropyl antipyrine)	150.00
50.00	3	Anhydrous caffeine	50.00
120.00	4	Avicel™ PH102	120.00
5.00	5	Pharmacoat® 603	5.00
3.25	6	Magnesium stearate	3.25
9.75	7	Talcum	9.75
1.30	8	Silicic acid	1.30
7.00	9	Methocel E-15	7.00
32.50	10	Esmaspreng fine	32.50
21.20	11	Maize starch	21.20
–	12	Water purified	QS

Manufacturing Directions

1. Place into a suitable vessel 5.00 g of Pharmacoat and 74.00 g of purified water; stir until homogeneous aqueous mucilage is obtained.
2. Mix in another vessel 250 g of acetaminophen powder and 17.50 g of Esmaspreng fine; add the above granulating solution and knead for approximately 10 minutes until an evenly moist mass of soft lumps is obtained.
3. Granulate by means of centrifugal granulator with 10-mm screen; dry the moist granulate overnight on trays in drying oven at 45°C (relative humidity of 20–30%).
4. Crush the dried cake through an oscillator with a 1.5-mm perforated plate.
5. In a suitable container, add 65 g of deionized water and 7.0 g of methocel.
6. Stir until homogeneous aqueous mucilage is obtained.
7. Mix into another vessel 150 g of isopropyl antipyrine, 50 g of caffeine, 15 g of Esmespreng fine, and 5.0 g of maize starch.
8. Pass through a centrifugal granulator with 1.0-mm screen; place the mixture into another vessel and knead for approximately 10 minutes until an evenly moist mass of small lumps is obtained.
9. Granulate through centrifugal granulator with 10-mm perforated screen.
10. Dry moist granulate overnight on trays in drying oven at 45°C (relative humidity of 10–20%).
11. Crush the dried granules through oscillator with a 1.5-mm perforated plate; store in airtight container.
12. Mix into a tumbling mixer 4.875 g of talc, 1.625 g of magnesium stearate, 0.65 kg of silicic acid, and 60.00 g of Avicel PH102.
13. Pass through a 0.5-mm round sieve, load acetaminophen granulate and isopropyl antipyrine/caffeine granulate, and add premixture of talc into blender.
14. Mix the mixture well for 30 minutes (relative humidity of 30–35%).
15. Store mix in airtight container.
16. Compress 650-mg tablet to 12.8–13.2 mm; hardness, 6 to 20 kPa; disintegration time, 5 minutes.

Acetaminophen, Salicylamide, Caffeine, and Codeine Tablets (150 mg/200 mg/50 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Salicylamide	200.00
150.00	2	Acetaminophen powder	150.00
50.00	3	Caffeine anhydrous	50.00
10.00	4	Codeine phosphate	10.00
130.00	5	Starch (maize)	130.00
5.00	6	Gelatin powder	5.00
8.00	7	PVP K30	8.00
1.00	8	Aerosil 200	1.00
30.00	9	Starch (maize)	30.00
–	10	Water, purified	300 mL
10.00	11	Talc powder	10.00
19.00	12	Starch (maize), dried	19.00
1.00	13	Aerosil 200	1.00

Manufacturing Directions

Note: The binding solution is prone to microbiological growth. Use only freshly prepared and properly stored solution.

1. Charge item 6 and about 25 mL of item 10 into a vessel to dissolve item 6. Mix for 10 minutes.
2. In a separate vessel, add and dissolve items 9 and 7 in about 12 mL of water.
3. Charge item 5 into a vessel; add about 40 mL of cold item 10 and 20 mL of hot (70–75°C) water, after first dissolving in cold water.
4. In a separate vessel, charge items 1 to 5 after passing them through a 630-μm sieve. Mix for 5 minutes at medium speed.
5. Add binding solution from step 3 and mix at medium speed. Continue until a satisfactory mass is obtained.
6. Dry the wet mass in a fluid-bed dryer at 50°C for 45 minutes to 1.5% to 2.5% LOD.
7. Pass the dried granules through a 1.5-mm sieve.
8. Load granules in a cone blender and mix for 5 minutes.
9. Add items 11 to 13 (passed through a 500-μm sieve) to blender, and blend for 5 minutes.
10. Compress into 634-mg tablets, using 12.7-mm flag bevel-edge punches.

Acetaminophen Sustained-Release Tablets

Manufacturing Directions

1. 300 g of acetaminophen and 60 g of hydroxypropylmethyl cellulose were dissolved in a mixture of 720 g of methanol and 720 g of dichloromethane.
2. 300 g of Celphere 102 (mean particle diameter of approximately 127 μm, particle diameter of approximately 50–150 μm) was introduced to a fluidized bed granulator and coated with the solution by the side spraying method (spraying liquid volume 14 g/min, spraying air pressure 3 kg/cm^2, product temperature 32°C, and inlet temperature 45°C) to obtain acetaminophen particles.
3. Separately, 48 g of ethyl cellulose and 12 g of hydroxypropylmethyl cellulose were dissolved in a mixture of 57 g of purified water and 1083 g of methanol.
4. Acetaminophen particles (300 g) were introduced to a fluidized bed granulator and coated with this solution by side spraying (spraying liquid volume of 8 g/min, spraying air pressure of 3 kg/cm^2, product temperature of 38°C, and inlet temperature of 67°C) to obtain sustained-release fine particles.
5. 66 g of these sustained-release fine particles and 314.25 g mannitol that had been pulverized by a pin mill pulverizing device were granulated (spraying liquid volume 15 g/min, spraying air pressure of 1.1 kg/cm^2, product temperature of 30°C, inlet temperature of 38°C, and spraying cycle of 30-seconds spraying and 30-seconds drying) with an aqueous 30% w/w solution containing 67.5 g of maltose in a fluidized bed granulator to obtain the final composition.
6. After further mixing 2.25 g of magnesium stearate with the composition that was obtained, 450-mg tablets containing 25-mg acetaminophen per tablet were made under a tableting pressure of 25 kg/punch and an initial hardness of 2.0 kPa, using a rotary tableting machine.
7. Next, these tablets were kept for 24 hours while heating and humidifying at 25°C/75% RH, using a thermostatic chamber at constant humidity. Then they were dried for 3 hours at 30°C and 40% RH.
8. The tablets that were obtained showed a hardness of 3.5 kPa and disintegration time in the buccal cavity of 12 seconds.

Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophen (fine powder)	500.00
44.15	2	Maize starch	44.15
0.84	3	Potassium sorbate	0.84
18.00	4	Povidone (PVP K-30)	18.00
4.00	5	Aerosil® 200	4.00
12.00	6	Gelatin (powder)	12.00
4.00	7	Glycerol	4.00
30.00	8	Cellulose (powder)	30.00
12.00	9	Primojel®	12.00
8.00	10	Stearic acid (fine powder)	8.00
2.00	11	Magnesium stearate	2.00
5.00	12	Talc (fine powder)	5.00
QS	13	Purified water	QS

Manufacturing Directions

1. Binder solution: Prepare in several batches. Add items 3 to 5 with about 50% quantity of water, dissolve item 1 in water, add item 4, and dissolve at medium speed. Avoid foaming.
2. Add item 5 and mix for 3 minutes.
3. Dissolve item 6 in 70°C to 80°C purified water, and mix until clear. Avoid foaming.
4. Add item 7 and mix gently; add to mixture from previous step.
5. Mix items 1 and 2 for 5 minutes.
6. Add binding solution and mix at slow speed until granules form; add extra water if necessary.
7. Dry in fluid-bed dryer at 55°C for 30 minutes; after 15 minutes, scrape granules to break up lumps to promote uniform drying. Dry to 1% to 1.5% LOD.
8. Grind through a 3.0-mm sieve and then through a 1.0-mm sieve; load into a double-cone blender.
9. Pass cellulose powder, Primojel, and stearic acid through a 500-μm sieve; bag-mix magnesium stearate and fine talc powder, and pass through a 250-μm sieve; then add portion of granules from the bulk to the bag and mix for 1 minute.
10. Add both of these parts to the granules.
11. Compress into 17.6 × 7.2-mm caplet punches of 10- to 14-kPa hardness and 5.8- to 6.0-mm thickness.

Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophen (crystalline)	500.00
137.00	2	Avicel™ PH102	137.00
35.00	3	Kollidon® VA 64	35.00
21.00	4	Kollidon® CL	21.00
3.00	5	Magnesium stearate	3.00
4.00	6	Aerosil® 200	4.00

Manufacturing Directions

1. Pass the lubricant through a 200-mm sieve and mix all other components.
2. Pass through 0.8-mm sieve, add the lubricant, and press with a high-compression force of 25 to 30 kN.
3. Fill 699 mg.

Acetaminophen Tablets

Bill of Materials			
Scale (g/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500	1	Acetaminophen (crystalline)	500
150	2	Avicel™ PH102	150
20	3	Kollidon® VA 64	20
15	4	Kollidon® CL	15
15	5	PEG-6000 (powder)	15
2	6	Aerosil® 200	2

Manufacturing Directions

1. Pass the lubricant through a 200-μm sieve and mix all other components.
2. Pass the mix through an 0.8-mm sieve, add the lubricant, and press with a high-compression force of 25 to 30 kN.
3. Weight should be 703 mg.

Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetaminophen (powder)	500.00
30.00	2	Dicalcium phosphate	30.00
12.00	3	Kollidon® CL	12.00
20.00	4	Kollidon® VA 64	20.00
10.00	5	Kollidon® 90F	10.00
–	6	Ethanol (96%)	70 mL (max.)
12.00	7	Kollidon® CL	12.00
10.00	8	Polyethylene glycol (powder)	10.00

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with the solution of items 5 and 6.
2. Dry, sieve, and mix with items 7 and 8.
3. Press with high-compression force of 25 to 30 kN.
4. Tablet weight is 587 mg for an 11-mm biconvex tablet.

Acetaminophen Tablets, Chewable

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
89.90	1	Acetaminophen, use acetaminophen particles coated with cellulose acetate and PVP	89.90
246.00	2	Mannitol granular	246.00
30.00	3	Microcrystalline cellulose	30.00
9.00	4	Aspartame	9.00
1.27	5	Dyes	1.27
2.10	6	Citric acid	2.10
2.30	7	Flavor	2.30
4.40	8	Magnesium stearate	4.40

Manufacturing Directions

1. Acetaminophen is coated with a layer of a taste-masking composition with a thickness of about 3 to 10 μm. The coating should be substantially free of cracks, holes, and other imperfections when examined under a scanning electron microscope at 100 to 500× magnification.
2. Charge items 1 to 7 in a suitable blender and mix for 20 minutes.
3. Add item 8 to step 2 and blend for 2 minutes.
4. Compress the appropriate quantity.

Acetaminophen Tablets for Children

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
210.00	1	Acetaminophen (Merck)	210.00
168.00	2	Avicel™ PH101	168.00
13.00	3	Kollidon® VA 64	13.00
6.00	4	Kollidon® CL	6.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with medium-compression force.
2. Tablet weight is 401 mg for a 12-mm biplanar tablet.

Acetaminophen-Tramadol Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Acetaminophen	200.00
20.00	2	Tramadol hydrochloride	20.00
50.40	3	Microcrystalline cellulose	50.40
19.20	4	Povidone K-90	19.20
4.80	5	Croscarmellose sodium	4.80
3.20	6	Colloidal silicon dioxide	3.20
3.20	7	Magnesium stearate	3.20

Manufacturing Directions

1. Mix the above amounts of items 1 through 6 listed in above formulation in a mixer, such as a high-shear mixer granulator or planetary mixer, to obtain homogeneity.
2. The mix is then granulated in water or other suitable granulation fluids and dried in a dryer.
3. The dried granular mass is then milled and then items 9 and 10 are added for blending.
4. The lubricated granular mass is then compressed into mini-tablets, using a tablet press for individual tablet weight of 160 mg and for regular tablet at 320 mg.
5. The mini-tablets are encapsulated in a capsule containing two immediate-release mini-tablets and two sustained-release mini-tablets.

Acetaminophen-Tramadol Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Acetaminophen	300.00
30.00	2	Tramadol hydrochloride	30.00
8.80	3	Microcrystalline cellulose	8.80
17.60	4	Povidone K-90	17.60
35.20	5	Sodium alginate (Keltone LV)	35.20
39.60	6	Hydroxypropylmethyl cellulose 4KM	39.60
4.40	7	Colloidal silicon dioxide	4.40
4.40	8	Magnesium stearate	4.40

Manufacturing Directions

1. For a portion of sustained release, mix the suitable amounts of items 1 through 3 and 7 and 8 listed in above formulation in a mixer, such as a high-shear mixer granulator or planetary mixer, to obtain homogeneity.
2. The mix is then granulated in water or other suitable granulation fluids and dried in a dryer. The dried granular mass is then milled and then items 9 and 10 are added for blending.
3. The lubricated granular mass is then compressed into mini-tablets, using a tablet press for individual tablet weight of 220 mg and for regular tablet 440 mg.
4. The mini-tablets are encapsulated in a capsule containing two immediate-release mini-tablets and two sustained-release mini-tablets.

Acetylsalicylic Acid, Acetaminophen, and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (crystalline)	250.00
250.00	2	Acetaminophen (crystalline)	250.00
50.00	3	Caffeine	50.00
50.00	4	Kollidon® 90°F	50.00
–	5	Isopropanol	QS
5.00	6	Magnesium stearate	5.00
16.00	7	Kollidon® CL	16.00

Manufacturing Directions

1. Granulate items 1 to 3 with the solution of items 4 and 5; dry and sieve through an 0.8-mm screen.
2. Add items 5 and 6 and press with low-compression force (hardness is 45 N); 12-mm biplanar tablet has an average weight of 670 mg.

Acetylsalicylic Acid, Acetaminophen, and Caffeine Tablets (Direct Compression)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (crystalline)	400.00
100.00	2	Acetaminophen (crystalline)	100.00
30.00	3	Caffeine	30.00
100.00	4	Ludipress®	100.00
20.00	5	Kollidon® CL	20.00
30.00	6	PEG-6000 (powder)	30.00
5.00	7	Stearic acid	5.00

Manufacturing Directions

1. Mix all components and pass through a 0.8-mm sieve.
2. Press with a compression force of 116 N; 12-mm biplanar tablet has an average weight of 683 mg.

Acetylsalicylic Acid Acetaminophen Caffeine Tablet (250 mg/250 mg/50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetaminophen (Merck)	250.00
50.00	2	Caffeine powder	50.00
250.00	3	Acetylsalicylic Acid	250.00
60.00	4	Kollidon VA 64	60.00
20.00	5	Kollidon CL	20.00
3.00	6	Aerosil 200 200	3.00
4.00	7	Magnesium stearate	4.00

Manufacturing Directions

1. The active ingredients and Kollidon® VA 64 are granulated in a roller compactor.
2. Pass the granules together with magnesium stearate, Aerosil® 200, and Kollidon® CL through an 800-μm sieve.
3. Blend for 10 minutes in a mixer.
4. Compress into tablets with a force of about 12 kN.

Acetylsalicylic Acid and Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (crystalline)	250.00
250.00	2	Acetaminophen (crystalline)	250.00
60.00	3	Avicel™ PH101	60.00
15.00	4	Kollidon® 30 (or Kollidon® VA 64)	15.00
25.00	5	Kollidon® CL	25.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with medium-compression force.
3. Tablet weight is 605 mg for a 12-mm biplanar tablet.

Acetylsalicylic Acid and Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (40 mesh)	250.00
250.00	2	Acetaminophen (40 mesh)	250.00
15.00	3	Avicel™ PH102	15.00
7.20	4	Croscarmellose sodium (Ac-Di-Sol)	7.20
7.20	5	Stearic acid	7.20
4.00	6	Fumed silica	4.00

Manufacturing Directions

1. Screen all ingredients through a 0.8-mm sieve.
2. Blend all ingredients in a V-blender and mix for 10 minutes.
3. Compress to 670-mg tablet weight, using appropriate tooling.

Acetylsalicylic Acid and Ascorbic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Acetylsalicylic acid (crystalline) (Merck)	325.00
250.00	2	Ascorbic acid (powder) (BASF)	250.00
120.00	3	Sorbitol (crystalline)	120.00
40.00	4	Avicel™ PH101	40.00
25.00	5	Kollidon® VA 64	25.00
20.00	6	Kollidon® CL	20.00
2.00	7	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with medium- to high-compression force (hardness is 92 N); 12-mm biplanar tablet has an average weight of 790 mg.

Acetylsalicylic Acid and Ascorbic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Acetylsalicylic acid (crystalline) (Merck)	325.00
250.00	2	Ascorbic acid (powder) (BASF)	250.00
100.00	3	Avicel™ PH101	100.00
12.00	4	Kollidon® VA 64	12.00
30.00	5	Kollidon® CL	30.00
3.00	6	Magnesium stearate	3.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with medium- to high-compression force (hardness is 100 N); 12-mm biplanar tablet has an average weight of 726 mg.

Acetylsalicylic Acid + Paracetamol (=Acetaminophen) Tablets (250 mg + 250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Acetylsalicylic acid	250.00
250.00	2	Acetaminophen	250.00
60.00	3	Avicel PH 101	60.00
15.00	4	Kollidon VA 64	15.00
3.00	5	Macrogel 6000 Powder	3.00

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force.

Acetylsalicylic Acid Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Acetylsalicylic acid crystalline	500.00
200.00	2	Avicel PH 101	200.00
15.00	3	Kollidon 30	15.00
25.00	4	Kollidon CL	25.00
3.00	5	Magneisum stearte	3.00

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with low-compression force.

Acetylsalicylic Acid Tablets (Direct Compression)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (crystalline) (Merck)	400.00
99.00	2	Ludipress®	99.00
1.00	3	Stearic acid	1.00
15.00	4	Kollidon® CL	15.00

Manufacturing Directions

1. Mix all components and pass through an 0.8-mm sieve.
2. Press with low-compression force (hardness is 90 N); 12-mm biplanar tablet has an average weight of 516 mg.

Acetylsalicylic Acid Tablets (Direct Compression)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Acetylsalicylic acid, 40 mesh	400.00
55.60	2	Cellulose (microcrystalline) (Avicel™ PH101)	55.60
21.40	3	Starch (pregelatinized)	21.40
2.20	4	Stearic acid	2.20
10.00	5	Croscarmellose sodium (Ac-Disol)	10.00
3.20	6	Fumed silica	3.20

Manufacturing Directions

1. Screen about half of item 1 through a mill, using 12-mesh screen with knives forward.
2. Preblend items 2 to 6 with 25% of item 1, and pass the mixture through the mill.
3. Pass the balance of item 1 through the mill.
4. Mix all the ingredients in a V-blender for 10 minutes and compress using 13/32-in. tooling.
5. For enteric coating, coat with Aquateric (FMC) dispersion.

Acetylsalicylic Acid Tablets (Direct Compression)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	2	Avicel™ PH101	200.00
15.00	3	Kollidon® 30	15.00
25.00	4	Kollidon® CL	25.00
3.00	5	Magnesium stearate	3.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with low-compression force of (hardness is 61 N); 12-mm biplanar tablet has an average weight of 707 mg.

Acetylsalicylic Acid Tablets, Buffered

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (40 mesh)	400.00
40.00	2	Magnesium hydroxide	40.00
40.00	3	Aluminum hydroxide	40.00
135.00	4	Cellulose (microcrystalline) (Avicel™ PH101)	135.00
15.30	5	Stearic acid	15.30
15.30	6	Croscarmellose sodium (Ac-D-Sol)	15.30
18.50	7	Hydroxy coatings	18.50

Manufacturing Directions

1. Screen all ingredients except item 7 through a 40-mesh sieve.
2. Blend items 2 and 3 in a V-blender for 10 minutes.
3. Coat items 2 and 3 using Aquacoat (FMC) aqueous polymer dispersion in a fluid-bed column with a 10% by weight formula.
4. Blend 50% of item 1 with items 4 and 5 for 10 minutes in a V-blender.
5. Add remaining item 1 and blend again for 10 minutes.
6. Blend item 7 with the mixture from the previous step for 10 minutes.
7. Add item 6 and blend for 7 minutes.
8. Compress into 625-mg tablets to the desired hardness using appropriate tooling.

Acetylsalicylic Acid + Vitamin C Tablets (400 mg + 250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Acetylsalicylic acid crystalline	400.00
250.00	2	Ascorbic acid	250.00
100.00	3	Ludipress	100.00
20.00	4	Kollidon CL	20.00
3.00	5	Macrogol 6000 powder	3.00

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force.

Acyclovir Fast Melt

Manufacturing Directions

1. Add and mix Acyclovir 50%, sodium bicarbonate 18%, citric acid anhydrous 18%, anhydrous lactose 7%, xylitol 5%, Crodesta F160 2%.
2. Dry the above ingredients to reduce moisture.
3. The ingredients are then blended for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) to form granules containing the effervescent ingredients.
4. Granules are then screened and blended with the following ingredients: ACY-EFG (30–60 mesh) 50%, microcrystalline cellulose 18%, Fujicalin SG 18%, L-HPC LH-11 10%, aspartame 3%, redberry flavor 0.4%, magnesium stearate 0.5%, Cab-O-Sil M5P 0.1%.
5. Mix the ingredients in step 4 for 5 minutes prior to compression.
6. Acyclovir tablets are then compressed to a hardness of approximately 1 to 3 kPa and tablets disintegrate in water in approximately 20 to 45 seconds.

Acyclovir Tablets (Zovirax)

Each 800-mg tablet of Zovirax contains 800 mg of acyclovir and the inactive ingredients FD&C Blue No. 2, magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate. Each 400-mg tablet of Zovirax contains 400 mg of acyclovir and the inactive ingredients magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate.

Acyclovir Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
800.00	1	Acyclovir	800.00
240.00	2	Lactose	240.00
100.00	3	Microcrystalline cellulose (Avicel PH 101)	100.00
24.00	4	Povidone	24.00
32.00	5	Sodium starch glycolate	32.00
8.00	6	Magnesium stearate	8.00
–	7	Alcohol	48.00

Manufacturing Directions

1. Pass items 1 to 3 through 250-μm mesh in a granulating vessel.
2. In a separate container, mix items 4 and 5 in item 6; now add the solution to step 1. Pass the wet mass through #8 mesh, dry, and size the granules.
3. Compress 1204 mg.

Acyclovir Water-Dispersible Tablets (800 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
800.00	1	Acyclovir	800.00
100.00	2	Microcrystalline cellulose (Avicel PH 101)	100.00
53.00	3	Veegum F	53.00
42.00	4	Sodium starch glucolate 42.00	42.00
9.40	5	Magnesium stearate	9.40
–	6	Alcohol	QS

Manufacturing Directions

1. Pass items 1 to 4 through 250-μm mesh into a granulating vessel.
2. Add a sufficient quantity of item 6 to make a wet mass. Pass it through a granulator, dry, and then pass through a #11 sieve.
3. Pass item 5 through a 250-μm sieve and add to step 2.
4. Compress into 1004-mg tablets, using a suitable punch.

Albendazole Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Albendazole	200.00
84.00	2	Starch (maize)	84.00
101.25	3	Lactose monohydrate	101.25
5.00	4	Sodium starch glycolate (Primojel)	5.00
13.00	5	Povidone (PVP K-30)	13.00
5.00	6	Saccharin sodium	5.00
1.00	7	Polysorbate 80 (Tween 80)	1.00
110.00	8	Microcrystalline cellulose (Avicel PH 102)	110.00
50.00	9	Sodium starch glycolate (Primojel)	50.00
5.00	10	Vanilla dry flavor	5.00
5.00	11	Blood orange dry flavor	5.00
4.00	12	Stearic acid	4.00
2.00	13	Magnesium stearate	2.00
2.75	14	Colloidal silicon dioxide (Aerosil 200)	2.75
2.00	15	Sodium lauryl sulfate	2.00
–	16	Alcohol (ethanol 95%)	105.00
–	17	Purified water	73.33

Manufacturing Directions

Note: Avoid overmixing the lubricants, or otherwise, hardness will be reduced.

1. Dissolve item 7 in item 16 by spatula. Dissolve items 5 and 6 in item 17 by stirring with a stirrer. Add item 7 (Tween-80) solution in items 5 and 6 (PVP-saccharin) solutions, while mixing with a stirrer.
2. Sift items 1 to 4 through a 500-μm stainless steel sieve. Collect in a polyethylene bag.
3. Load the sifted powder into the mixer. Mix for 2 minutes at low speed.
4. Add the binding solution from steps 1 and 2, while mixing at low speed over a period of 2 minutes. Scrape the sides and blades of the mixer. Mix and chop at low speed for 2 minutes. Check the end point of granulation. If required, add item 17 to get the end point. (The end point of the granulation is the point when the wet mass consists of little or no lumps of granules.) Unload the wet mass on stainless steel trays to dry.
5. Dry the wet granules in an oven at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break the lumps for uniform drying.
6. Check the LOD. The limit is 1.0% to 1.5%.

7. Grind the dried granules through a 1.25-mm sieve, using the granulator at medium speed.
8. Sift items 8 to 11 through a 500-μm sieve. Add the sieved powder from step 1. Mix manually for 2 minutes.
9. Mix items 12 to 15 in a polyethylene bag. Sift through a 250-μm stainless steel sieve. Collect in a polyethylene bag. Add into step 1. Mix manually for 1 minute.
10. Compress into 10 tablets with weight = 5.900 g ± 2% and hardness = 9 to 11 kPa.
11. Coat using the hydroxypropylmethylcellulose (HPMC) system and add a finishing coat. (See the Appendix.)

Albendazole Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Albendazole	100.00
288.00	2	Ludipress	288.00
4.00	3	Magnesium stearate	4.00
8.00	4	Aerosil 200	8.00

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.

Alendronate Tablets (Fosamax)

Fosamax tablets for oral administration contain either 6.53, 13.05, or 52.21 mg of alendronate monosodium salt trihydrate, which is the molar equivalent of 5, 10, and 40 mg, respectively, of free acid, and the following inactive ingredients: microcrystalline cellulose, anhydrous lactose, croscarmellose sodium, and magnesium stearate.

Alendronate Tablets, Effervescent (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Alendronate, use alendronate sodium	13.05
650.00	2	Citric acid anhydrous	650.00
367.00	3	Sodium bicarbonate granular	367.00
40.00	4	Sodium carbonate anhydrous	40.00
25.00	5	Flavor	25.00
5.00	6	Color	5.00
7.50	7	Sodium benzoate	7.50
–	8	Water, purified	2.00

Note: For other strengths, adjust with lactose.

Manufacturing Directions

1. Premix sodium benzoate with sodium bicarbonate and alendronate sodium. Mix the color with sodium carbonate. Place citric acid in a bowl of a suitable blender.
2. Slowly add 2 mg of water to the citric acid and mix thoroughly to form a moist blend. Add to the blend, in sequence, while mixing, the sodium bicarbonate mix and the sodium carbonate–color mix. Mix until uniformly distributed.
3. Compress tablets using suitably sized tooling. Cure the tablets, cool, and package in aluminum foil.

Alendronate Sodium Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
13.05	1	Sodium alendronate	13.05
103.95	2	Lactose anhydrous	103.95
80.00	3	Microcrystalline cellulose granular	80.00
2.00	4	Sodium carboxymethylcellulose	2.00
1.00	5	Magnesium stearate	1.00

Manufacturing Directions

Alendronate is first blended with one-third of microcrystalline cellulose and with one-half of anhydrous lactose. The premixture obtained is then blended with both remaining excipients and it is mixed again. Sodium salt of carmellose is added under mixing to be followed with magnesium stearate to finish the mixture blending. When homogenized by forth mixing the mixture is subjected to the compression.

Alendronate Sodium Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
13.05	1	Sodium alendronate	13.05
11.15	2	Maize starch	11.15
104.50	3	Mannitol	104.50
1.30	4	Magnesium stearate	1.30

Manufacturing Directions

A mixture containing alendronate, mannitol, maize starch, and microcrystalline cellulose is blended in a container at the stirrer speed of 14 rpm and under the normal temperature and humidity (25°C, 60% R.H.). Magnesium stearate is added to the premixed mixture. After homogenization, the precompression mixture is compressed on a rotary compression machine to form flat (cylindrical) or oval-shaped tablets of 130 mg in the mass.

Alendronate Sodium Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
13.05	1	Sodium alendronate	13.05
42.00	2	Calcium hydrogen phosphate	42.00
62.50	3	Granulated microcrystalline cellulose	62.50
11.15	4	Maize starch	11.15
1.30	5	Magnesium stearate	1.30

Alendronate Sodium Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Alendronate, use alendronate sodium	52.00
10.00	2	Polyvinyl pyrrolidone	10.00
100.00	3	Lactose anhydrous	100.00
1.50	4	Sodium stearyl fumarate	1.50
–	5	Water, purified	100.00

Manufacturing Directions

1. Pass items 1 to 3 through a 500-μm sieve and blend for 10 minutes.
2. Add item 2 and mix it well with item 5. Add to this to step 1 to granulate, dry, size, and then add item 4.
3. Compress into 163.50-mg tablets, using a suitable punch.

Allopurinol Tablets, 100 mg (Zyloric)

Each scored white tablet contains 100 mg of allopurinol and the inactive ingredients lactose, magnesium stearate, potato starch, and povidone. Each scored peach tablet contains 300 mg of allopurinol and the inactive ingredients cornstarch, FD&C Yellow No. 6 Lake, lactose, magnesium stearate, and povidone.

Allopurinol Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Allopurinol	100.000
1.00	2	Sorbitan monooleate	1.000
73.00	3	Starch (maize)	73.000
100.00	4	Lactose	100.00
10.00	5	Starch (maize)	10.000
8.00	6	Sodium starch glycolate	8.000
QS	7	Purified water (deionized), approximately	65.00 mL
4.50	8	Talc purified	4.5000
1.50	9	Silicon dioxide	1.5000

Manufacturing Directions

Caution: Wear gloves, mask, and protective glasses during all manufacturing operations.

1. Granulation
   a. Prescreen the allopurinol through a 75-μm aperture screen and transfer it to a suitable mass mixer. Dissolve the sorbitan monoleate in 10 mL of water and add the solution to the mixer. Mix until the allopurinol is wetted.
   b. Pass the wetted allopurinol through a 2.00-mm aperture screen on an oscillating granulator and dry in a tray dryer at 50°C until the LOD (Brabender 105°C, 1 hour or equivalent) is less than 2%.
   c. Rescreen the dried allopurinol through a 75-μm aperture screen and transfer it to the mass mixer. Add the starch (item 3) and lactose and mix for 15 minutes.
   d. Add the starch (item 5) to about 15 mL of water and mix until a smooth slurry, free from lumps, is formed.
   e. Heat 40 mL of water to boiling. Reduce the heat, and then, while mixing, add the slurry from step 1d. Continue mixing well, until a smooth translucent paste is formed. Allow to cool to 50°C before moving to the next step in the process. (*Caution:* Control the heat to avoid charring of the paste.)
   f. Add half of the starch paste from step 1e to the blended powders in the mixer and mix for 1 minute. Stop mixing, and scrape the blades and sides of the mixer. Add the second half of the starch paste and mix for another 1 minute. Stop mixing, scrape the blades and sides of the mixer, and examine the mass.
   g. If necessary, add more water at 50°C, in small quantities, mixing for 1 minute after each addition, until a good wet, holding mass is formed. (*Caution:* Do not overwet or overmix the mass.)
   h. Pass the mass through a 2.00-mm aperture screen on an oscillating granulator and dry in a tray dryer at 50°C until the LOD (Bra-bender 105°C, 1 hour or equivalent) is in the range of 1% to 2%.
   i. Arrange for sample.
   j. Pass the granules through a 595-μm aperture screen on an oscillating granulator into tared, polyethylene-lined drums, seal, and weigh.
2. Lubrication
   a. Transfer the dried granulation to a suitable blender.

   b. Screen the sodium starch glycolate, talc, magnesium stearate, and colloidal silicon dioxide through a 595-μm aperture screen. Add to the blender and blend for 15 minutes.
   c. Discharge the granule into polyethylene-lined drums, seal, and weigh for yield.
3. Compression
   a. Compress using 9.52-mm (0.375-in.) diameter concave punches with the bisect on the upper punch.
   b. Compress to the following specifications:
      i. Weight of 10 tablets—3.025 g
      ii. Weight variation—Average weight differs from theoretical weight by not more than 3%
      iii. Thickness—3.5 to 4.3 mm (range: not more than 5%)
      iv. Hardness—NTL 8 kPa
      v. Disintegration time—Not more than 15 minutes in water

Allopurinol Tablets (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Allopurinol	300.00
180.00	2	Lactose	180.00
20.00	3	Povidone (K 29)	20.00
50.00	4	Starch (maize)	50.00
QS	5	Water, purified (deionized)	65.00 mL
20.00	6	Croscarmellose sodium	20.00
30.00	7	Starch (maize), dried	30.00

Manufacturing Directions

Caution: Wear gloves, mask, and protective glasses during all manufacturing operations.

1. Granulation
   a. Transfer allopurinol, lactose, povidone, and starch (item 4) to a suitable mass mixer. Mix for 15 minutes and then pass through a 250-μm sieve aperture screen.
   b. Return the screened mix from step 1 to the mixer and add sufficient water until a good wet, holding mass is formed. Pass the mass through a 2.00-mm aperture screen on an oscillating granulator and dry in a tray dryer at 50°C until the LOD (Barbender 105°C, 1 hour or equivalent) is in the range of 1% to 2%.
   c. Pass the granules through a 595-μm aperture screen on an oscillating granulator into tared, polyethylene-lined drums, then seal, and weigh.
2. Lubrication
   a. Transfer the dried granulation to a suitable blender.
   b. Screen the croscarmellose sodium and dried starch through a 595-μm aperture screen and add to the blender. Blend for 15 minutes.
   c. Discharge the granule into polyethylene-lined drums, then seal, and weigh for yield.
3. Compression: Compress using 11.11-mm (0.4375-in.) diameter concave punches with the bisect on the upper punch. (Weight of 10 tablets: 6.00 g; weight variation: average weight differs from theoretical weight by not more than 3%.)

Alprazolam Tablets (0.25 mg/0.50 mg/1.0 mg), Xanax

Each Xanax tablet, for oral administration, contains 0.25, 0.5, 1, or 2 mg of alprazolam and the following inactive ingredients: cellulose, cornstarch, docusate sodium, lactose, magnesium stearate, silicon dioxide, and sodium benzoate. In addition, the 0.5-mg tablet contains FD&C Yellow No. 6, and the 1-mg tablet contains FD&C Blue No. 2.

Alprazolam Tablets (0.25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.25	1	Alprazolam, with excess	0.252
82.50	2	Dicalcium phosphate	82.50
2.25	3	Starch (maize)	2.25
2.25	4	Gelatin	2.25
33.50	5	Starch (maize)	33.50
0.082	6	Propyl paraben	0.082
0.082	7	Methyl paraben	0.082
1.00	8	Magnesium stearate	1.00
1.00	9	Sodium starch glycolate	1.00
0.30	10	Dye yellow	0.30
–	11	Water, purified, ca	100 mL

Manufacturing Directions

1. Charge items 2 and 5 in a suitable vessel after sifting through an 80-mesh sieve. Mix for 2 minutes.
2. Sift item 1 through a 60-mesh sieve and add to step 1. (*Note:* Because of the small quantity of item 1, use a geometric dilution method to mix the entire amount.)
3. Mix for 5 minutes.
4. In a separate vessel, sift (through 80 mesh) and charge items 3, 4, 6, 7, and 10 and then mix for 2 minutes. Add a sufficient quantity of item 11 to form a suitable lump-free paste.
5. Add step 4 into step 3, and knead and chop to prepare a suitable mass without lumps.
6. Spread the wet mass from step 5 on trays and dry at 50°C for 12 hours to an LOD of not more than 2%; dry for an additional hour, if necessary.
7. Pass dried granules through 20 mesh.
8. Sift items 8 and 9 through a 250-μm sieve screen and add to step 7. Blend for 2 minutes.
9. Compress into 125-mg tablets, using 6-mm punches. For 0.5-mg and 1.0-mg strengths, adjust with item 2 and compress the same weight and size.

Aluminum Acetylsalicylate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Aluminum acetylsalicylate, excess	255.00
213.00	2	Mannitol	213.00
28.00	3	Cornstarch	28.00
10.00	4	Kollidon® 90F	10.00
5.00	5	Lutrol E 6000	5.00
–	6	Isopropanol, QS	50.00 mL
23.00	7	Kollidon® CL	23.00
5.00	8	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with solution of items to 6.
2. Dry, pass through an 0.8-mm sieve, and mix with items 7 and 8.
3. Compress with medium-compression force; 12-mm biplanar tablet has an average weight of 540 mg.

Aluminum Hydroxide and Magnesium Hydroxide Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Aluminum hydroxide (Rorer)	200.00
200.00	2	Magnesium hydroxide (Rorer)	200.00
100.00	3	Lactose monohydrate	100.00
30.00	4	Kollidon® VA 64	30.00
QS	5	Water	260.00 mL
315.00	6	Sucrose (crystalline)	315.00
100.00	7	Sorbitol (crystalline) (Merck)	100.00
60.00	8	PEG-6000 (powder)	60.00
12.00	9	Aerosil® 200	12.00
6.00	10	Talc	6.00
6.00	11	Magnesium stearate	6.00

Manufacturing Directions

1. Granulate mixture of items 1 to 5 with solution of items 4 and 5.
2. Dry and pass through an 0.8-mm sieve, add items 6 to 11, and press with high-compression force (20 kN).
3. The 16-mm biplanar tablet has an average weight of 1013 mg.

Aluminum Hydroxide and Magnesium Hydroxide Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
320.00	1	Aluminum hydroxide (dried gel)	320.00
320.00	2	Magnesium hydroxide powder	320.00
32.00	3	Sucrose	32.00
288.40	4	Mannitol	288.40
QS	5	Povidone (Plasdone®) (10% solution in equal parts water and alcohol)	QS
12.90	6	Glycerin	12.90
19.20	7	Magnesium stearate	19.20
6.40	8	Fumed silica	6.40
0.30	9	Oil of peppermint	0.30

Manufacturing Directions

1. Mix items 1 to 4 in a suitable blender, add items 5 and 6, and use this combination to moisten the mix of items 1 to 4.
2. Granulate by passing through a 20-mesh screen.
3. Add and thoroughly mix items 7 to 9, and compress using 0.5-in., flat-face, beveled-edge punches.

Aluminum Hydroxide and Magnesium Hydroxide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
405.00	1	Aluminum hydroxide gel (dried)	405.00
100.00	2	Magnesium hydroxide powder	100.00
108.00	3	Mannitol	108.00
38.80	4	Sorbitol powder	38.80
2.50	5	Saccharin sodium	2.50
16.70	6	Povidone (PVP K-30)	16.70
7.00	7	Magnesium stearate	7.00
2.00	8	Mint flavor (dry)	2.00
299.00	9	Purified water	299.00

Manufacturing Directions

1. Dissolve items 4 and 5 in 59.0 g of purified water by using stirrer.
2. Add item 6 while mixing until clear solution is obtained.
3. Add items 1 to 3 into mixer and mix for 5 minutes, with mixer and chopper at high speed.
4. Dilute concentrate binding solution with 240.0 g of purified water.
5. Add binding solution at a rate of 9 to 11 g/min to the dry powders in the mixer while mixing at low speed. Mix for 2 to 3 minutes. Scrape the sides, blade, and lid of the mixer. Mix and chop at low speed for an additional 2 to 3 minutes or until the granules stop flying around the chopper. Add extrapurified water, if required, and continue mixing until a satisfactory mass is obtained. Record extra quantity of purified water added.
6. Unload the wet mass into a clean aeromatic bowl for drying. Avoid big lump formation, as this leads to nonuniform drying.
7. Dry the wet mass in an Aeromatic fluid-bed dryer at 60°C for 120 minutes. After 30 minutes of drying, scrape the semidried granules to break the lumps for uniform drying. Check the LOD (limit: NMT 5.5%).
8. Pass the dried granules through 1.5-mm sieve, using granulator at medium speed. Collect in stainless steel drums. Set aside 7 to 9 g of granules for later step.
9. Load the rest of the granules into blender. Pass items 8 and 7 through a sifter, using a 250-μm sieve. Collect in a polyethylene bag.
10. Add about 7 to 9 g of granules and mix gently.
11. Load into blender and blend for 3 minutes.
12. Check temperature and humidity of the room before beginning compression (humidity limit: NMT 60%; temperature, 25 ± 1°C).
13. Compress the granules using a rotary tabletting machine. Compress into 680-mg tablets, using 12.7-mm, flat, beveled-edge punches.

Aluminum Hydroxide, Magnesium Carbonate (or Oxide), and Simethicone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
576.00	1	Sucrose	576.00
157.00	2	Aluminum hydroxide	157.00
160.00	3	Magnesium carbonate (or oxide)	160.00
97.00	4	Magnesium oxide	97.00
45.00	5	Kollidon® 90F	45.00
22.00	6	Aerosil® 200	22.00
300.00	7	Simethicone suspension (30%)	300.00
9.00	8	Menthol	9.00
1.00	9	Saccharin sodium	1.00
49.00	10	Talc	49.00
13.00	11	Magnesium stearate	13.00

Manufacturing Directions

1. Granulate mixture of items 1 to 6 with the simethicone suspension, dry, sieve through an 0.8-mm screen, add items 8 to 11, and press with high-compression force.
2. Tablet has an average weight of 1295 mg.

Aluminum Hydroxide and Magnesium Silicate Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
120.00	1	Aluminum hydroxide dried gel (Giulini)	120.00
250.00	2	Magnesium trisilicate	250.00
232.00	3	Ludipress®	232.00
6.00	4	Aerosil® 200	6.00
6.00	5	Magnesium stearate	6.00
12.00	6	Cyclamate sodium	12.00
1.50	7	Menthol	1.50

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with a compression force of 20 kN.
2. Because of the poor flowability of the powder, the tabletting machine should be equipped with a special technical device to provide a continuous and homogeneous filling of the dies.
3. The 16-mm biplanar tablet has an average weight of 640 mg.

Ambroxol HCl Sustained-Release Pellets Releasing Tablets

Formulation for 500 tablets: ambroxol HCl/Kollicoat® SR 30D pellets,* 250.0 g; microcrystalline cellulose Vivapur® 200, 250.0 g; magnesium stearate, 2.5 g.

Manufacturing Directions

Mix the ingredients together, pass through a 0.8-mm sieve, and compress into tablets with a force of about 15 kN. This gives 500 tablets.

Aminophylline Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Aminophylline	100.00
196.00	2	Starch (maize)	196.00
2.00	3	Talc	2.00
3.00	4	Magnesium stearate	3.00
QS	5	Water, purified	QS

Manufacturing Directions

1. Charge item 2 in a suitable vessel and add a sufficient quantity of item 5 to prepare a 30% smooth slurry.
2. Add item 1 into step 1 and mix well to form a suitable mass.
3. Pass the wet mass through a #6 sieve to granulate.
4. Dry the granules at 60°C for 10 hours to an LOD of not more than 3%.
5. Pass the dried granules through 1.19-mm sieve and transfer to a blending vessel.
6. Sift items 3 and 4 through a 250-μm sieve and add to step 5. Blend for 2 minutes.
7. Compress into 300-mg tablets, using 9-mm punches.

4-Amino-1-Hydroxybutylidene-1,1-Bisphosphonic Acid Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid; use monosodium trihydrate	6.55
110.45	2	Lactose anhydrous	110.45
80.00	3	Microcrystalline cellulose	80.00
1.00	4	Magnesium stearate	1.00
2.00	5	Croscarmellose sodium type A	2.00

Manufacturing Directions

1. The active ingredient (equivalent to 5 mg of anhydrous free acid per tablet) is premixed with one-third quantity of the microcrystalline cellulose and one-half the quantity of the anhydrous lactose in a ribbon blender for 5 minutes at 20 rpm.
2. To the premix is added the remaining two-thirds of the microcrystalline cellulose and the remaining one-half of the anhydrous lactose. Blend for 10 minutes at 20 rpm.
3. Add croscarmellose sodium to the blended powders in step 2 and mix for 5 minutes at 20 rpm.
4. Add item 4 to the mixture after passing it through a 90-mesh screen and blend for an additional 5 minutes at 20 rpm.
5. Compress into 192-mg tablets, using a suitable punch.

Aminosalicylic Acid Tablets

Formulation: 5-Aminosalicyclic acid (5-ASA), 73.3%; sodium chloride, 11.7%; povidone, 4.4%; alcohol SDA-3A, q.s.; lactose, 8.8%; calcium stearate/sodium lauryl sulfate, 1.76%; sodium starch glycolate, 0.29%.

Manufacturing Directions

1. Sodium chloride is milled through a Whistler mill, using a small slotted screen.
2. 5-ASA is combined with the sodium chloride and mixed for 5 minutes in a ribbon blender. The powder blend is milled through a FitzMill at high speed (1B band) and returned to the ribbon blender.
3. Povidone/alcohol solution is added to the powder blend while the mixer is running to form a wet mass.
4. The wet mass is passed through a FitzMill (1/2 in., perforated band) with hammers forward at high speed. The wet granulation is trayed and dried for 16 hours at 55°C. The dried mixture is passed through a FitzMill (2A band) with knives forward at medium speed.
5. The resultant blend is placed in a ribbon blender. Lactose, calcium stearate/sodium lauryl sulfate, and sodium starch glycolate is passed through a 40-mesh screen.
6. The screened powders are added to the ribbon blender and mixed for 5 minutes.
7. On a conventional tablet press, the finished granulation is compressed into 3/8-in. tablets, using standard concave tooling. The tablets meet the target weight requirements, are about 0.175-in. thick, have a hardness of 8 to 15 kPa, and a friability of NMT 0.4%.
8. 100 kg of compressed tablets is placed into an Accela-Cota pan and warmed to about 40°C exhaust temperature.
9. 5 kg of Opadry Enteric (Colorcon, Inc.) is dispersed in an alcohol (SDA-3A) and water mixture (composition of alcohol/water is 25.5 and 2.8 kg, respectively).
10. This solution is spray coated on tablets using an air-atomization system as follows: 2 spray guns at 35 psi each set to deliver about 60 g/min, maintaining an exhaust temperature of 35°C to 45°C. The coated tablets are dried in the Accela-Cota pan for 1 hour at 35°C to 45°C.
11. The tablets are polished in the pan, using 1 g powdered carnauba wax.

Amiodarone Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.000	1	Amiodarone hydrochloride	200.000
86.000	2	Lactose monohydrate	86.000
27.500	3	Starch (maize)	27.500
8.500	4	Povidone (PVP K-30)	8.500
25.000	5	Starch (maize)	25.000
2.000	6	Magnesium stearate	2.000
1.000	7	Colloidal silicon dioxide (Aerosil 200)	1.000
–	8	Purified water	116.67

Manufacturing Directions

Note: Avoid overmixing lubricants because it reduces hardness.

1. Sieving and dry mixing: Sift items 1, 3, and 2 through a 500-μm stainless steel sieve. Load into the mixer. Mix for 5 minutes at low speed.
2. Preparation of binder
   a. Dissolve item 4 in 16.67 g of item 8 by using a stirrer at a slow speed in a stainless steel container.
   b. Pass item 5 through a 250-μm sieve.
   c. Make a homogeneous slurry of item 5 in 25.0 g of item 8 (30°C) in a stainless steel container. Ensure that it is free of lumps.
   d. Heat 75.0 g of item 8 to 90°C in a stainless steel container. Add the slurry from step 2. Stir until complete gelatinization occurs. Cool to 50°C.
   e. Add the solution from step 2 into step 3 and stir for 5 minutes.
   f. Check the quantity of the binder: theoretical weight, 150 g. Adjust the weight with purified water by mixing if required.
3. Kneading
   a. Knead the powder in a mixer (Diosna) with the binder, while mixing at low speed over a period of 2 minutes. Scrape the sides and the blades. Mix and chop at low speed for 2 minutes.
   b. Check the end point of granulation. If required, add more purified water to get the end point. (The end point of the granulation is the point when the wet mass consists of little or no lumps of the granules.)
   c. Unload the wet granules in a stainless steel tray for drying.
4. Drying
   a. Dry the wet granules at 550°C for 5 hours.
   b. Check the LOD: the limit is 1.0% to 1.5%. If required, dry further at 550°C for 1 hour. Check the LOD.
   c. Transfer the dried granules to a polyethylene bag.
5. Grinding: Grind the dried granules through a 1.25-mm sieve, using a granulator at medium speed. Collect in a polyethylene bag.
6. Lubrication
   a. Sift items 6 and 7 through a 250-μm sieve in a stainless steel sieve. Collect in a polyethylene bag. Take approximately 66.67 g of granules from step 5 into the polyethylene bag. Mix manually. Add into step 5. Mix for 1 minute.
   b. Store in a polyethylene bag.
7. Compression and specifications: Compress the granules by using a rotary tabletting machine, 10-mm round plain convex punch. (Weight of 10 tablets: 3.5 g ± 3%.)

Amitriptyline Tablets (50 mg), Elavil

Elavil® (amitriptyline HCl) is supplied as 10-, 25-, 50-, 75-, 100-, and 150-mg tablets and as a sterile solution for intramuscular use. Inactive ingredients in the tablets are as follows: calcium phosphate, cellulose, colloidal silicon dioxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, magnesium stearate, starch, stearic acid, talc, and titanium dioxide. The 10-mg amitriptyline HCl tablets also contain FD&C Blue No. 1. The 25-mg amitriptyline HCl tablets also contain D&C Yellow No. 10, FD&C Blue No. 1, and FD&C Yellow No. 6. The 50-mg amitriptyline HCl tablets also contain D&C Yellow No. 10, FD&C Yellow No. 6, and iron oxide. The 75-mg amitriptyline HCl tablets also contain FD&C Yellow No. 6. The 100-mg amitriptyline HCl tablets also contain FD&C Blue No. 2 and FD&C Red No. 40. The 150-mg amitriptyline HCl tablets also contain FD&C Blue No. 2 and FD&C Yellow No. 6.

Amitriptyline Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Amitriptyline	50.00
20.00	2	Starch (maize)	20.00
20.00	3	Lactose monohydrate	20.00
15.00	4	Dicalcium phosphate	15.00
2.00	5	Magnesium stearate	2.00
3.00	6	Talc	3.00
20.00	7	Starch (maize)	20.00
–	8	Water, purified, ca	100 mL

Manufacturing Directions

1. Sift items 1 to 4 through a 250-μm sieve and charge in a suitable mixer.
2. In a separate vessel, charge item 2 and add item 8 at 80°C. Mix until a good paste is formed. Cool to 50°C.
3. Add step 2 into step 1, and knead and chop until granules are formed without lumps.
4. Spread the wet mass onto trays and dry in an oven at 50°C for 15 hours to an LOD of not more than 1.5%.
5. Pass the dried granules through No. 18 mesh and transfer to a suitable blender.
6. Pass item 5 though a 250-μm sieve and item 7 through a 500-μm sieve; add to step 5 and blend for 2 minutes.
7. Compress into 130-mg tablets, using a suitable punch.
8. Coat the tablet with an organic base coating. (See Appendix.)

Amlodipine Besylate Tablets

Amlodipine besylate tablets are formulated as white tablets equivalent to 2.5, 5, and 10 mg of amlodipine for oral administration. In addition to the active ingredient, amlodipine besylate, each tablet contains the following inactive ingredients: microcrystalline cellulose, dibasic calcium phosphate anhydrous, sodium starch glycolate, and magnesium stearate.

Amlodipine Besylate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	(–)Amlodipine	0.50
183.00	2	Lactose anhydrous	183.00
15.00	3	Starch pregelatinized	15.00
1.50	4	Magnesium stearate	1.50

Manufacturing Directions

1. Sieve the active ingredient, (–)amlodipine, through a suitable sieve, and blend with lactose and pregelatinized maize starch.
2. Add suitable volumes of purified water to granulate.
3. After drying, screen the granules and blend with the magnesium stearate.
4. Compress using 7-mm-diameter punches to a total weight of 200 mg. Adjust the formula for other strengths with lactose (2.5 and 5.0 mg).

Amlodipine Free Base Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.5	1	Amlodipine base	2.5
31.50	2	Calcium hydrogen phosphate anhydrate	31.50
62.05	3	Microcrystalline cellulose	62.05
2.00	4	Sodium starch glycollate	2.00
1.00	5	Magnesium stearate	1.00

Manufacturing Directions

1. Amlodipine base is sieved through a 500-μm screen and other excipients are sieved through a 850-μm screen.
2. All excipients except magnesium stearate are mixed in a free fall mixer for 15 minutes at about 25 rpm.
3. Magnesium stearate is added and the powder blend is mixed for another 5 minutes at about 25 rpm. Compress into 2.5-mg and 10-mg tablets with total weight of 100 or 400 mg, respectively.

Amlodipine Maleate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3.21	1	Amlodipine maleate	3.21
31.50	2	Calcium hydrogen phosophate anhydrous	31.50
62.05	3	Microcrystalline cellulose	62.05
2.00	4	Soodium startch glycolate	2.00
1.00	5	Magnesium stearate	1.00

Manufacturing Directions

1. Amlodipine maleate is milled to a particle size of 10 to 20 μm.
2. Amlodipine maleate is sieved through a 500-μm screen and other excipients are sieved through a 850-μm screen.
3. All excipients except magnesium stearate are mixed in a free fall mixer for 15 minutes at about 25 rpm. Value of pH is checked at 20% aqueous slurry (should be around 5.9).
4. Magnesium stearate is added and the powder blend is mixed for another 5 minutes at about 25 rpm.
5. Tablets are compressed at approximately 100 mg to give 2.5 mg strength and proportionally higher for amounts up to 10 mg per tablet.

Amoxacillin and Clavulanate Potassium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Amoxicillin, use amoxicillin trihydrate compacted, with excess	587.50
125.00	2	Clavulanate, use clavulanate potassium with Avicel (1:1)	305.00
25.00	3	Sodium starch glycolate	25.00
30.00	4	Aerosil 200	30.00
10.00	5	Sodium carmellose	10.00
10.00	6	Talc	10.00
5.00	7	Magnesium stearate	5.00

Manufacturing Directions

1. Dry item 1 at 45°C for 2 hours.
2. Dry items 6, 7, 5, and 3 at 80°C for 4 hours.
3. Sift items 1 to 7 through #40 mesh screen, charge in a drum mixer, and mix for 30 minutes.
4. Slug the mixture in step 3 using 16-mm punches and a hardness of 6 to 7 kPa.
5. Break the slugs by passing through 2.5-mm mesh sieves on a mill.
6. Transfer the comminuted slugs to a blender and add items 6 and 7 for 15 minutes.
7. Compress using 19 × 9 mm punches.
8. Coat the tablets with HPMC organic coating. (See Appendix.)

Amoxacillin Fast-Disintegrating Tablets

1. 970 g of cefaclor (as monohydrate) and 30 g of microcrystalline cellulose and sodium carboxymethyl cellulose (Avicel RC591) are mixed for 5 minutes in a planetary mixer.
2. Gradually about 320 mL of water is added to this blend and mixing is continued for another 5 minutes.
3. The wet granulate is dried in a fluidized bed dryer at an air inlet temperature of 50°C and subsequently sieved through a 1.00- and 0.630-mm screen, respectively.
4. 864 g of the granulate obtained in step 3 is mixed with 98 g of a mixture of microcrystalline cellulose and crosslinked polyvinylpyrrolidone (1:1), flavors, and sweetening agents in a TURBULA-mixer for 10 minutes.
5. After a lubricant is added, mixing is continued for another 3 minutes and the mixture is compressed into tablets with a mean weight of 625 mg. Friability, <0.01%; hardness, 6.9 kPa; disintegration time, 22 seconds.

Amoxicillin and Potassium Clavulanate Tablets (250 mg/62.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Amoxicillin, use amoxicillin trihydrate	250.00
62.50	2	Clavulanic acid, use potassium clavulanate	62.50
23.00	3	Polyplasdone XL, dried	23.00
23.00	4	Syloid AL1	23.00
4.50	5	Magnesium stearate	4.50
450.00	6	Microcrystalline cellulose	450.00

Manufacturing Directions

1. Polyplasdone XL, dried, is present as a disintegrant. Syloid AL1 is a desiccant used to prevent hydrolytic degradation of the actives. Magnesium stearate is present as a lubricant. Microcrystalline cellulose is a tablet binder and disintegrant.
2. Mill amoxicillin trihydrate, using a swing hammer mill at fast speed through a 0.063-in. screen, with knives forward.
3. Mix the milled amoxycillin trihydrate with potassium clavulanate, polyplasdone, Syloid AL1, part of magnesium stearate, and part of microcrystalline cellulose.
4. Slug the blend from step 3, or use a roller compacted.
5. Mill the compacts or flake from step 4 through a swing hammer mill at medium speed, with knives forward, and fitted with a 0.063-in. screen.
6. Blend granules with remaining magnesium stearate and remaining microcrystalline cellulose.
7. Compress to a core weight of 450 mg and a hardness of 15 to 20 kPa.
8. Provide a film subcoating with an aqueous suspension of hydroxypropyl methyl cellulose, further coated with a Eudragit enteric coating, and finally, with a further overcoating of hydroxypropyl methyl cellulose. (See Appendix.)

Amoxicillin Tablets (250 mg/500 mg/1 g), Acid Trihydrate

Tablets—Each tablet contains 500 or 875 mg of amoxicillin as the trihydrate. Each film-coated, capsule-shaped, pink tablet is embossed with AMOXIL, centered over 500 or 875, respectively. The 875-mg tablet is scored on the reverse side. The inactive ingredients are colloidal silicon dioxide, crospovidone, FD&C Red No. 30 Aluminum Lake, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide.

Chewable tablets—each cherry-/banana-/peppermint-flavored tablet contains 125, 200, 250, or 400 of amoxicillin as the trihydrate. The 125- and 250-mg pink oval tablets are imprinted with the product name AMOXIL on one side and 125 or 250 on the other side. The inactive ingredients are citric acid, cornstarch, FD&C Red No. 40, flavorings, glycine, mannitol, magnesium stearate, saccharin sodium, silica gel, and sucrose. Each 125-mg chewable tablet contains 0.0019 mEq (0.044 mg) of sodium; the 250-mg chewable tablet contains 0.0037 mEq (0.085 mg) of sodium. Each 200-mg chewable tablet contains 0.0005 mEq (0.0107 mg) of sodium; the 400-mg chewable tablet contains 0.0009 mEq (0.0215 mg) of sodium. The 200- and 400-mg pale pink, round tablets are imprinted with the product name AMOXIL and 200 or 400 along the edge of one side. The inactive ingredients are aspartame, crospovidone, FD&C Red No. 40 Aluminum Lake, flavoring, magnesium stearate, and mannitol.

Amoxacillin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Amoxicillin (871 mcg/mg activity)[a]	287.00
28.50	2	Cellulose microcrystalline NC (Avicel PH 101)	28.50
20.00	3	Povidone K 29–32	20.00
QS	4	Alcohol 190 proof, approximately	70.00 mL
3.50	5	Magnesium stearate	3.50

[a]Adjust according to potency. Adjust the tablet size as given below to yield 1-g, 500-mg, and 250-mg tablets.

Manufacturing Directions

Caution: Handle with extreme care. Protect face and hands because some individuals may be sensitive and reactions may occur.

1. Granulation
   a. Pass amoxicillin through a 595-μm aperture screen using a FitzMill, with knives forward, at medium speed.
   b. Charge the following ingredients in a suitable mixer: cellulose microcrystalline, sodium starch glycolate, and milled amoxicillin. Mix for 30 minutes.
   c. Add 100 g of alcohol and mix for an additional 15 minutes.
   d. Dissolve povidone in approximately 150 g of alcohol. Add povidone solution to the mixture from step 3, with continuous mixing. Mix for 15 minutes, until a suitable granulating mass is obtained. If necessary, add more alcohol.
   e. Pass the wet mass through a 4.76-mm aperture screen.
   f. Spread the wet granulation onto trays. Oven dry at 38°C or until the LOD is 2% to 3.5% (vacuum 60°C, 3 hours).
   g. Pass the dry granulation through a 1.2-mm aperture screen in an oscillating granulator.
2. Lubrication
   a. Charge half of the amount of dried granulation into a suitable mixer. Pass magnesium stearate through a 500-μm aperture screen and add to the mixer. Mix for 10 minutes.
   b. Add the balance of granulation and mix for an additional 5 minutes.
   c. Charge into polyethylene-lined drums.
3. Compression
   a. Compress into 1-g tablets, using 20 × 9 mm bisected ovaloid punches (thickness 9.6–10.6 mm; hardness not less than 15 kPa).
   b. Compress into 500-mg tablets, using 18 × 8.5-mm ovaloid punches (thickness is 6.5–6.7 mm; hardness is 12–18 kPa).
   c. Compress into 250-mg tablets, using 10.3-mm-diameter punches (thickness is 5.1–5.3 mm; hardness is 12 kPa).

Amoxicillin Trihydrate and Clavulanate Potassium Tablets (500 mg/125 mg) Augmentin

Each Augmentin tablet contains 0.63 mEq of potassium. Each 125-mg chewable tablet and each 5 mL of reconstituted Augmentin 125 mg/5 mL oral suspension contain 0.16 mEq of potassium. Each 250-mg chewable tablet and each 5 mL of reconstituted Augmentin 250 mg/5 mL oral suspension contain 0.32 mEq of potassium. Each 200-mg chewable tablet and each 5 mL of reconstituted Augmentin 200 mg/5 mL oral suspension contain 0.14 mEq of potassium. Each 400-mg chewable tablet and each 5 mL of reconstituted Augmentin 400 mg/5 mL oral suspension contain 0.29 mEq of potassium.

Inactive ingredients:

Chewable tablets—colloidal silicon dioxide, flavorings, magnesium stearate, mannitol, and one or more of the following: aspartame, D&C Yellow No. 10, FD&C Red No. 40, glycine, sodium saccharin, and succinic acid.

Tablets—colloidal silicon dioxide, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide.

Amphetamine Salts Tablets

This is a single-entity amphetamine product combining the neutral sulfate salts of dextroamphetamine and amphetamine, with the dextroisomer of amphetamine saccharate, and 6,L-amphetamine aspartate.

Each Tablet Contains	5 mg	10 mg	20 mg	30 mg
Dextroamphetamine saccharate	1.25 mg	2.5 mg	5 mg	7.5 mg
Amphetamine aspartate	1.25 mg	2.5 mg	5 mg	7.5 mg
Dextroamphetamine sulfate	1.25 mg	2.5 mg	5 mg	7.5 mg
Amphetamine sulfate	1.25 mg	2.5 mg	5 mg	7.5 mg
Total amphetamine base equivalence	3.13 mg	6.3 mg	12.6 mg	18.8 mg

Inactive ingredients: Sucrose, lactose, cornstarch, acacia, and magnesium stearate.

Ampicillin Tablets (250 mg)

Formulation: Ampicillin trihydrate, 250 g; Ludipress, 250 g; magnesium stearate, 10 g.

Manufacturing Directions

Mix all components, pass through a sieve, and press with low-compression force at 500 mg.

Apomorphine and Nicotine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Apomorphine hydrochloride	4.00
1.00	2	Nicotine base	1.00
4.00	3	Acesulfame-K	4.00
37.50	4	Microcrystalline cellulose	37.50
2.50	5	Peppermint flavor	2.50
2.00	6	Chocolate natural flavor	2.00
3.00	7	Citric acid	3.00
13.00	8	Hydroxypropyl methylcellulose	13.00
80.00	9	Mannitol	80.00
3.00	10	Magnesium stearate	3.00

Manufacturing Directions

1. Pass all ingredients through a #35 mesh screen (sieve opening of about 0.51 mm) to ensure granulation.
2. A solution containing apomorphine HCL, citric acid, half the acesulfame-K, half the peppermint flavor, and half the chocolate flavor is prepared by dissolving the ingredients into a mixture of equal volumes of purified water and ethanol, USP.
3. The solution is mixed until clear, and then absorbed into the listed amount of microcrystalline cellulose (Avicel 302).
4. The resulting wet mass, labelled "part A," is mixed in a porcelain dish at room temperature (20°C) for 30 minutes, and then partially dried to obtain a solid mass.
5. The mass is next granulated by screening through a #50 mesh (ASTM) (sieve opening of about 0.297 mm) stainless steel screen. The wet granules are dried at about 60°C to 70°C for about 1 to 1.5 hours. The resulting dried granules are then passed through a #35 mesh screen (sieve opening of about 0.51 mm).
6. Separately, nicotine is added to and blended with all the remaining ingredients except for the magnesium stearate. More specifically, nicotine is added to the second half of the acesulfame-K, half the peppermint flavor, half the chocolate flavor, the hydroxypropylmethylcellulose (methocel E4M, premium), and the mannitol.
7. The resulting blend is labelled "part B." Parts A and B are then combined and mixed for about 5 minutes in a V-shaped blender. Next, magnesium stearate is added to the blender and blended continuously for about 2 minutes.
8. The final mix is removed from the blender and compressed into 150-mg tablets.

Apomorphine and Prochlorperazine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Apomorphine hydrochloride	4.00
5.00	2	Prochlorperazine hydrochloride	5.00
4.00	3	Acesulfame-K	4.00
37.50	4	Microcrystalline cellulose	37.50
2.50	5	Peppermint flavor	2.50
2.00	6	Chocolate natural flavor	2.00
3.00	7	Citric acid	3.00
10.00	8	Hydroxypropyl methylcellulose	10.00
80.00	9	Mannitol	80.00
3.00	10	Magnesium stearate	3.00

Manufacturing Directions

1. Pass all ingredients through a #35 mesh screen (sieve opening of about 0.51 mm) to ensure granulation.
2. A solution containing prochlorperazine HCL, citric acid, half the acesulfame-K, half the peppermint flavor, and half the chocolate flavor is prepared by dissolving the ingredients into a mixture of equal volumes of purified water and ethanol, USP.
3. The solution is mixed until clear, and then absorbed into the listed amount of microcrystalline cellulose (Avicel 302).
4. The resulting wet mass, labelled "part A," is mixed in a porcelain dish at room temperature (20°C) for 30 minutes, and then partially dried to obtain a solid mass.
5. The mass is next granulated by screening through a #50 mesh (sieve opening of about 0.297 mm) stainless steel screen. The wet granules are dried at about 60°C to 70°C for about 1 to 1.5 hours. The resulting dried granules are then passed through a #35 mesh screen (sieve opening of about 0.51 mm).
6. Separately, nicotine is added to and blended with all the remaining ingredients except for magnesium stearate. More specifically, nicotine is added to the second half of the acesulfame-K, half the peppermint flavor, half the chocolate flavor, the hydroxypropylmethylcellulose (methocel E4M, premium), and the mannitol.
7. The resulting blend is labelled "part B." Parts A and B are then combined and mixed for about 5 minutes in a V-shaped blender. Next, magnesium stearate is added to the blender and blending continued for about 2 minutes.
8. The final mix is removed from the blender and compressed into 150-mg tablets.

Asparagus Extract + Parsley Extract Tablets (200 mg + 200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Asparagus extract powder	200.00
200.00	2	Parsley extract powder	200.00
200.00	3	Sorbitol crystalline	200.00
20.00	4	Kollidon VA 64	20.00
10.00	5	Kollidon CL	10.00
4.00	6	Magnesium stearate	4.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve and mix.
2. Press to tablets with low-compression force at 636 mg.

Aspartame Effervescent Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
00.00	1	Aspartame	20.00
10.40	2	Sorbitol crystalline	10.40
14.30	3	Tartaric acid powder	14.30
18.70	4	Sodium carbonate	18.70
1.70	5	Kollidon 25	1.70
1.10	6	PEG 6000 powder	1.10

Manufacturing Directions

1. Mix all components and pass through a 0.5-mm sieve.
2. Press to tablets at 66 mg.

Aspartame Tablets (25 mg), DC

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
27.00	1	Aspartame	27.00
76.00	2	Ludipress	76.00
12.00	3	Kollidon® CL	12.00
1.00	4	Magnesium stearate	1.00
3.00	5	Lutrol F68	3.00

Manufacturing Directions

1. Mix all components and pass through a 0.8-mm sieve.
2. Press to tablets with low-compression force at 120 mg.

Aspartame Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Aspartame	20.00
4.00	2	Cellulose (microcrystalline) (Avicel™ PH101), NF	4.00
4.00	3	Sodium starch glycolate (pH 5.5–7.5), NF International	4.00
0.50	4	Silicon dioxide (colloidal)	0.50
0.50	5	Povidone (PVP K-29–32), USP	0.50
14.00	6	Anhydrous alcohol (isopropyl, refined) USP	~14.00
34.00	7	Lactose (granulated)	34.00
4.00	8	Leucine, USP	4.00
3.00	9	Sodium benzoate (powder), NF	3.00

Manufacturing Directions

1. Charge aspartame, cellulose microcrystalline, sodium starch glycolate, silicon dioxide, and Povidone in a suitable mixer.
2. Blend for 20 minutes or until uniform.
3. While mixing, slowly add isopropyl alcohol to blended powders until a suitable granulating mass is obtained. Avoid overwetting.
4. Pass wet mass through a 2.38-mm screen on an oscillating granulator and spread onto paper-lined trays.
5. Oven dry at 45°C to 50°C until LOD is NMT 1.2%.
6. Pass dried granulation through an 840-μm screen on an oscillating granulator.
7. Charge dried granulation into a suitable mixer.
8. Add granulated lactose, leucine, and sodium benzoate, and blend for ~10 minutes.
9. Discharge into polyethylene-lined drums.
10. Compress tablets in a low-humidity area not to exceed 40% relative humidity at 23°C.
11. Compress, using 7/32-in. concave punches, to the following specifications: weight of 10 tablets is 0.7 g; thickness of a tablet is 2.9 to 3.3 mm.

Aspartame Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25	1	Aspartame	25
25	2	Dibasic calcium phosphate	25
3	3	Kollidon® VA 64	3
10	4	Water	10
3	5	Kollidon® CL	3
3	6	PEG-6000 (powder)	3

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with items 4 and 5.
2. Pass through an 0.8-mm sieve and mix with item 6.
3. Press to tablets (60 mg in weight) with a 5-mm biplanar shape.

Aspartame Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Aspartame	27.00
76.00	2	Ludipress®	76.00
12.00	3	Kollidon® CL	12.00
1.00	4	Magnesium stearate	1.00
3.00	5	Lutrol F 68	3.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press to tablets with low-compression force.
2. Each 8-mm biplanar tablet has an average weight of 120 mg.

Aspartame Tablets, Effervescent

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Aspartame	20.00
10.40	2	Sorbitol (crystalline)	10.40
14.30	3	Tartaric acid (powder)	14.30
18.70	4	Sodium bicarbonate	18.70
1.70	5	Kollidon® 25	1.70
1.10	6	PEG-6000 (powder)	1.10

Manufacturing Directions

1. Mix all items, pass through a 0.5-mm sieve, and press to tablets.
2. Each 6-mm biplanar tablet has an average weight of 66 mg.

Aspirin, Acetaminophen, and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
225.00	1	Aspirin (40 mesh)	225.00
250.00	2	Acetaminophen (20 mesh)	250.00
30.00	3	Caffeine (granular)	30.00
100.00	4	Cellulose (microcrystalline) (Avicel™ PH-102)	100.00
45.00	5	Anhydrous lactose	45.00
10.00	6	Croscarmellose sodium (Ac-Di-Sol)	10.00
5.00	7	Fumed silica	5.00
10.00	8	Stearic acid	10.00

Manufacturing Directions

1. Mix items 1 to 6 in a suitable blender.
2. Pass the mixture through a mill, using a 12-mesh screen with knives forward.
3. Add items 7 and 8, and blend the milled mixture for 20 minutes in a V-blender.
4. Compress to tablet weight of 675 mg.

Aspirin, Acetaminophen, Caffeine, and Salicylamide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Aspirin (40 mesh)	200.00
100.00	2	Salicylamide	100.00
100.00	3	Acetaminophen (40 mesh)	100.00
60.00	4	Caffeine (Granular)	60.00
150.00	5	Cellulose (microcrystalline) (Avicel™ PH101)	150.00
13.00	6	Stearic acid, USP	13.00
3.00	7	Fumed silica	3.00

Manufacturing Directions

1. Screen all ingredients through a 20-mesh sieve.
2. Blend all the ingredients in a V-blender for 20 minutes.
3. Compress into 615-mg tablets, using 5/8-in. tooling.

Aspirin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Aspirin	325.00
25.52	2	Starch 1500	25.52
21.33	3	Microcrystalline cellulose (50 um)	21.33
6.33	4	Powdered cellulose	6.33

Manufacturing Directions

1. Blend in a twin-shell blender.
2. Compress into 378.00-mg tablets.

Atenolol Tablet

Formulation: Atenolol, 100.00 mg; citric acid (anhydrous), 4.00 mg; microcrystalline cellulose, 169.00 mg; sodium starch glycollate, 3.00 mg; magnesium stearate, 4.00 mg. Total 280.00 mg.

Manufacturing Directions

1. Citric acid is dissolved in purified water to provide a 20% citric acid solution.
2. Atenolol is granulated with this solution in a planetary mixer and the resultant granules were dried in a tray dryer to less than 3% by weight loss on drying.
3. The atenolol/citric acid premixture is hammer milled and blended with the other excipients. This material is compressed into 280-mg tablets.

Atenolol Tablets (50 mg/100 mg), Tenormin

Tenormin is available as 25-, 50-, and 100-mg tablets for oral administration. The inactive ingredients are magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate.

Atenolol Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Atenolol	50.00
87.50	2	Magneisum carbonate heavy	87.50
29.70	3	Starch (corn)	59.70
3.30	4	Sodium lauryl sulfate	3.30
30.00	5	Starch (corn)	30.00
2.00	6	Gelatin	2.00
5.00	7	Magnesium stearate	5.00
QS	8	Purified water	QS

Note: The above formula is used for both 50- and 100-mg strengths; see below for fill weights to obtain the correct strengths.

Manufacturing Directions

1. Massing
   a. Mix starch (item 5) with approximately 27.3 mL of purified water (item 8) in a glass or stainless steel vessel, avoiding the formation of lumps.
   b. Boil the remaining 52.8 mL of purified water (item 8), and add the mix from step 1 with continuous stirring until a gel is formed. Further heat may be necessary. (*Note:* A mix temperature greater than 95°C must be exceeded before a gel is formed.)
   c. Pass gelatin through a 1.59-mm aperture, and add water at 50°C, dissolve, and add to step 2.
   d. Add sodium lauryl sulfate to step 3 without excessively mixing (to avoid foaming).
   e. Mill the atenolol through a 1.59-mm aperture screen at medium speed with knives forward, then charge into a suitable mixer.
   f. Pass magnesium carbonate heavy, starch (corn) (#3) through a 1.00-mm aperture stainless screen, and add to the mixer. Mix at 60 rpm for 10 minutes.
   g. Pass the mixed powders from step 4 through a 1-mm aperture stainless steel screen, and return to the mixer.
   h. Add, in one charge, the starch and gelatin and sodium lauryl sulfate gel from step 4 at 70°C to 80°C, and mix for 5 minutes at 60 rpm.
   i. Stop the mixer and inspect the mass. Add the extra 6.88 mL of purified water (#9) at 50°C to complete the granulation while mixing. Mix for a further 5 minutes at 60 rpm.
2. Drying/granulation: Proceed to step 1 or 2.
   a. Oven drying
      i. Pass the wet mass through a granulator fitted with a 4.76-mm aperture stainless steel screen. Collect the granules on paper-lined trays.
      ii. Dry the granules in a hot air oven at 60°C (not more than 65°C). After 1 hour of drying, pass the granules through a granulator fitted with a 2.38-mm aperture stainless steel screen. Collect the granules on paper-lined trays and return to the hot air oven at 60°C.
   b. Fluid-bed drying
      i. Pass the wet mass through a granulator fitted with a 4.76-mm aperture stainless steel screen into the fluid-bed dryer bowl.
      ii. Dry the granules in the fluid-bed dryer at 60°C for 30 minutes, turning over after 15 minutes. Then pass the granules through a granulator fitted with a 2.38-mm aperture stainless steel screen, and then return to the fluid-bed dryer bowl with the air inlet and outlet fully open. Proceed to step 3.
   c. Continue drying the granules until the LOD is between 1.5 and 2%.
   d. Pass the dried granules through a granulator fitted with a 1-mm aperture stainless steel screen. Collect the granules in a polyethylene-lined drum, and close securely.
3. Lubrication
   a. Place the dried granules from step 2 ("drying/granulation") in a suitable blender.
   b. Add magnesium stearate and the remainder of the starch via a 0.6-mm aperture stainless steel screen, and mix for 25 minutes.
   c. Transfer to a polyethylene-lined drum and close securely until ready for compression.
4. Compression: Compress on a suitable tablet machine using round punches—weight of 10 tablets is 2.075 g for 50-mg strength and 4.15 g for 100-mg strength; hardness more than 5 kPa; disintegration time not more than 15 minutes.
5. Coating: Use either organic coating or aqueous methocel as needed. Follow with a clear gloss.

Atenolol Tablets (90 mg)

Formulation: Atenolol (Stober), 93.0 g; Ludipress, 287.0 g; Kollidon CL, 52.0 g; magnesium stearate, 2.2 g; aerosil 200, 0.9 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press to tablets with low-compression force at 436 mg.

Atorvastatin Tablets (10 mg/20 mg), Atrovastatin Calcium Lipitor

Lipitor tablets for oral administration contain 10, 20, or 40 mg of atorvastatin and the following inactive ingredients: calcium carbonate, USP; candelilla wax, FCC; croscarmellose sodium, NF; hydroxypropyl cellulose, NF; lactose monohydrate, NF; magnesium stearate, NF; microcrystalline cellulose, NF; Opadry White YS-1–7040 (hydroxypropylmethylcellulose, polyethylene glycol, talc, titanium dioxide); polysorbate 80; and simethicone emulsion.

Atorvastatin Calcium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00 11.00	1	Atorvastatin, use atorvastatin calcium trihydrate	10.00 11.00
36.00	2	Calcium carbonate	36.00
65.00	3	Lactose monohydrate	65.00
30.00	4	Microcrystalline cellulose (Avicel PH 102)	30.00
3.00	5	Polyvinylpyrrolidone (Povidone K-30)	3.00
0.40	6	Polysorbate 80 (Tween 80)	0.40
4.00	7	Croscarmellose sodium (Ac-Di-Sol)	4.00
0.60	8	Magnesium stearate	0.60
–	9	Purified water	QS

Manufacturing Directions

1. Sift atorvastatin calcium trihydrate, calcium carbonate, lactose monohydrate, and Avicel PH 102 through a 0.500-mm stainless steel sieve.
2. Dissolve PVP K-30 and Polysorbate-80 in purified water (50°C) by slow stirring until it becomes clear. Cool the solution to 30°C. This is the granulating solution.
3. Knead the powder mix with granulating solution to get the desired granules.
4. Dry the granules to a targeted LOD of 2%.
5. Pass the dried granules through #16 mesh.
6. Sift Ac-Di-Sol and magnesium stearate through 0.500 mm.
7. Load the ground granules from step 5 and the powder mix from step 6 into a suitable blender. Blend for 1 minute.
8. Compress into 150-mg tablets, using 12-mm punches. For 20-mg strength, compress 300 mg in 15-mm punches.
9. Prepare a hypromellose and polyethylene glycol 4000 solution in the mixture of purified water and ethanol 95%. Keep overnight for complete gelation. (See Appendix.)
10. Add talc and titanium dioxide into step 10, and homogenize for a uniform coating dispersion.
11. Coat the tablets using the coating dispersion Accel Cota to a targeted weight.

Attapulgite Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
475.00	1	Attapulgite (regular)	475.00
275.00	2	Attapulgite (colloidal)	275.00
12.00	3	PVP K 30	12.00
7.00	4	Ac-Di-Sol	7.00
15.00	5	Kollidon® CL	15.00
30.00	6	Sucrose	30.00
50.00	7	Klucel® EF	50.00
40.00	8	Sucrose	40.00
35.00	9	Ac-Di-Sol	35.00
25.00	10	Kollidon® CL	25.00
14.00	11	Talc (fine powder)	14.00
5.00	12	Pectin	5.00
7.00	13	Glyceryl behenate	7.00
5.00	14	Aerosil 200	5.00
5.00	15	Magnesium stearate	5.00
–	16	Purified water	32.00
–	17	Ethanol (95%)	23.00

Manufacturing Directions

Caution: Use face-mask, hand gloves, and clean uniform. Avoid dust and inhalation of powder.

1. Dissolve sucrose (item 6) in purified water by using an appropriate stirrer at slow speed in a stainless steel container.
2. Dissolve Klucel EF in the ethanol by using an appropriate stirrer at slow speed in stainless steel container.
3. Mix the contents of steps 1 and 2 in a stainless steel drum by using an appropriate stirrer at slow speed.
4. Take item 8 (sucrose) and pass through a FitzMill using sieve number 24250 (impact forward, high speed). Collect the sieved contents in a stainless steel drum.
5. Add items 1 to 5 and sift the material through a 500-μm sieve using a Russell sifter.
6. Mix for 3 minutes.
7. Add the binding solution prepared earlier at a speed of 6 to 8 kg/min to the dry powder in an appropriate mixer at slow speed. After addition, scrape sides and blades, and then mix and chop further for 1 minute at slow speed. Check for satisfactory wet mass. Add additional purified water, if required, to obtain satisfactory wet mass.
8. Spread the granules onto stainless steel trays to a thickness of 1/4th of the tray thickness and load the trays on the trolley.
9. Load the trolleys into the oven and dry the granules at 55°C for 16 hours.
10. After 4 hours of drying, stir the granules on the trays and change the position of the trays for uniform drying.
11. Check the LOD of dried granules (limit: 2.5–3.5%).
12. The LOD should be strictly maintained; otherwise, tablet hardness and friability are affected. If required, dry further to obtain the desired LOD.
13. Grind the dried granules first using a 2.5-mm sieve and then with a 1.25-mm sieve.
14. Load the ground material into a double-cone blender.
15. Sift items 9, 10, 12, and 14 through a 500-μm sieve and add mixture to the double-cone blender.
16. Mix for 5 minutes.
17. Sift items 11, 13, and 15 through a 250-μm sieve and collect in a polyethylene bag.
18. Add about 2 to 3 kg bulk granules from earlier step, mix, and add to the double-cone blender.
19. Mix for 1 minute.
20. Compress the granules using an 18 × 8 mm, oblong, capsule-shaped, parallel, concave, plain punch for a 1-g tablet weight of hardness 12 to 18 kPa.
21. Coat the tablets using one of the HPMC coating solutions (see Appendix).

Azithromycin Chewable Tablets

Formulation: Azithromycin dihydrate (1619.870 g, 60% of total composition), F.D. and C. Red #40 (1.125 g), magnesium oxide (309.757 g, 11.5% of total composition), calcium gluconate (46.4160 mg, 1.7% of total composition), and sodium starch glycolate (139.248 g) are combined in an eight-quart V-blender and blended for 30 minutes.

Manufacturing Directions

1. The blend is passed through a Fitzpatrick JT Comminutor fitted with a #0 plate (0.027 in. opening) at medium speed with the hammers forward.
2. The mixture is then returned to the blender and blended for an additional 30 minutes. The blend is transferred to an eight-quart Hobart Planetary Mixer (Model C-100) and mixed at slow (#1) setting.
3. During mixing, the mixture is wet massed by adding 50 g of hydroxypropyl cellulose solution (prepared by adding 45 g of hydroxypropyl cellulose to 405 g of warm (60°C) water with stirring). Water (108 g) is added and the mixture is mixed for 10 minutes. An additional 85 g of water is added to the granulation to achieve the endpoint.
4. The mixer is continued at the slow setting for an additional 5 minutes to granulate the mass. The wet mixture is transferred to a polyethylene-lined tray and heated at 50°C in a forced air over overnight (16 hours).
5. The dried mass is passed through a Fitzpatrick JT Comminutor fitted with a #2 A plate (0.093-in. opening) at slow speed with the knives forward.
6. The granulation is transferred to an eight-quart V-blender, flavors are added, and the flavored granulation is blended for 30 minutes.
7. Magnesium stearate (45 g) is added and the mixture is blended for 5 minutes. The mixture is compressed into tablets to achieve a final tablet weight of 750 mg.

Azithromycin Dihydrate Tablets (600 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
630.00	1	Azithromycin dihydrate equivalent to azithromycin 600 mg	630.00
107.25	2	Dibasic calcium phosphate anhydrous, DC grade	107.25
50.00	3	Pregelatinized starch	50.00
35.00	4	Sodium croscarmellose	35.00
12.75	5	Sodium lauryl sulfate	12.75
15.00	6	Magnesium stearate	15.00
16.00	7	Hypromellose	16.00
5.00	8	Triacetin	5.00
7.00	9	Lactose	7.00
2.00	10	Titanium dioxide	2.00
–	11	Water, purified	200.00

Manufacturing Directions

1. Pass item 1 and 75% of item 5 (=9.5 g) through 0.5-mm sieve and charge in a tumbler. Mix for 5 minutes.
2. Pass item 2, item 3, and 70% of item 4 (=24.5 g) through 0.5-mm sieve and add to step 1.
3. Mix the contents of step 1 for 10 minutes, using tumbler.
4. Pass 50% of item 6 (=7.5 g) through 0.250-mm sieve and add to step 3.
5. Mix the contents of step 4 for 2 minutes.
6. Slug the granules of step 5 with a suitable punch (18.0 mm, round).
7. Grind the slug into granules with 1.25-mm sieve followed by 3-mm sieve.
8. Charge the granules of step 7 in a tumbler.
9. Pass the rest quantity of item 5 and item 4 through 0.5-mm sieve and add to step 8.
10. Mix the contents of step 9 for 5 minutes.
11. Pass the rest quantity of step 6 through 0.250-mm sieve and add to step 10.
12. Mix the contents of step 11 for 2 minutes.
13. Compress into 850-mg tablets, using a suitable punch (19.5 mm × 9.5 mm, oblong).
14. Charge item 11 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
15. Add items 8 through 10 to step 14 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
16. Load core tablets from step 13 in coating pan and apply coating dispersion from step 15 to get 2.75% to 3.25% weight gain.

Azithromycin Tablets (250 mg), Zithromax

Zithromax is supplied for oral administration as film-coated, modified capsule-shaped tablets containing azithromycin dihydrate equivalent to 250 mg of azithromycin and the following inactive ingredients: dibasic calcium phosphate anhydrous, pregelatinized starch, sodium croscarmellose, magnesium stearate, sodium lauryl sulfate, hydroxypropyl methylcellulose, lactose, titanium dioxide, triacetin, and D&C Red No. 30 Aluminum Lake.

Azithromycin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Azithromycin, 5% excess	262.50
22.50	2	Microcrystalline cellulose	22.50
5.00	3	Sodium carmellose	5.00
10.00	4	Starch (maize)	10.00
3.50	5	Talc	3.50
3.50	6	Magnesium stearate	3.50
3.50	7	Aerosil 200	3.50
1.00	8	Sodium lauryl sulfate	1.00
32.50	9	Starch (maize)	32.50

Manufacturing Directions

1. Sift items 1 to 3 through a 250-μm sieve and charge in a mixer.
2. Mix for 15 minutes.
3. Charge item 4 in a suitable vessel, add hot item 10 (80°C), and mix. Allow to cool to room temperature.
4. Add the contents of step 3 to those of step 2, and mix to make wet mass without lumps.
5. Spread wet mass on trays and dry at 50°C for 12 hours.
6. Pass dried granules through #20 mesh and transfer to a tumble mixer.
7. Add items 5 to 9 (sifted through a 250-μm sieve) and mix for 2 minutes.
8. Compress into 340-mg tablets, using 16 × 6 mm punches.
9. Coat tablets with HPMC methylene chloride coating. (See Appendix.)

Benazepril Hydrochloride Tablets Lotensin

Lotensin is supplied as tablets containing 5, 10, 20, and 40 mg of benazepril for oral administration. The inactive ingredients are cellulose compounds, colloidal silicon dioxide, crospovidone, hydrogenated castor oil (5-, 10-, and 20-mg tablets), iron oxides, lactose, magnesium stearate (40-mg tablets), polysorbate 80, propylene glycol (5- and 40-mg tablets), starch, talc, and titanium dioxide.

Benazepril Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Benazepril hydrochloride	20.00
32.90	2	Lactose monohydrate	32.90
5.00	3	Starch, pregelatinized	5.00
1.00	4	Silicon dioxide colloidal	1.00
2.00	5	Crospovidone	2.00
10.00	6	Microcrystalline cellulose	10.00
4.00	7	Hydrogenated castor oil	4.00
–	8	Water, purified	QS

Manufacturing Directions

1. Mill items 1 to 3 and blend together.
2. Add water to granulate the blend, screen wet granules, and oven dry.
3. Mill dried granules after mixing with items 5 to 7.
4. Screen item 4 and add to step 3; blend for 1 minute.
5. Compress.
6. Coat using HPMC 2910 3 cps (4.88 mg) and polysorbate 80 (0.119 mg) in aqueous dispersion; dust tablets with talc.

Benzafibrate Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Benzafibrate	200.00
84.00	2	Lactose monohydrate	84.00
25.00	3	Starch (maize)	25.00
5.800	4	Methocel E5	5.80
13.00	5	Gelatin	13.00
14.90	6	Microcrystalline cellulose (Avicel PH 102)	14.90
14.90	7	Premojel	14.90
6.90	8	Talc	6.90
5.80	9	Magnesium stearate	5.80
QS	10	Water, purified, ca	80 mL

Manufacturing Directions

1. Dissolve item 5 into 50% of item 10 at 70°C to 80°C by mixing at medium speed and avoiding foam formation.
2. Cool to 50°C prior to use.
3. In a separate mixer, drymix items 1 to 4 at medium speed for 5 minutes.
4. Add the gelatin solution from step 2 slowly to the powder mix; add more of item 10, if necessary, to achieve a satisfactory mass, avoiding big lumps.
5. Spread the granules on stainless steel trays to a 10-mm thickness, and load in the oven for drying at 55°C for 12 hours to an LOD of not more than 1%.
6. Grind the dried granules through a 1.25-mm sieve in a granulator and transfer to a double-cone blender.
7. Pass items 6 to 8 through a 250-μm sieve in a sifter, load the mixture in a double-cone blender (step 6), and blend for 5 minutes.
8. Pass item 9 through a 250-μm sieve sifter and collect in a bag. Take a small amount of granules from step 7, mix with item 9 manually, and then add the mixture to the double-cone blender in step 7.
9. Compress into 370-mg tablets, using 11-mm round, concave punches.
10. Coat the tablets with hypermellose. (See Appendix.)

Berberine Tablets (5 mg)

Formulation: Berberine sulfate, 5.7 g; lactose monohydrate, 54.1 g; Ludipress, 54.1 g; magnesium stearate, 1.2 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.

Berberine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Berberine sulfate	5.70
54.10	2	Lactose monohydrate	54.10
54.10	3	Ludipress®	54.10
1.20	4	Magnesium stearate	1.20

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with low-compression force.
2. The 6-mm biplanar tablet has an average weight of 115 mg.

Betamethasone Tablets (0.50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	Betamethasone base, 10% excess	0.55
20.00	2	Maize starch	20.00
85.90	3	Lactose monohydrate	85.95
3.00	4	Maize starch	3.00
0.50	5	Magnesium stearate	0.50
QS	6	Purified water	25.00

Manufacturing Directions

1. Pass item 2 through a 250-μm sieve, and make a homogenous slurry in cold purified water (5 kg) to assure it is free of lumps.
2. Add the slurry to a container with water (20 kg) at 80°C, stir until completely gelatinized, and cool to 50°C.
3. Mix item 1 gradually with item 3 and pass through a 250-μm sieve; pass item 4 through a similar sieve and mix the powders for 15 minutes.
4. Add starch paste and mix for 10 minutes; pass the wet mass through a FitzMill sieve 24205 at medium speed.
5. Dry granules at 55°C for 10 hours; do not exceed a moisture content of 2%. Pass dried granules through a 1-mm sieve into a double-cone blender.
6. Pass item 5 through a 250-μm sieve, mix with granules, and mix for 1 minute.
7. Compressed average tablet weight is 1.10 g; hardness not less than 2.0 kPa.

Beta Carotene Effervescent Tablets (7 mg)

Formulation: Lucarotin® dry powder 10% CWD (BASF), 70 g; Ludipress, 113 g; citric acid, anhydrous, 200 g; sodium bicarbonate, 120 g; sodium carbonate, 12 g; sodium cyclamate, 20 g; aspartame, 15 g; orange flavor, 20 g; polyethylene glycol 6000, powder, 30 g.

Manufacturing Directions

Pass all components through an 0.8-mm sieve, mix, and press with medium- or high-compression force at maximum 30% of relative atmospheric humidity.

Beta-Carotene Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
7.00 mg	1	Beta-carotene; use Lucarotin® CWD (dry powder, 10%) (BASF)	70.00
113.00 mg	2	Ludipress®	113.00
200.00 mg	3	Anhydrous citric acid	200.00
120.00 mg	4	Sodium bicarbonate	120.00
12.00 mg	5	Sodium carbonate	12.00
20.00 mg	6	Sodium cyclamate	20.00
15.00 mg	7	Aspartame	15.00
20.00 mg	8	Orange flavor	20.00
30.00 mg	9	PEG-6000 (powder)	30.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with medium- or high-compression force at maximum 30% relative humidity.
3. Use 12-mm biplanar punches for 602-mg tablets.

Beta-Carotene Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Beta-carotene (dry powder, 10% with excess)	160.00
240.00	2	Ludipress®	240.00
175.00	3	Dicalcium phosphate, granulated with 5% Kollidon® 30	175.00
6.00	4	Kollidon® CL	6.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with medium-compression force.
2. Compress into 400-mg tablets, using 12-mm biplanar punches.

Beta-Carotene Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Beta-carotene (dry powder, 10%)	150.00
175.00	3	Dicalcium phosphate, granulated with 5% Kollidon® 30	175.00
100.00	4	Avicel™ PH101	100.00
5.00	5	Kollidon® CL	5.00
2.50	6	Aerosil® 200	2.50
20.00	7	Talc	20.00
2.50	8	Calcium arachinate	2.50

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with a medium-compression force.
2. Compress into 502-mg tablets, using 12-mm biplanar punches.

Beta-Carotene Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Beta-carotene (dry powder, 10%)	220.00
250.00	2	Avicel™ PH101	250.00
20.00	3	Kollidon® CL	20.00
2.00	4	Aerosil® 200	2.00

Manufacturing Directions

1. Mix all components, and press with a low-compression force.
2. Compress into 518-mg tablets, using 12-mm biplanar punches.

Beta-Carotene, Vitamin C, and Vitamin E Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Beta-carotene (dry powder, 10%)	100.00
250.00	2	Ascorbic acid (crystalline) (BASF)	250.00
280.00	3	Sodium ascorbate (crystalline)	280.00
500.00	4	Vitamin E acetate (dry powder, SD 50)	500.00
600.00	5	Sorbitol (crystalline)	600.00
500.00	6	Ludipress®	500.00
350.00	7	Fructose	350.00
50.00	8	PEG-6000 (powder)	50.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with high-compression force.
2. The 20-mm biplanar tablet has an average weight of 2.6 g.

Beta Carotene + Vitamin C + Vitamin E Chewable Tablets (10 mg + 500 mg + 250 mg)

Formulation: Beta carotene dry powder 10%, 100 g; Ascorbic acid, crystalline (BASF), 250 g; Sodium ascorbate, crystalline, 280 g; Vitamin E acetate dry powder SD 50, 500 g; (BASF) sorbitol, crystalline [10], 600 g; Ludipress, 500 g; fructose, 350 g; polyethylene glycol 6000, powder, 50 g.

Manufacturing Directions

Mix all components, pass through a sieve and press with high-compression force at 2600 mg.

Beta Carotene + Vitamin C + Vitamin E Effervescent Tablets (12 mg + 150 mg + 25 mg)

Formulation: Lucarotene dry powder 10% CWD G/Y (BASF), 120 g; Ascorbic acid, crystalline (BASF), 150 g; Dry vitamin E acetate 50% DC (BASF), 50 g; Ludipress LCE [1], 705 g; Kollidon VA64 [1], 50 g; citric acid, anhydrous, 450 g; sodium bicarbonate, 320 g; polyethylene glycol 6000, powder [10], 75 g; orange flavor (Dragoco), 50 g; aspartame (Searle), 30 g.

Manufacturing Directions

1. Mix all components, and pass through a sieve.
2. Press with high-compression force at a maximum of 30% of relative atmospheric humidity at 2.045 mg.

Beta Carotene + Vitamin C + Vitamin E Tablets (12 mg + 250 mg + 125 mg)

Formulation: Beta Carotene dry powder 10%, 125 g; Ascorbic acid, crystalline (BASF), 125 g; Sodium ascorbate, crystalline (BASF), 141 g; Vitamin E acetate dry powder SD 50, 250 g; (BASF) Ludipress or Sorbitol, crystalline [10], 119 g; Polyethylene glycol 6000, powder [10], 5 g; Orange flavor (FDO), 15 g; Sodium cyclamate, 10 g.

Manufacturing Directions

Mix all components, pass through a sieve, and press with medium-compression force at 790 mg.

Beta Carotene + Vitamin C + Vitamin E Tablets (7 mg + 60 mg + 25 mg)

Formulation: Betavit® dry powder 10% (BASF), 75 g; ascorbic acid, powder (BASF), 60 g; vitamin E acetate dry powder 50%, 50 g; sorbitol, crystalline [10], 240 g; Kollidon CL, 30 g; magnesium stearate, 5 g.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and then press with low-compression force at 497 mg.

Beta-Carotene, Vitamin C, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
12.00	1	Beta-carotene (dry powder, 10% with excess)	125.00
125.00	2	Ascorbic acid (crystalline) (BASF)	125.00
141.00	3	Sodium ascorbate (crystalline) (BASF)	141.00
250.00	4	Vitamin E acetate (dry powder, SD 50)	250.00
119.00	5	Ludipress® or sorbitol (crystalline)	119.00
5.00	6	PEG-6000 (powder)	5.00
15.00	7	Orange flavor (FDO)	15.00
10.00	8	Sodium cyclamate	10.00

Manufacturing Directions

1. Mix all components, and pass through a sieve.
2. Press with medium-compression force.
3. Compress into 790-mg tablets, using 12-mm biplanar tablets.

Beta-Carotene, Vitamin C, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.00	1	Beta-carotene; use Betavit® (dry powder, 10% with excess) (BASF)	65.00
100.00	2	Ascorbic acid (powder) (BASF)	100.00
60.00	3	Vitamin E acetate (dry powder, 50%)	60.00
369.00	4	Ludipress®	369.00
6.00	5	Magnesium stearate	6.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix.
2. Press with medium- or high-compression force.
3. Compress into 790-mg tablets, using 12-mm biplanar tablets.

Beta-Carotene, Vitamin C, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.00	1	Beta-carotene; use Betavit® (dry powder, 10% with excess) (BASF)	65.00
100.00	2	Ascorbic acid (powder) (BASF)	100.00
60.00	3	Vitamin E acetate (dry powder, 50%)	60.00
233.00	4	Sorbitol (crystalline) (Merck)	233.00
30.00	5	Kollidon® VA 64	30.00
8.00	6	Kollidon® CL	8.00
4.00	7	Magnesium stearate	4.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with medium- or high-compression force.
3. Compress into 502-mg tablets, using 12-mm biplanar tablets.

Beta-Carotene, Vitamin C, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
7.00	1	Beta-carotene; use Betavit® (dry powder, 10% with excess) (BASF)	75.00
60.00	2	Ascorbic acid (powder) (BASF)	60.00
50.00	3	Vitamin E acetate (dry powder, 50%)	50.00
240.00	4	Sorbitol (crystalline)	240.00
30.00	5	Kollidon® CL	30.00
5.00	6	Magnesium stearate	5.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve and mix.
2. Press with low-compression force.
3. A colorant pigment should be added to obtain a homogeneous appearance of tablets.
4. Use 12-mm biplanar punches for 497-mg tablets.

BIRB 796 Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	BIRB 796	100.00
200.00	2	3-cyclodextrin	200.00
225.00	3	Microcrystalline cellulose	225.00
165.00	4	Lactose	165.00
7.50	5	Colloidal silicon dioxide	7.50
30.00	6	Starch, pregelatinized	30.00
15.00	7	Sodium starch glycolate	15.00
7.50	8	Magnesium stearate	7.50

Note: Item 2 can be replaced with item 4 (a total of 365 mg of lactose).

Manufacturing Directions

1. Charge items 1 to 7 in a suitable mixer after passing through a 250-μm sieve; mix for 10 minutes.
2. Add item 8 and blend for 3 minutes.
3. Compress into 750-mg tablets, using a 15-mm biplanar punch.

Bisacodyl Delayed-Release Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
05.00	1	Bisacodyl	5.00
20.00	2	Cellulose (microcrystalline) (Avicel™ PH102)	20.00
45.27	3	Lactose (spray dried)[a]	45.27
04.00	4	Maize starch (dried)[b]	4.00
00.73	5	Magnesium stearate	0.73

[a] Particle size distribution: minimum, 98% 250 μm, 30% to 60% 100 μm; maximum 15% 45 μm.
[b] LOD NMT 4.5%, when dried at 120°C for 4 hours.

Manufacturing Directions

Handle bisacodyl carefully; it can cause itching if it comes into contact with skin. Over-mixing of lubricants reduces the hardness. Check the temperature and relative humidity of the room before beginning processing. Limit relative humidity to 50% to 60% and temperature to 27°C to 30°C.

1. Mix items 1 and 2 in a stainless steel drum for 2 to 3 minutes.
2. Pass the mixed powder through a 500-μm sieve using sifter.
3. Collect in stainless steel drum.
4. Pass item 3 through a 500-μm sieve using sifter.

5. Collect in stainless steel drum.
6. Load the sieved material into the drum mixer, and mix for 5 minutes.
7. Mix items 4 and 5 in a polyethylene bag for 1 minute.
8. Pass the mix through a 250-μm sieve.
9. Collect in a polyethylene bag.
10. Add 3 to 5 g powder to it, and mix for 1 minute.
11. Add this mixture, and mix for 1 minute in a drum blender.
12. Check the moisture content (limit: 1.0–1.5%).
13. Compress the granules using a rotary tabletting machine; 6-mm biconvex tablets have an average weight of 750 mg and hardness of 4 to 5 kPa.
14. Apply enteric coating.

Bismuth Subsalicylate and Calcium Carbonate Tablets

Formulation: Bismuth subsalicylate, 262.5 mg; microcrystalline cellulose, NF, 213.3 mg; calcium carbonate, 67.5 mg; mannitol, 67.5 mg; sodium starch glycolate, 40.5 mg; polyvinyl pyrrolidone, 13.5 mg; magnesium stearate, 5.4 mg; polysorbate, 80 3.4 mg; silica, 0.7 mg; dye, 0.7 mg. Total 675.0

Manufacturing Directions

1. The ingredients are added to a mixer or granulator in the following order: part of microcrystalline cellulose, calcium carbonate, part of sodium starch glycolate, Polysorbate 80, dye, and bismuth subsalicylate.
2. After adding bismuth subsalicylate and mixing at high shear, the mixture is dried at 86°C to less than 2% moisture.
3. Additional powders (microcrystalline cellulose, sodium starch glycolate, mannitol, and polyvinyl pyrrolidone) are added, and granules are formed by spraying water (approximately 10% by weight of the composition) onto the mixture under high shear.
4. After additional drying to less than 3% moisture, silica (glidant) and magnesium stearate (lubricant) are added and mixed for about 1 minute.
5. Caplets are then formed on a rotary tablet press.

Bismuth Subsalicylate Swallow Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
262.50	1	Bismuth subsalicylate	262.50
213.30	2	Microcrystalline cellulose	213.30
67.50	3	Calcium carbonate	67.50
67.50	4	Mannitol	67.50
40.50	5	Sodium starch glycolate	40.50
13.50	6	Polyvinylpyrrolidone	13.50
5.40	7	Magnesium stearate	5.40
3.40	8	Polysorbate 80	3.40
0.70	9	Silica	0.70
0.70	10	Dye	0.70

Manufacturing Directions

1. Mix the above ingredients in a mixer in the following order: part of microcrystalline cellulose, calcium carbonate, part of sodium starch glycolate, Polysorbate 80, dye, and bismuth subsalicylate.
2. After adding bismuth subsalicylate and mixing at high shear, the mixture is dried at 86°C to less than 2% moisture.
3. Additional powders (microcrystalline cellulose, sodium starch glycolate, mannitol, and polyvinyl pyrrolidone) are added, and granules are formed by spraying water (approximately 10% by weight of the composition) onto the mixture under high shear.
4. After additional drying to less than 3% moisture, silica (glidant) and magnesium stearate (lubricant) are added and mixed for about 1 minute.
5. Caplets are then formed on a rotary tablet press.

Bisoprolol Fumarate and Hydrochlorothiazide Tablets

Each bisoprolol fumarate HCTZ 2.5-mg/6.25-mg tablet for oral administration contains bisoprolol fumarate 2.5 mg and hydrochlorothiazide 6.25 mg. Each bisoprolol fumarate HCTZ 5-mg/6.25-mg tablet for oral administration contains bisoprolol fumarate 5 mg and hydrochlorothiazide 6.25 mg. Each bisoprolol fumarate HCTZ 10-mg/6.25-mg tablet for oral administration contains bisoprolol fumarate 10 mg and hydrochlorothiazide 6.25 mg. Inactive ingredients include colloidal silicon dioxide, cornstarch, dibasic calcium phosphate, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, and titanium dioxide. The 5-mg/6.25-mg tablet also contains red and yellow iron oxide. The 2.5-mg/6.25-mg tablet also contains crospovidone, pregelatinized starch, and yellow iron oxide.

Bran Sucrose Gelatin Calcium Carbonate Tablets

Manufacturing Directions

1. Gelatin–sucrose syrup is prepared by placing the following ingredients in a mixing kettle equipped with a heater and agitator: distilled water, 24000.0 g; gelatin, 3000.0 g; sucrose, granular, 31995.0 g.
2. The mixture is heated up to about 150°F with agitation until solution is effected and the gelatin–sucrose syrup then slowly stirred and held at a temperature of about 150°F until needed.
3. Wheat bran is comminuted in a Schutz-O'Neill Airswept Pulverizer to provide a particle size whereby a minimum of 94% passes through a United States Standard number 20-mesh screen and a maximum of 60% passes through a United States Standard number 80-mesh screen. [The required amount of bran for the batch is calculated by the following formula: 44250 g × 100/(100 –percent moisture in bran.]
4. After pulverizing, the bran is transferred to a heavy-duty double sigma arm mixer and mixed with 1500 g of calcium carbonate, and the previously prepared gelatin–sucrose syrup added rapidly thereto with stirring.
5. When the bran appears to be damp, the mixture is stirred for a 30-minute period and then stopped.
6. Powdered sucrose (16600.0 g) is added and the mixture agitated for an additional 2 to 5 minutes.
7. The wet mix is then discharged through an Ambrette screw extruder and the extrudate spread on drying trays and dried in an oven at 225°F to 3% moisture content.
8. The dried extrudate is granulated employing a FitzMill (2A plate) and then pressed into 1-g tablets by a conventional tableting machine.

Bran Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Bran wheat (milled <1 mm)	250.00
200.00	2	Ludipress®	200.00
5.00	3	Kollidon® 30	5.00
4.00	4	Aerosil® 200	4.00
4.00	5	Magnesium stearate	4.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with medium-compression force.
2. If the bran is not milled, the hardness of the tablet is higher but the content uniformity is less.
3. Compress into 477-mg tablets, using 12-mm punches.

Bromhexine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
8.00	1	Bromhexine HCl	8.00
78.00	2	Lactose monohydrate	78.00
30.40	3	Cornstarch	30.40
3.00	4	Gelatin (powder)	3.00
QS	5	Purified water	12.00
0.60	6	Magnesium stearate	0.60

Manufacturing Directions

Note: The binding solution is susceptible to microbiological growth, and so prepare the solution immediately before the granulation process. Protect bromhexine HCl from light.

1. Make slurry in a separate container by dissolving item 4 in hot item 5 (70–80°C).
2. Mix for 10 minutes using stirrer at medium speed.
3. Pass items 2, 1, and 3 through a 630- μm sieve using a sifter.
4. Charge the sieved material into the mixer.
5. Mix, using mixer and chopper, for 5 minutes at high speed. Add binding solution to the dry powders in the mixer while mixing at low speed.
6. After the addition is complete, mix for an additional 4 minutes at low speed or until a satisfactory mass is obtained.
7. Spread the wet granules onto the trays.
8. Load the trolleys into the drying oven.
9. Dry the granules at 60°C for 10 hours.
10. Turn the granules after 4 hours of drying in order to obtain uniform drying.
11. Transfer the dried granules in stainless steel drums.
12. Check moisture content (limit: NMT 2.0%).
13. Pass the dried granules first through a 1.5-mm and then a 1.0 mm sieve using a granulator. Collect in stainless steel drums.
14. Load the granules into the blender.
15. Pass item 6 through a 250- μm sieve using a sifter, and add to the granules in blender; blend for 2 minutes.
16. Compress the granules using a rotary tabletting machine.
17. Use a 7-mm flat, beveled edge punch to compress 1.20 g per tablet at a hardness of NLT 3.0 kPa.

Bromazepam Tablets (3 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3.00	1	Bromazepam	3.00
0.23	2	Aluminum lake erythrosine (19.4%)[a]	0.23
1.80	3	Talc	1.80
100.00	4	Microcrystalline cellulose (Avicel PH 102)	100.00
94.37	5	Lactose crystalline	94.37
0.60	6	Magnesium stearate	0.60

[a]If a different dye is used, adjust the weight with lactose crystalline (item 5).

Manufacturing Directions

1. Charge item 1 and 3% of item 5 in a mixer and mix for 10 minutes.
2. Pass the mixture through an oscillating granulator with a 0.5-mm screen.
3. Rinse the oscillator with 2% of item 5 and add it to the mixture in step 2.
4. In a separate mixer, add item 2 (if used), item 3, and 5% of item 4, and then mix for 3 minutes.
5. Pass the mixture in step 4 through a mill at medium speed.
6. Transfer the mixture in steps 5 and 3 into an oscillating granulator, add the balance of item 5, add item 3, pass through a 0.5-mm sieve, and then mix for 1 hour.
7. Transfer the mixture to a blender, add item 6, and blend for 30 minutes.
8. Compress at 4- to 5-ton pressure; compress into 200-mg tablets, using 9 mm × 2.5 mm cylindrical biplanar punches.

Bromhexine Tablets (8 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
8.00	1	Bromhexine hydrochloride	8.00
78.00	2	Lactose monohydrate	78.00
30.40	3	Starch (maize)	30.40
3.00	4	Gelatin	3.00
–	5	Water, purified, ca	120 mL
0.60	6	Magnesium stearate	0.60

Manufacturing Directions

1. Charge item 4 in a suitable vessel, add item 5 at 70°C to 80°C to dissolve item 4, and mix for 10 minutes.
2. Charge items 1 to 3 in a suitable container after passing them through a 630-μm sieve. Mix and chop for 5 minutes.
3. Add binding solution from step 1 to the mixer in step 2, and mix for 5 minutes at high speed and then slow speed until a suitable mass is obtained (add more of item 5 if needed).
4. Spread the wet mass on trays and dry at 60°C for 10 hours, turning granules over every 4 hours until not more than 2% moisture remains.
5. Pass the dried granules through a 1.5-mm sieve and then a 1.0-mm sieve.
6. Pass item 6 through a 250-μm sieve, add to step 5, and blend for 2 minutes.
7. Compress into 120-mg tablets, using 7-mm flat punches.

Bromocriptine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.00	1	Bromocriptine mesylate, with excess	6.10
205.50	2	Ludipress	205.50
2.20	3	Magnesium stearate	2.20

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force.
2. Compress to 214-mg tablets, using 9-mm biconvex punches.

Buflomedil Hydrochloride Tablets (150 mg/300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Buflomedil hydrochloride	300.00
74.00	2	Lactose	74.00
14.00	3	Povidone K 29–32	14.00
2.00	4	Magnesium stearate	2.00
QS	5	Water, purified	55.00 mL

Note: For 150-mg strength, adjust all components proportionally.

Manufacturing Directions

1. Granulation
   a. Dissolve povidone in purified water, using a glass or stainless steel vessel.
   b. Pass through a 500-μm aperture screen and add buflomedil hydrochloride and lactose. Charge into a suitable planetary or ribbon mixer. Mix at 15 to 30 rpm for 10 minutes.
   c. Granulate the mixed powders with povidone solution, adding 20-mL aliquots every 2 to 3 minutes, with a mixer speed of 30 rpm.
   d. Stop the mixer and inspect the mass. Additional purified water may be added to complete the granulation.
   e. Pass the wet mass through a suitable granulator fitted with a 2000-μm aperture stainless steel screen. Collect granules on paper-lined trays and spread out evenly, 1/2 to 1 in. (1–2.5 cm) deep.
   f. Dry the granules in a hot air oven at 40°C for 3 hours or until the LOD is between 0.7 and 2.8%.
2. Lubrication
   a. Pass the dry granules through a 100-μm aperture stainless steel screen and charge into a cone or ribbon blender.
   b. Mix the magnesium stearate with one scoopful of granules from the previous step and add to the bulk. Blend for 10 minutes at 20 to 30 rpm, and empty the blender into polyethylene-lined drums for compression.
3. Compression: The tablet can be compressed using 9.5-mm or 11.11-mm punches: 385.40 mg per tablet. The weight of a 150-mg tablet is 246 mg.
4. Coating: Use a clear CAP/Carbowax coating to control the release of the active ingredient. (See Appendix.)

Buflomedil Hydrochloride Tablets (600 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Buflomedil hydrochloride	600.00
160.00	2	Sodium calcium alginate (Kelset)	160.00
30.00	3	Povidone K 29–32	30.00
QS	4	Water, purified, ca	300 mL
4.35	5	Magnesium stearate	4.35

Manufacturing Directions

Caution: Wear a face mask and rubber gloves. When wett, alginate materials result in slippery surfaces—exercise care.

1. Granulation (standard method using planetary or horizontal mixer). (*Note:* Temperature of the water used should not exceed 30°C, so cool it if necessary.)
   a. Pass any agglomerated materials through a 375-μm screen.
   b. Load buflomedil, sodium alginate, sodium calcium alginate, and povidone into suitable mixing equipment. Blend for 10 minutes. Add while mixing 250 mL water over a period of 5 to 10 minutes and then mix for 5 minutes. Add additional water in small portions with mixing, until granulation is complete. Record the amount of water added. Stop mixing and allow the mixture to stand for approximately 5 minutes. (The granulation end point occurs when the mass is of a slightly wet but crumbly consistency. Avoid overwetting. The quantity of water and the mixing time must be sufficient to dissolve the povidone.)
   c. Load granules onto paper-lined oven trays, and dry at 50°C until the LOD is 3% to 5% (IR balance or similar at 100°C for 15 minutes). The drying time is 5 to 8 hours depending on tray loading. Should the LOD be above 5% at the completion of the drying period, increase the temperature of the drying oven to 60°C and continue until the LOD is satisfactory. It is important that you do not increase the temperature until the initial drying period is complete.
   d. After drying, screen granules through an 840-μm screen fitted on the oscillating granulator. Pack into tightly sealed polyethylene-lined drums and store in an air-conditioned area.
2. Lubrication
   a. Blend magnesium stearate with a portion of granules and then screen through a 600-μm screen fitted to the oscillating granulator. Incorporate the remaining granules by serial dilution, mixing between additions. Do not overblend.
3. Compression: Compress into oval-shaped tablets.
4. Coating: Coat using methocel coatings. (See Appendix.)

Bupropion Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Bupropion hydrochloride	150.00
9.00	2	Kollidon 90F	9.00
171.00	3	Purified water	171.00
3.20	4	Stearic acid	3.20

Manufacturing Directions

1. Povidone is first dissolved in water.
2. Bupropion hydrochloride is placed in the top spraying chamber of Glatt GPCG1 fluidized bed apparatus. The solution of povidone is sprayed onto the active ingredient, with the following parameters: Air flow = 100–110 m^3/h, liquid flow = 6–7 g/min, inlet temperature = 65°C, and spraying pressure = 2.8 bar.
3. Once the granulation is completed, granules are passed through a sieve (1 mm mesh) and stearic acid is weighed, added, and blended in a drum mixer (Turbula T2C, Bachoffen, Switzerland). The resulting mixture is pressed into tablets (7-mm diameter and 7-mm curvature) with average hardness being between 60 and 120 N.
4. The tablet cores (step 3) are then coated with the following formulation: Tablet cores (step 3) 162.20 mg, Ethocel PR100 (ethylcellulose) 7.05 mg, Kollidon 90F (povidone USP) 7.05 mg, PEG 1450 2.10 mg, Denatured alcohol 210.00 mg to give total dry weight of 178.40 mg.

   Ethocel, povidone, and PEG 1450 are first dissolved in denatured alcohol. The coating solution is then sprayed onto the tablet cores in a coating pan (Vector LCDS), with the following spraying parameters: Air flow = 100–110 m^3/h, liquid flow = 6–7 g/min, inlet temperature = 65°C, and spraying pressure = 2.8 bar.

Bupropion Hydrochloride Tablets Wellbutrin

Immediate-release tablets—Wellbutrin is supplied for oral administration as 75-mg (yellow-gold) and 100-mg (red) film-coated tablets. Each tablet contains the labeled amount of bupropion HCl and the following inactive ingredients: (a) *75-mg tablet*— D&C Yellow No. 10 Lake, FD&C Yellow No. 6 Lake, hydroxypropyl cellulose, hydroxypropyl methylcellulose, microcrystalline cellulose, polyethylene glycol, talc, and titanium dioxide. (b) *100-mg tablet*—FD&C Red No. 40 Lake, FD&C Yellow No. 6 Lake, hydroxypropyl cellulose, hydroxypropyl methylcellulose, microcrystalline cellulose, polyethylene glycol, talc, and titanium dioxide.

Sustained-release tablets—(a) *Wellbutrin SR:* Wellbutrin SR tablets are supplied for oral administration as 100-mg (blue) and 150-mg (purple), film-coated, sustained-release tablets. Each tablet contains the labeled amount of bupropion HCl and the following inactive ingredients: carnauba wax, cysteine hydrochloride, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, and titanium dioxide and is printed with edible black ink. In addition, the 100-mg tablet contains FD&C Blue No. 1 Lake and polysorbate 80; the 150-mg tablet contains FD&C Blue No. 2 Lake, FD&C Red No. 40 Lake, and polysorbate 80. (b) *Zyban:* Zyban (bupropion HCl for smoking cessation) is supplied for oral administration as 150-mg (purple), film-coated, sustained-release tablets. Each tablet contains the labeled amount of bupropion HCl and the following inactive ingredients: carnauba wax, cysteine HCl, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, and titanium dioxide and is printed with edible black ink. In addition, the 150-mg tablet contains FD&C Blue No. 2 Lake and FD&C Red No. 40 Lake.

Bupropion Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Bupropion hydrochloride	100.00
68.50	2	Microcrystalline cellulose	68.50
6.90	3	Sodium starch glycolate	6.90
3.80	4	L-Cysteine hydrochloride	3.80
17.30	5	Talc	17.30
0.20	6	Silicon dioxide colloidal	0.20
–	7	Water, purified	8.00
–	8	Alcohol SD3A anhydrous	24.00

Manufacturing Directions

1. Sift bupropion hydrochloride, microcrystalline cellulose, and sodium starch glycolate through a 30-mesh Russell–Finex sifter.
2. Blend the sifted items in 1 for 15 minutes in a slant-cone blender.
3. In a separate container, dissolve cysteine hydrochloride in purified water.
4. Add item 8 to step 3 and mix thoroughly.
5. Add to step 1 in a granulating vessel: make a wet mass, dry granules in a fluid-bed dryer until the LOD is between 1% and 2%.
6. Sift dried granule through a 20-mesh Russell–Finex sifter.
7. Sift items 4 and 6 and blend with step 6.
8. Compress into 172.6-mg tablets, using round 7.8-mm punches.

Bupropion Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Bupropion hydrochloride uncoated	100.00
121.30	2	Pharmatose DCL	121.30
15.00	3	Methocel A4M	15.00
121.30	4	Pharmatose DCL21	121.30
27.00	5	Talc	27.00
0.70	6	Magnesium stearate	0.70
85.00	7	Kollidon SR	85.00

Manufacturing Directions

Mix, granulate, and compress into 334.00-mg tablets.

Buspirone Fast-Melt Tablets

Formulations: Mix buspirone, 8%; sodium bicarbonate, 25%; citric acid anhydrous, 25%; avicel PH113, 12%; anhydrous lactose, 17%; xylitol, 11%; crodesta f160, 2%.

Manufacturing Directions

1. Dry all ingredients at 40°C to 60°C to significantly reduce the moisture content of each material.
2. Blend for 10 minutes and extrude in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
3. Mix BUS-EGF (20–80 mesh) 50%, microcrystalline cellulose (Avicel PH113) 31%, mannitol (Mannogen 3215) 10%, AcDiSol 5%, aspartame 3%, redberry flavor 0.4%, magnesium stearate 0.5, and fumed silicon dioxide 0.1%.
4. Screen and blend for 5 minutes prior to compression.
5. Buspirone tablets are then compressed to a hardness of approximately 1–3 kPa and tablets disintegrate in water in approximately 15–35 seconds.

Buspirone Hydrochloride Tablets, BusPar

BuSpar is supplied for oral administration in 5-mg and 10-mg, white, ovoid-rectangular, scored tablets. BuSpar tablets, 5 mg and 10 mg, contain the following inactive ingredients: colloidal silicon dioxide, lactose, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate.

Buspirone Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Buspirone hydrochloride	15.00
7.00	2	Polyvinylpyrrolidone	7.00
1.50	3	Silicon dioxide	1.50
150.00	4	Lactose	150.00
1.50	5	Glyceryl behenate	1.50
	6	Water qs	

Manufacturing Directions

1. Buspirone and lactose are placed in a fluidized bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1-mm mesh) and glyceryl behenate is weighed, added, and blended in a drum mixer.
4. The resulting mixture is pressed into 175-mg tablets.
5. These tablet cores are then coated with the following formulation: ethylcellulose 10.00, hydroxypropylcellulose 10.00, stearic acid 2.00, and alcohol 188.00 g.
6. Ethocel, povidone, and stearic acid are first dissolved in denatured alcohol (188 g). The coating solution is then sprayed onto the tablet cores in a coating pan.

Buspirone Hydrochloride Tablets, Controlled-Release (30 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Buspirone hydrochloride	30.00
120.00	2	Polyvinyl chloride	120.00
11.00	3	Polyvinyl acetate C10-V7	11.00
1.60	4	Magnesium stearate	1.60
–	5	Alcohol	QS

Manufacturing Directions

1. Dry mix buspirone hydrochloride with polyvinyl chloride.
2. Granulate the powder mixture with a solution of polyvinyl acetate in ethanol.
3. Mill dried granules and compress into 7-mm round tablets (162.60 mg).

Cabenoxolone Tablets

Formulations: Carbenoxolone sodium, 20 mg; mannitol, 400 mg; alginic acid, 200 mg; sodium alginate, 200 mg; aluminium hydroxide, dried gel 80 mg; sodium bicarbonate, 70 mg; magnesium trisilicate, 20 mg; magnesium stearate, 12 mg; gum acacia, 35 mg; peppermint oil, 2 mg. Total 1039 mg.

Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Caffeine powder	150.00
36.00	2	Cellulose (microcrystalline) (Avicel™ PH-102)	36.00
46.00	3	Anhydrous lactose	46.00
48.50	4	Di-Pac granular	48.50
3.00	5	Croscarmellose sodium (Ac-Di-Sol SD-711)	3.00
1.50	6	Fumed silica	1.50
0.75	7	Stearic acid	0.75
0.75	8	Magnesium stearate	0.75
1.20	9	Flavor	1.20

Manufacturing Directions

1. Screen items 1, 7, and 8 separately through a 40-mesh sieve.
2. Blend items 1 to 6 and 9 in a V-shaped blender, and mix for 3 minutes.
3. Add item 8 to the blender and mix for another 5 minutes.
4. Compress, using 7 kg pressure and 3/8-in., flat, beveled-edge punches to produce tablets with an average weight of 311 mg.

Calcium and Vitamin D Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Anhydrous calcium phosphate (dibasic)	500.00
133 IU	2	Vitamin D (as vitamin D3) (3.33 μg/tablet)	3.33 mg
15.00	3	Starch (pregelatinized, NF)	15.00
55.00	4	Cellulose (microcrystalline, NF)	55.00
6.00	5	Magnesium stearate, NF	6.00
5.00	6	Talc (powder), USP	5.00
12.00	7	Wax (hydrogenated vegetable oil) (Sterotex K)	12.00
15.50	8	Sodium starch glycolate, NF	15.50

Manufacturing Directions

1. Charge one half of the dibasic calcium phosphate through a mesh screen into a blender.
2. Premix by hand the pregelatinized starch with vitamin D3 beadlets in a suitable container, and sift through a mesh screen into the blender.
3. Charge the microcystalline cellulose and the remaining calcium phosphate through a mesh screen into the blender.
4. Mix for 20 minutes.
5. Discharge approximately one third of the granulation into polyethylene-lined drums.
6. Mix the magnesium stearate, talc, hydrogenated vegetable oil wax, and sodium starch glycolate.
7. Mill through a #40-mesh screen into the blender.
8. Return granulation from step above to the blender. Blend together.
9. Compress.

Calcium Carbonate and Glycine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Calcium carbonate (precipitated)	400.00
200.00	2	Glycine (aminoacetic acid)	200.00
QS	3	Starch	QS
6.50	4	Mineral oil (light)	6.50
QS	5	Purified water	QS

Manufacturing Directions

1. Add starch to a planetary mixer, and add 10 times the quantity of purified water.
2. Heat to boil with constant stirring until a thick, translucent white paste is formed. Use this paste in granulation.
3. Charge calcium carbonate and glycine in a sigma-blade or a planetary mixer, and mix for 10 minutes.
4. Granulate this powder with the starch paste until a suitable mass is obtained.
5. Force the wet mass through a #12-mesh screen onto dryer trays.
6. Dry in an air-forced oven at 130°F to 140°F or in a fluid-bed dryer.
7. Pass the dried granules through a #12-mesh screen, then through a #18-mesh screen.
8. Pass the granules over a 30-mesh screen, remove the portion passing through the screen, and regranulate.
9. Charge the particles retained on 30-mesh screen in a tumble mixer, add mineral oil, and mix for 8 minutes.
10. Compress into 640-mg tablets, using 7/16-in. punches.

Calcium Carbonate and Vitamin D Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Calcium (elemental); use calcium carbonate (90%) for direct compression	1665.00
0.235	2	Vitamin D3 (200.00 IU); use vitamin D3 beadlets	0.282
4.16	3	Magnesium stearate	4.16
83.25	4	Sodium starch glycolate	83.25

Manufacturing Directions

1. Make a premix of vitamin D3 successively in three portions of calcium carbonate (total amount equivalent to ~3% of total calcium carbonate), using the geometric dilution.
2. Mix for 10 minutes each time (total time: 30 minutes).
3. Add the premix to the sodium starch glycolate. Mix for 10 minutes.
4. Set the blend aside, protected from light, until the next step.
5. Pass the magnesium stearate through a 420-μm aperture screen, if required, and blend it with another portion of calcium carbonate (~10% of total calcium carbonate).
6. Mix for 5 minutes. Set aside.
7. Add the blended material to the balance of the calcium carbonate. Mix for 10 minutes.
8. Add the premix to blend from above. Mix for 5 minutes.
9. Compress on specially shaped, 0.8100 × 0.3700-in., ovaloid, bisected punches with a monogram on one side.
10. Theoretical weight of 10 tablets = 17.527 g.
11. Coat using one of the HPMC formulae (see Appendix).

Calcium Carbonate Chewable Tablets

Formulations: Granulated calcium carbonate (93.3% calcium carbonate, 6.3% glucose and 0.4% gelatin), 42.87%; magnesium stearate, 2.50%; colored speckles, 0.75%; flavorants, 0.78%; MPD (31-menthoxy propane 1,2diol), 0.07%; WS-3 (methyl-*p*-menthane-3-carboxamide), 0.05%; aspartame, 0.198%; sodium saccharin, 0.102%; mannitol Q.S.

Manufacturing Directions

1. The above ingredients are dry blended in a mixer until homogeneous, and then direct compressed in a tabletting machine to approximately 8.5 Strong Cobb units hardness to produce chewable antacid tablets each weighing 1.25 g (500 mg calcium carbonate per tablet).
2. These tablets may also be prepared by using granulated calcium carbonate, which is a 50/50 coblend of calcium carbonate/mannitol.

Calcium Carbonate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Calcium carbonate (precipitated)	500.00
65.00	2	Kollidon® 30	65.00
97.00	3	Water	97.00
32.00	4	Kollidon® CL	32.00
53.00	5	Ludipress®	53.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with the water (item 3).
2. Pass through a 0.8-mm sieve, mix the dry granules with items 4 and 5, and press with low-compression force.
3. Fill 656 mg in 12-mm planar punches.

Calcium Chewable Tablets (200 mg Ca)

Formulation: Calcium gluconate (Merck), 845.0 g; calcium citrate (Merck), 500.0 g; Ludipress LCE [1], 297.5 g; citric acid anhydrous, fine granular, 100.0 g; polyethylene glycol 6000, powder, 80.0 g; orange flavor (Dragoco), 30.0 g; aerosil 200, 17.0 g. aspartame, potassium (Searle), 5.0 g.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with high-compression force at 2417 mg.

Calcium D-Pantothenate Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Calcium D-pantothenate (BASF)	610.00
150.00	2	Sorbitol (crystalline)	150.00
140.00	3	Avicel™ PH101	140.00
30.00	4	Kollidon® CL	30.00
50.00	5	PEG-6000 (powder)	50.00
QS	6	Flavors	QS

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with low-compression force.
2. Compress into 987-mg tablets, using 12-mm biplanar punches.
3. Kollidon® CL may be omitted and the tablet weight adjusted.

Calcium D-Pantothenate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Calcium D-pantothenate (BASF)	100.00
150.00	2	Ludipress®	150.00
10.00	3	Kollidon®	10.00
3.00	4	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve.
2. Press into 252-mg tablets using medium-compression force and biplanar 8-mm punches.

Calcium D-Pantothenate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
280.00	1	Calcium D-pantothenate (BASF)	285.00
50.00	2	Avicel™ PH101	50.00
150.00	3	Dibasic calcium phosphate	150.00
20.00	4	Kollidon® CL	20.00
3.00	5	Stearic acid	3.00
3.00	6	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, and pass through an 0.8-mm sieve.
2. Press into 518-mg tablets using medium-compression force and 12-mm biplanar punches.

Calcium Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
634.00	1	Calcium lactate	634.00
610.00	2	Calcium gluconate	610.00
185.21	3	Calcium carbonate	185.21
400.00	4	Sodium bicarbonate	400.00
468.25	5	Tartaric acid	468.25
46.25	6	Povidone (Kollidon® 30)	46.25
11.75	7	Povidone (Kollidon® 30)	11.75
QS	8	Isopropyl or ethyl alcohol (96%)	QS
97.50	9	Crospovidone (Kollidon® CL)	97.50
46.25	10	PEG-6000	46.25
QS	11	Flavor	QS

Manufacturing Directions

1. Granulate items 1 to 6 in a solution of items 7 and 8.
2. Dry, sieve, and mix well with items 9 to 11.
3. Compress at low pressure to form 2.5-g tablets, 20 mm in diameter.

Calcium Gluconate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
350.00	1	Calcium gluconate (powder)	360.00
117.00	2	Lactose monohydrate	117.00
11.00	3	Kollidon® 30	11.00
QS	4	Isopropanol	90.00
25.00	5	Kollidon® CL	25.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with item 4.
2. Dry, pass through an 0.8-mm sieve, and mix with items 5 and 6.
3. Press into 500-mg tablets using high-compression force and 12-mm biplanar punches.

Calcium Glycerophosphate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Calcium glycerophosphate	500.00
117.50	2	Cornstarch	117.50
15.00	3	Kollidon® 90F	15.00
60.00	4	Water	60.00
15.00	5	Kollidon® CL	15.00
2.50	6	Magnesium stearate	2.50

Manufacturing Directions

1. Granulate items 1 to 3 with item 4; dry, sieve, and mix with items 5 and 6.
2. Press into 650-mg tablets using medium- to high-compression force and 12-mm biplanar punches.

Calcium Glycerophosphate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Calcium glycerophosphate	200.00
297.50	2	Ludipress®	297.50
2.50	3	Magnesium stearate	2.50
QS	4	Aerosil® 200	QS

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, and mix.
2. Press into 470-mg tablets using high-compression force and 12-mm biplanar punches.

Calcium Glycerophosphate Tablets (200 mg)

Formulation: Calcium glycerophosphate, 200.0 g; Ludipress, 297.5 g; Magnesium stearate, 2.5 g; Aerosil 200. q.s.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with high-compression force at 470 mg.

Calcium Phosphate Tablets for Cats and Dogs

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Dicalcium phosphate	400.00
100.00	2	Wheaten flour	100.00
1.00	3	Citric acid crystalline	1.00
262.00	4	Lactose monohydrate	262.00
QS	5	Flavors	QS
30.00	6	Kollidon® 30F	30.00
150.00	7	Water	150.00 mL
4.00	8	Magnesium stearate	4.00

Manufacturing Directions

1. Granulate items 1 to 6 in item 7, dry, add item 8, and pass through an 0.8-mm sieve.
2. Compress 800-mg tablets, using 12-mm biplanar punches.

Calcium Phosphate Tablets for Cats and Dogs (Direct Compression)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Dicalcium phosphate	400.00
100.00	2	Wheaten flour	100.00
1.00	3	Citric acid crystalline	1.00
272.00	4	Lactose monohydrate	272.00
QS	5	Flavors	QS
20.00	6	Kollidon® 90F	20.00
4.00	7	Magnesium stearate	4.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix.
2. Press with medium- to high-compression force (20 kN).
3. Compress into 800-mg tablets, using 12-mm biplanar punches.

Captopril Tablets (25 mg), Capoten

Capoten is available in potencies of 12.5, 25, 50, and 100 mg as scored tablets for oral administration. Inactive ingredients include microcrystalline cellulose, cornstarch, lactose, and stearic acid.

Captopril Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Captopril	25.00
91.00	2	Ludipress	91.00
2.00	3	Kollidon CL	2.00
2.00	4	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force to meet the following specifications.
2. Compress into 122-mg tablets, using 8-mm biplanar punches.

Carbamazepine Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.000	1	Carbamazepinea	208.00
25.880	2	Microcrystalline cellulose (Avicel PH 101)	25.880
9.000	3	Croscarmellose sodium (Ac-Di-Sol)	9.000
1.520	4	Carboxymethylcellulose sodium (CMC sodium)	1.520
1.500	5	Poloxyl 40 stearate	1.500
0.500	6	Colloidal silicon dioxide (Aerosil 200)	0.500
6.000	7	Sodium starch glycolate (Primojel)	6.000
7.000	8	Croscarmellose sodium (Ac-Di-Sol)	7.000
0.600	9	Magnesium stearate	0.600
–	10	Purified water	104.000

Carbamazepine 8.0 mg/tablet added to compensate the assay (98.0–102.0%) and LOD of the material.

Manufacturing Directions

Note: Avoid overmixing lubricants, otherwise hardness is reduced. *Critical note:* Hardness is critical for this product. Increasing or decreasing hardness from the specified limit will affect the dissolution.

1. Sieving and dry mixing: Sift items 1 to 3 through a 630-μm stainless steel sieve in the sifter. Load into the mixer. Mix for 5 minutes at low speed.
2. Preparation of the binder: Dissolve item 5 in 104 g of item 10 (55–65°C). Cool to 30°C. Dissolve item 4 while stirring with a stirrer. Check the weight (theoretical weight: 107.02 g).
3. Kneading
   a. Knead the powder mix with the binding solution at a rate of 28 to 32 g/min while mixing at low speed. Scrape sides and blades. Mix and chop at low speed for 2 minutes. Check the end point of granulation, consisting of free-flowing granules with little lumps. If required, add more purified water to get to the end point.
   b. Sift the granules in the granulator through a 3.5-mm stainless steel sieve, and follow by sifting through a 1-mm stainless steel sieve.
   c. Unload the wet granules into stainless steel trays for drying.
4. Drying
   a. Dry the wet granules in an oven at 55°C for 8 hours.
   b. Check the LOD (limit: 0.5% to 1%).
   c. If required, dry further at 55°C for 1 hour.
5. Grinding and lubrication
   a. Grind the dried granules through a 1-mm sieve using a granulator at medium speed. Collect in stainless steel drums. Load the granules into a drum blender.
   b. Sift items 6 to 8 through a 500-μm sieve, using a sifter, and add it to the drum blender. Mix for 2 minutes.
   c. Sift item 9 through a 250-μm sieve. Add 4- to 8-g granules from the bulk (step 5a). Mix in a polyethylene bag for 1 minute. Add to blender and blend for 1 minute.
   d. Unload in stainless steel drums. Check and record the weight of the granules (theoretical weight: 260 g).
6. Compression
   a. Check temperature and humidity before starting compression.
   b. Limits are that the temperature should not exceed 27°C, and the recommended relative humidity is 55% to 60%.
   c. Compress the granules using a rotary tabletting machine. At 9 mm, the weight of 10 caplets is 2.6 g ± 2%.

Carbamazepine Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Carbamazepine	200.00
300.00	2	Ludipress	300.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 496-mg tablets, using 12-mm biplanar punches.

Carbetapentane Tannate and Chlorpheniramine Tannate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Carbetapentane tannate	60.00
5.00	2	Chlorpheniramine tannate	5.00
65.00	3	Starch	65.00
150.00	4	Methylcellulose	150.00
32.00	5	Polygalacturonic acid	32.00
65.00	6	Dibasic calcium phosphate dehydrate	65.00
25.00	7	Povidone	25.00
5.40	8	Talc	5.40
3.93	9	FD&C Red #40 Aluminum Lake 40%	3.93
1.00	10	D&C Blue #1 Aluminum Lake 29%	1.00
4.00	11	Magnesium stearate	4.00
qs	12	Alcohol denatured 190 proof	qs

Carbidopa and Levodopa Tablets Sinemet

The inactive ingredients are cellulose, magnesium stearate, and starch. Tablets Sinemet 10–100 and 25–250 also contain FD&C Blue No. 2. Tablets Sinemet 25–100 also contain D&C Yellow No. 10 and FD&C Yellow. Sinemet CR (car-bidopa–levodopa) is a sustained-release combination of carbidopa and levodopa for the treatment of Parkinson's disease and syndrome. The inactive ingredients in Sinemet CR 50–200 are D&C Yellow No. 10, magnesium stearate, iron oxide, and other ingredients. Inactive ingredients in Sinemet CR 25–100 are magnesium stearate, red ferric oxide, and others. The Sinemet CR tablet is a polymeric-based drug delivery system that controls the release of carbidopa and levodopa as it slowly erodes. Sinemet CR 25–100 is available to facilitate titration and as an alternative to the half-tablet of Sinemet CR 50–200.

Carbidopa and Levodopa Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Carbidopa	25.00
100.00	2	Levodopa	100.00
224.00	3	Microcrystalline cellulose (Avicel PH 101)	224.00
15.00	4	Croscarmellose sodium	15.00
3.00	5	Silicon dioxide colloidal	3.00
3.00	6	Magnesium stearate	3.00
50.00	7	Carbidopa	50.00
200.00	8	Levodopa	200.00
80.00	9	Methocel E4M premium CR	80.00
61.00	10	Microcrystalline cellulose	61.00
2.00	11	Silicon dioxide colloidal	2.00
2.00	12	Magnesium stearate	2.00

Manufacturing Directions

1. This is a bilayer or two-compartment tablet consisting of a core layer of sustained-release carbidopa–levodopa overcoated with a layer of immediate-release carbidopa–levodopa.
2. The core ingredients (items 7–10) are blended separately (as are the outer layer [items 1–4] ingredients), compressed to produce core tablets, and then overcoated with the compressed outer-layer blend using a suitable coating press.

Carbinoxamine Maleate, Phenylpropanolamine, and Acetaminophen Sustained-Release Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Cabinoxamine maleate	5.00
75.00	2	Phenylpropanolamine hydrochloride	75.00
50.00	3	Acetaminophen	50.00
143.35	4	Sucrose and maize starch microgranules	143.35
6.34	5	Polyvidone (PVP)	6.34
0.01	6	Dye	0.01
0.075	7	Dye	0.075
0.025	8	Dye	0.025
23.99	9	Talc	23.99

Manufacturing Directions

Note: This product requires separate preparation of microgranules for each active ingredient. This preparation requires a coating pan equipped with air suction and hot air heating system, mixer, automatic airless pump with a spray gun, vibrating sieve, and capsule-filling machine with triple-feed microgranular system.

1. Place the neutral microgranules in the coating pan; prepare a 20% solution of PVP.
2. Maintain the temperature of microgranules at 20 ± 2°C.
3. Using the pump, apply the solution of PVP, then project the active ingredient onto the microgranules with a plastic scoop until they are dry.
4. Repeat these operations until all the active ingredients have been incorporated.
5. Sieve the microgranules with a 1.11-mm sieve.
6. Dry the microgranules at 30 ± 5°C for 3 hours.
7. Prepare a 40% solution of shellac in alcohol and the required quantity of talc.
8. Apply the shellac solution, maintaining a microgranule temperature of 20 ± 2°C, and add talc simultaneously.
9. Sieve the microgranules through a 1.18-mm sieve.
10. Dry the microgranules at 18°C to 23°C for 8 hours. Store until used.
11. Test for dissolution and rework if necessary.

Carbonyl Iron, Copper Sulfate, and Manganese Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
24.00	1	Carbonyl iron (BASF)	24.00
0.16	2	Copper sulfate	0.16
3.50	3	Manganese sulfate	3.50
100.00	4	Ludipress	100.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, and mix.
2. Press into131-mg tablets using medium-compression force and 8-mm biplanar punches.

Carisoprodol Tablets Soma

Soma tablets are available as 350-mg round, white tablets. Carisoprodol is present as a racemic mixture. Other ingredients include alginic acid, magnesium stearate, potassium sorbate, starch, and tribasic hydrogen phosphate.

Carvedilol Tablets Coreg

Coreg (carvedilol) is a white, oval, film-coated tablet containing 3.125, 6.25, 12.5, or 25 mg of carvedilol. The 6.25-, 12.5-, and 25-mg tablets are Tiltab® tablets. Inactive ingredients consist of colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, lactose, magnesium stearate, polyethylene glycol, polysorbate 80, povidone, sucrose, and titanium dioxide.

Carvedilol Talets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Carvedilol	25.00
25.00	2	Saccharose	25.00
28.00	3	Lactose monohydrate	28.00
1.78	4	Polyvinyl pyrrolidone 25 K	1.78
20.17	5	Polyvinyl pyrrolidone cross-linked	20.17
10.00	6	Microcrystalline cellulose	10.00
5.32	7	Silicon dioxide colloidal	5.32
2.17	8	Magnesium stearate	2.17
–	9	Purified water	115.00

Manufacturing Directions

1. Charge the following in a mixing vessel: item 3 sieved, item 2 (half), and item 4; add and mix item 9, and then mix by stirring for 30 minutes.
2. Add item 7 and item 1, and stir for another 30 minutes until a homogenous suspension is obtained.
3. Pass the suspension in step 2 through a colloid mill, and keep circulating.
4. Add items 2 and 5 to a fluid-bed dryer, and then pour the suspension in step 3 to obtain dry granules.
5. Sieve the granules through a 1.2-mm mesh sieve.
6. Lubricate granules and compress.

Cefadroxil Dispersible Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Cefadroxil, use cefadroxin anhydrous	268.65
2.00	2	PVP potassium 30	2.00
–	3	Isopropyl alcohol	10.80
77.00	4	Lactose monohydrate	77.00
93.50	5	Starch (maize)	93.50
13.00	6	Aspartame	13.00
1.50	7	Aerosil 200	1.50
0.45	8	Methyl paraben	0.45
0.05	9	Propyl paraben	0.05
4.00	10	Starch (maize)	4.00
5.00	11	Magnesium stearate	5.00
5.00	12	Talc	5.00
QS	13	Water, purified	QS

Manufacturing Directions

1. Charge items 2 and 3, and prepare a binding solution.
2. Sift item 1 through a 250-µm sieve.
3. Add step 1 into step 2, and prepare a wet mass.
4. Spread granules on trays, and dry in a dehumidified room.
5. Pass dried granules through a 595-µm sieve.
6. Prepare a paste of item 5 using purified water.
7. Sift items 4 and 6 into 9 through a 250-µm sieve. Mix for 15 minutes.
8. Add the paste from step 6, and mix until a wet mass is obtained without lumps.
9. Dry the granules obtained in step 8 in a fluid-bed dryer at 50°C for 2 hours.
10. Mix granules from steps 5 and 9, and charge into a tumble mixer.
11. Sift items 10 to 12 through a 250-µm sieve, add to step 10, and blend for 2 minutes.
12. Compress into 630-mg tablets, using 11.3-mm punches.

Cefdinir Tablets (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Cefdinir bulk powder	306.80
29.20	2	Microcrystalline cellulose (Avicel PH 101)	29.20
29.20	3	L-HPC (LH-21, Shin-Etsu Chemical)	29.20
3.70	4	Polyvinylpyrrolidone (Kollidon 30)	3.70
0.90	5	Silicic acid light anhydorus (Aerosil 200)	0.90
4.40	6	Magnesium stearate	4.40
15.00	7	Saccharin sodium	15.00
5.60	8	Strawberry flavor	5.60

Manufacturing Directions

1. Charge items 1 to 4 after passing through a 250-µm mesh into a mixing vessel. Mix for 10 minutes.
2. Add items 5 to 8, one at a time, and blend for 1 minute each time.
3. Compress 395 to 400 mg.

Cefixime and Amoxacillin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Cefixime	100.00
250.00	2	Amoxacillin	250.00
90.00	3	Microcrystalline cellulose	90.00
8.00	4	Hydroxypropylcellulose	8.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Cefixime, amoxicillin, microcrystalline cellulose, and hydroxypropylcellulose are thoroughly blended and the mixture is granulated.
2. The granules are vacuum-dried at 40°C and subjected to grain size adjustment on a duplex sieve.
3. Magnesium stearate is added to these granules and the resulting mixture is compressed.
4. The above tablets are coated with the coating solution (hydroxypropylmethylcellulose 10 mg in water) at a feed air temperature of 55°C and an exhaust gas temperature of 40°C.

Cefixime Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Cefixime bulk powder	448.90
38.90	2	Microcrystalline cellulose (Avicel PH 101)	38.90
38.90	3	L-HPC (LH-21, Shin-Etsu Chemical)	38.90
4.90	4	Polyvinylpyrrolidone (Kollidon® 30)	4.90
1.20	5	Silicic acid light anhydrous (Aerosil 200)	1.20
5.90	6	Magnesium stearate	5.90
20.00	7	Saccharin sodium	20.00
7.50	8	Strawberry flavor	7.50

Manufacturing Directions

1. Charge items 1 to 4 after passing through a 250-μm mesh into a mixing vessel. Mix for 10 minutes.
2. Add items 5 to 8, one at a time, and blend for 1 minute each time.
3. Compress 566 to 570 mg.

Cefpoxomine Tablets

Manufacturing Directions

1. The tablet formula consisted of cefpodoxime proxetil (53.6%), HPMC 4000 cps (35%), Avicel PH 101 (10.4%), and magnesium stearate (1%).
2. Materials are blended in a polybag, using the geometric dilution principle.
3. The blend is compressed using 19.0 mm × 8.8 mm caplet-shaped concave punches with a target weight of 1.1 g/tablet.

Cefprozil Tablets (250 mg) Cefzil

Cefzil® tablets contain cefprozil equivalent to 250 or 500 mg of anhydrous cefprozil. In addition, each tablet contains the following inactive ingredients: cellulose, hydroxypropylmethylcellulose, magnesium stearate, methylcellulose, simethicone, sodium starch glycolate, polyethylene glycol, polysorbate 80, sorbic acid, and titanium dioxide. The 250-mg tablets also contain FD&C Yellow No. 6.

Cefprozil Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Cefprozil	250.00
30.00	2	Starch (maize)	30.00
3.00	3	Magnesium stearate	3.00

Manufacturing Directions

1. Dry blend items 1 and 2 for 20 minutes.
2. Sieve item 3 through a 250-μm mesh, and blend with step 1. Blend for 2 minutes.
3. Compress.

Cephalexin Tablets Keflex

Each pulvule contains cephalexin monohydrate equivalent to 250 mg (720 mcmol) or 500 mg (1439 mcmol) of cephalexin. The pulvules also contain cellulose, FD&C Yellow No. 10, FD&C Blue No. 1, FD&C Yellow No. 6, gelatin, magnesium stearate, silicone, titanium dioxide, and other inactive ingredients. Each tablet manufactured by Biocraft contains cephalexin monohydrate equivalent to 250 mg (720 mcmol) or 500 mg (1439 mcmol) of cephalexin. Inactive ingredients include hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 90, sodium starch glycolate, and titanium dioxide.

Cetirizine and Pseudoephedrine Delayed-Release Tablets (5 mg/120 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Cetirizine dihydrochloride, excess	6.25
120.00	2	Pseudoephedrine hydrochloride	120.00
25.00	3	Hydroxypropyl methylcellulose (Methocel DE5)	25.00
110.00	4	Hydroxypropyl methylcellulose (Methocel F4N)	110.00
10.00	5	Hydroxypropyl methylcellulose (Methocel K5M)	10.00
174.00	6	Microcrystalline cellulose	174.00
1.00	7	Dye yellow	1.00
2.50	8	Aerosil 200	2.50
2.50	9	Magnesium stearate	2.50
5.00	10	Ethyl cellulose (7PPS)	5.00
0.001 mL	11	Propylene glycol	1.00 mL
0.06 mL	12	Dichloromethane	60.00
0.16 mL	13	Water, purified	16.60 mL

Manufacturing Directions

1. Charge items 2 to 6 and 8 in a suitable mixer. Mix for 5 minutes.
2. Compress the mixture in step 1 at 445 mg per tablet.

Cetirizine Chewable Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Cetirizine hydrochloride	10.00
130.8	2	Mannitol DC grade	130.80
25.00	3	Lactose monohydrate	25.00
15.00	4	Microcrystalline cellulose	15.00
10.00	5	Betadex	10.00
2.00	6	Acesulfame potassium	2.00
0.70	7	Blue dye	0.70
1.50	8	Red dye (carmine)	1.50
2.00	9	Grape flavor	2.00
2.00	10	Colloidal silicon dioxide (Aerosil-200)	2.00
1.00	11	Magnesium stearate	1.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 5, and 6 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 10% (=6.5 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity of step 4 into step 2.
6. Charge 10% (=6.5 g) powder from step 1 in a stainless steel container.
7. Pass item 7 and item 8 through 0.5-mm sieve and add to step 6 and mix well.
8. Transfer half quantity of step 7 into step 2.
9. Pass item 3, item 4 and item 10 through 0.7-mm sieve and add to step 2.
10. Transfer balance quantity of step 4 into step 2.
11. Transfer balance quantity of step 7 into step 2.
12. Transfer balance quantity of step 1 into step 2.
13. Mix step 2 for 20 minutes using tumbler.
14. Pass item 11 through 0.250-mm sieve and add to step 13.
15. Mix step 14 for 2 minutes.
16. Compress into 200-mg tablets, using a suitable punch (8 mm, round).

Cetirizine Hydrochloride Tablets (10 mg) Zyrtec

Zyrtec tablets are formulated as white, film-coated, rounded-off rectangular-shaped tablets for oral administration and are available in 5- and 10-mg strengths. The inactive ingredients are as follows: lactose, magnesium stearate, povidone, titanium dioxide, hydroxypropyl methylcellulose, polyethylene glycol, and cornstarch.

Cetirizine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Cetirizine hydrochloride	10.20
39.00	2	Maize starch	39.00
70.55	3	Lactose monohydrate	70.55
2.60	4	PVP K-30	2.60
7.00	5	Maize starch, dried	7.00
0.65	6	Magnesium stearate	0.65
QS	7	Purified water	30.00

Manufacturing Directions

1. Prepare the binding solution by dissolving item 4 in item 7 at 25°C to 30°C until the solution becomes clear.
2. Sift item 1 through a 500-μm sieve in portions.
3. Add binding solution slowly, and granulate.
4. Add water if necessary. Dry granules at 55°C for 10 hours.
5. Pass granules through a 1.25-mm sieve in a V-shaped blender. Add items 5 and 6, and mix for 1 minute. Compress tablets of 130 mg with hardness of 5 to 8 kPa.
6. Coat using the HPMC. (See Appendix.)

Cetirizine Hydrochloride Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Cetirizine hydrochloride	5.00
90.75	2	Mannitol DC Grade	90.75
25.00	3	Lactose monohydrate	25.00
15.00	4	Microcrystalline cellulose	15.00
7.50	5	Betadex	7.50
1.50	6	Acesulfame potassium	1.50
0.50	7	Blue Dye	0.50
1.00	8	Red dye (carmine)	1.00
1.50	9	Grape flavor	1.50
1.50	10	Colloidal silicon dioxide (Aerosil-200)	1.50
0.75	11	Magnesium stearate	0.75

For other strengths adjust quantity with item 2.

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 5, and 6 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (=6.8 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity of step 4 into step 2.
6. Charge 10% (=4.5 g) powder from step 1 in a stainless steel container.
7. Pass item 7 and item 8 through 0.5-mm sieve and add to step 6 and mix well.
8. Transfer half quantity of step 7 into step 2.
9. Pass items 3, 4, and 10 through 0.7-mm sieve and add to step 2.
10. Transfer balance quantity of step 4 into step 2.
11. Transfer balance quantity of step 7 into step 2.
12. Transfer balance quantity of step 1 into step 2.
13. Mix step 2 for 20 minutes using tumbler.
14. Pass item 11 through 0.250-mm sieve and add to step 13.
15. Mix step 14 for 2 minutes.
16. Compress into 150-mg tablets, using a suitable punch (6.0 mm $\times$ 7.0 mm, oval).

Cetirizine Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Cetirizine hydrochloride	5.00
87.2	2	Lactose spray dried	87.2
5.00	3	Cornstarch	5.00
2.00	4	Povidone K30	2.00
0.80	5	Magnesium stearate	0.80
2.20	6	Hypromellose	2.20
0.50	7	Polyethylene glycol 4000	0.50
0.80	8	Titanium dioxide	0.80
–	9	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 3, and 4 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 10% (=4.4 g) lactose from step 1 to step 3 and mix well.
5. Transfer step 4 into step 2.
6. Transfer balance quantity of lactose from step 1 into step 2.
7. Mix step 2 for 15 minutes using tumbler.
8. Pass item 5 through 0.250-mm sieve and add to step 7.
9. Mix step 8 for 2 minutes.
10. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).
11. Charge item 9 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
12. Add item 7 and item 8 to step 11 with stirring. Stir for 5 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
13. Load core tablets from step 10 in coating pan and apply coating dispersion from step 12 to get 2.5% to 3.0% weight gain.

Cetirizine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Cetirizine hydrochloride	15.00
3.00	2	Polyvinylpyrrolidone	3.00
1.50	3	Silicon dioxide	1.50
135.00	4	Lactose	135.00
1.50	5	Glyceryl behenate	1.50
	6	Water qs	

Manufacturing Directions

1. Cetirizine and lactose are placed in a fluidized-bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1 mm mesh) and glyceryl behenate is weighed, added, and blended in a drum mixer.
4. The resulting mixture is pressed into tablets 156.00 mg.
5. These tablet cores are then coated with the following formulation: ethylcellulose 10.00, hydroxypropylcellulose 10.00, stearic acid 2.00, and alcohol 188.00 g.
6. Ethocel, povidone, and stearic acid are first dissolved in denatured alcohol (188 g).
7. The coating solution is then sprayed onto the tablet cores in a coating pan.

Cetylpyridinium Lozenges (2.5 mg)

Formulation: Cetylpyridinium chloride (Merck), 2.5 g; Ludipress LCE [1], 370.0 g; polyethylene glycol 6000, powder, 20.0 g; menthol, crystalline, 6.0 g; aspartame, potassium (Searle), 1.5 g.

Manufacturing Directions

1. Mix all components, and pass through a 0.8-mm sieve.
2. Press with low-compression force at 402 mg.

Charcoal Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Activated charcoal	250.00
150.00	2	Bolus alba (Merck)	150.00
28.00	3	Kollidon® 25	28.00
38.00	4	Acacia gum	38.00
QS	5	Water + isopropanol (10 + 3)	575.00 mL
15.00	6	Cremophor EL	15.00
QS	7	Isopropanol	300.00 mL

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with item 5, and pass through a 1-mm sieve.
2. Dry until a relative powder humidity of 90% is reached.
3. Add solution of items 6 and 7, and pass again through a 0.8-mm sieve.
4. Dry the granules, and press into 481-mg tablets using low-compression force and 12-mm planar punches.
5. Dry the obtained tablets.

Chlorcyclizine Hydrochloride Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Chlorcyclizine hydrochloride	50.00
109.75	2	Lactose monohydrate	109.75
4.28	3	Povidone (K 29–32)	4.28
11.30	4	Alcohol ethanol 190 proof	11.30
QS	5	Water, purified	QS
95.71	6	Starch (corn)	95.71
6.21	7	Talc	6.21
2.60	8	Magnesium stearate	2.60

Manufacturing Directions

1. Charge chlorcyclizine hydrochloride, lactose, and povidone into a mass mixer. Mix well.
2. Add alcohol (diluted with an equal weight of purified water) and QS to mass.
3. Granulate through a 15.88-mm aperture or similar.
4. Dry at 41°C to less than 1% LOD (1 hour Bra-bender or equivalent at 105°C).
5. Sift and grind through a 1.19-mm aperture or similar screen.
6. Lubricate by adding cornstarch (#6), talc, and acid stearic (or magnesium stearate) sifted through a 600-μm aperture or similar.
7. Compress using 7.94-mm standard round convex punches with logo.
8. Coating is optional; use organic coatings, preferably.

Chlordiazepoxide and Clinidium Bromide Tablets (5 mg/2.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Clinidium bromide, 5% excess	2.625
5.00	2	Chlordiazepoxide, 5% excess	5.25
131.02	3	Lactose powder	131.02
8.50	4	Starch (maize)	8.50
2.30	5	Talc	2.30
0.30	6	Magnesium stearate	0.30
QS	7	Water, purified	QS

Manufacturing Directions

1. Prepare a paste with maize starch and water. Use this for separately granulating items 1 and 2. Use a 1:4 starch and water mixture, and heat to 50°C with continuous stirring.
2. Knead, granulate, dry, and sieve item 1 using step 1 paste. Mix a 1:5 ratio of items 1 to 3, and mix together for 5 minutes. Pass the mixture through an oscillating granulator using a 1-mm sieve. Add paste from step 1 and mix for 5 minutes. Add item 3 (part) and pass the wet mass through a 7-mm sieve. Dry at an humidity of 40% to 50%. Pass the dried granules through a 1.5-mm perforated sieve.
3. Knead, granulate, dry, and sieve item 2 using step 1 paste. Use a 1:3 ratio of item 2 to lactose, and mix for 5 minutes. Then pass the mixture through a 1-mm oscillating granulator. Pass the wet mass through a 7-mm sieve and dry at 60°C overnight in a relative humidity of granules that is 34% to 43%. Pass the dried granules through a 1.5-mm perforated sieve.
4. Mix the granules from steps 2 and 3, and tumble the mix for 1 hour at low rpm.
5. Premix items 5 and 6 for 5 minutes, and then blend this mixture with step 4. Tumble the mix for a half hour at low rpm.
6. Compress into 150-mg tablets, using 8-mm cylindrical biconvex punches at 4 to 5 tons of pressure.
7. Apply a sugar coating (see Appendix) to the final weight of 300 mg.

Chlordiazepoxide Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Chlordiazepoxide	10.00
61.70	2	Lactose	61.70
6.17	3	Starch (maize)	6.17
0.60	3	Talc	0.60
0.30	4	Magnesium stearate	0.30
QS	5	Water, purified	QS

Manufacturing Directions

1. Mix items 1 and 2 in a blender for 10 minutes at medium speed.
2. In a separate vessel, prepare a paste of item 3 with item 5, at 50°C, and maintain this temperature until fully gelatinized without lumps.
3. Transfer the hot paste to the blender in step 1, and mix for 30 minutes. Then pass it through a granulator with a 10-mm perforated screen.
4. Dry the granules overnight at 45°C.
5. Sift the dry granules in an oscillating granulator with a 1-mm sieve.
6. Add item 4, and mix in a tumbler for 10 minutes.
7. Compress into 80-mg tablets, using 6 × 3-mm cylindrical biconvex punches.
8. Sugarcoat the tablets. (See Appendix.)

Chlorhexidine Lozenges

Bill of Materials			
Scale (mg/lozenge)	Item	Material Name	Quantity/1000 lozenges (g)
5.00	1	Chlorhexidine	5.00
150.00	2	Sorbitol (crystalline)	150.00
5.00	3	Kollidon® VA 64	5.00
5.00	4	Menthol (crystalline)	5.00
5.00	5	Eucalyptol (crystalline)	5.00
1.00	6	Aspartame, potassium	1.00
0.10	7	Saccharin sodium	0.10
2.00	8	Aerosil® 200	2.00
1.00	9	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with medium-compression force.
2. Compress into 175-mg lozenge, using 8-mm biplanar punches.

Chloroquine Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Chloroquine diphosphate	250.00
100.00	2	Dicalcium phosphate (Ditab)	100.00
10.00	3	Kollidon 30	10.00
–	4	Isopropyl alcohol	83.00
10.00	5	Kollidon CL	10.00
2.00	6	Aerosil 200	2.00
3.00	7	Talc	3.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4. Then dry, pass through a 0.8-mm sieve, add the mixture of items 5 to 7, and press with low-compression force.
2. Compress into 361-mg tablets, using 8-mm biplanar punches.

Chlorpheniramine and Pseudoephedrine Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3.35	1	Chlorpheniramine maleate	3.35
100.00	2	Pseudoephedrine hydrochloride	100.00
396.65	3	Cab-o-sil MS	396.65
200.00	4	Water	200.00

Manufacturing Directions

1. Chlorpheniramine maleate and pseudoephedrine hydrochloride are mixed in the water until thoroughly dissolved.
2. Cab-o-sil M5 (silicon dioxide) is poured into a planetary mixer to which the dissolved drug solution is added and mixed at slow speed.
3. This is continued for 5 minutes until the solution and Cab-o-sil are completely mixed.
4. The mixture is dried in a forced hot air oven for 5 hours to an LOD of less than 2.0%.
5. Magnesium stearate is then added as a lubricant, and tartaric acid is added as an acidulent.
6. The excipients are then thoroughly mixed and the entire composition is compressed into 1-g tablets, each one possessing a potency of 4.0-mg chlorpheniramine maleate and 120-mg pseudoephedrine hydrochloride.

Chlorpheniramine, Pseudoephedrine, and Dextromethorphan Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
8.00	1	Chlorpheniramine maleate	8.00
120.00	2	Pseudoephedrine hydrochloride	120.00
60.00	3	Dextromethorphan hydrobromide	60.00
812.00	4	Cab-o-Sil M5	812.00
200.00	5	Water	200.00

Manufacturing Directions

1. Chlorpheniramine maleate dextromethrophan HBr and pseudoephedrine hydrochloride are mixed in the water until throughly dissolved.
2. Cab-o-sil M5 (silicone dioxide) is poured into a planetary mixer to which the dissolved drug solution is added and mixed at slow speed.
3. This is continued for 5 minutes until the solution and Cab-o-sil are completely mixed.
4. The entire composition is dried in a forced hot air oven for 7 hours at 50°C.
5. The composition is dried to an LOD of 1.25%.
6. The dried material is then screened through a No. 30 U.S. standard mesh screen.
7. The excipients are added as mentioned before and the blend is compressed into 1.0 g. tablets, each one possessing a potency of 4 mg; chlorpheniramine maleate and 60 mg; pseudoephedrine hydrochloride and 30 mg dextromethorphan HBr.

Chlorpheniramine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Chlorpheniramine maleate	4.00
75.00	2	Starch 1500	75.00
65.62	3	Microcrystalline cellulose (50 um)	65.62
2.96	4	Stearic acid	2.96
1.11	5	Fumed silica	1.11
0.37	6	Magnesium stearate	0.37

Manufacturing Directions

1. Blend half of the Starch 1500 with the fumed silica and chlorpheniramine for 5 minutes.
2. Pass this mixture through a 40-mesh screen and return to blender.
3. Add the remaining starch 1500 to the material in step 1 and blend for 5 additional minutes.
4. Add the microcrystalline cellulose and stearic acid to the material from step 2 and blend for an additional 10 minutes.
5. Add the magnesium stearate to the material from step 3 and blend for an additional 5 minutes.

Choline Theophyllinate Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Choline theophylline	100.00
244.00	2	Ludipress	244.00
6.00	3	Magnesium stearate	6.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve. Mix and press with very low-compression force.
2. Compress into 350-mg tablets, using 8-mm biplanar punches.

Chymotrypsine Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Chymotrypsin	27.50
71.50	2	Ludipress	71.50
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm screen, and press with low-compression force.
2. Compress into 100-mg tablets, using 8-mm biplanar punches.

Cilazapril Tablets (2.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Cilazapril anhydrous	2.50
37.00	2	Lactose powder	37.00
2.87	3	Talc	2.87
57.43	4	Starch (maize)	57.43
7.65	5	Hydroxypropyl methylcellulose 2910/3C	7.65
1.91	6	Sodium stearyl fumarate	1.91
QS	7	Water, purified	QS

Manufacturing Directions

1. Disperse item 5 in 50 mL of item 7, and allow this to stand overnight.
2. In a tumble mixer, add item 1 and 10 g of item 2, and mix for 5 minutes.
3. Add the balance of item 2 and 20 g of item 4, and mix well.
4. Add the granulating solution from step 1, and knead. Then pass through a 7-mm sieve in a granulator.
5. Spread on paper-lined trays, and dry at 45°C overnight.
6. Pass the dried granules through a 1.5-mm sieve at 20% to 25% RH.
7. In a tumble mixer, add the balance of item 4, and then add items 3 and 6. Mix for 6 minutes.
8. Compress into 200-mg tablets, using a suitable punch.
9. Coat using the Opadry coating. (See Appendix.)

Cimetidine Chewable Tablets

Manufacturing Directions

1. Cimetidine Premix Granules—Cimetidine, 200.0 mg; Eudragit E100, 20.0 mg; antacid (Al/Mg) granules sorbitol: direct compression grade, 590.0 mg; lactose: direct compression grade spray dried, 325.0 mg; lactose crystalline, 325.0 mg; dried aluminium hydroxide gel, 250.0 mg; magnesium hydroxide, 200.0 mg; croscarmellose sodium type A, 30.0 mg; magnesium stearate, 15.0 mg. Total 1735.0 mg.
2. Tableting mix for compression—Cimetidine 220.0 mg; premix granules antacid (Al/Mg), 1735.0 mg; granules microcrystalline cellulose, 200.0 mg (Avicel PH102); aspartame, 10.0 mg; aniseed, 20.0 mg, butterscotch, 20.0 mg; magnesium stearate, 15.0 mg. Total 2220.0 mg.
3. A 40% (w/w) solution of the Eudragit E100 in methylene chloride is added with mixing to the cimetidine and blended until granules are formed.
4. The resulting granules are dried and then sieved through a 16-mesh screen.
5. Aluminium hydroxide, magnesium hydroxide, and other ingredients for the antacid granules are sieved through a 12-mesh (1.4 mm) screen and mixed together.
6. The resulting mix is compressed on a rotary tablet press and the resulting compacts are milled using a 12-mesh screen.
7. Cimetidine granules, antacid granules, and extragranular excipients are put into a cone blender and mixed thoroughly.
8. The resulting mix is discharged from the blender and compressed on a suitable rotary tablet press fitted with the appropriate punches.

Cimetidine Tablets (200 mg)

Formulation: Cimetidine, 200 g; Ludipress, 295 g; magnesium stearate, 5 g.

Manufacturing Directions

1. Pass the mixture through 0.8-mm screen.
2. Press with low-compression force at 510 mg at low humidity 30%.

Cimetidine Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Cimetidine[a]	202.00
48.89	2	Microcrystalline cellulose (Avicel PH 102)	48.89
6.00	3	Povidone (PVP K-30)	6.00
0.40	4	Sodium lauryl sulfate	0.40
0.26	5	Dispersed blue E132	0.26
0.26	6	Ferric oxide (iron oxide yellow)	0.26
13.11	7	Starch (maize)[b]	14.41
9.44	8	Sodium starch glycolate (Primojel)	9.44
1.40	9	Magnesium stearate	1.40
–	10	Purified water	77.78

Note: For higher strength (400- and 800-mg tablets), adjust formula and fill weights accordingly.
[a]Cimetidine 2.0 mg/tablet (1%) is added as an extra to compensate for the moisture.
[b]Maize starch 1.3 mg/tablet (10%) is added as an extra to compensate for the moisture.

Manufacturing Directions

1. Prepare a slurry of item 7 in 15.56 g of item 10 (30–40°C). Then make a translucent paste by adding 44.44 g of item 10 (90–95°C). Cool to 45°C to 50°C.
2. Disperse items 5 and 6 in 4.44 g of item 10 (25–30°C) by homogenizing. Add the color dispersion to the starch paste at step 1, and mix well.
3. Dissolve item 3 in 13.33 g of item 10. Stir until the solution is clear. Add item 4 to the solution. Stir just to dissolve. Do not produce foam by stirring. Add this solution to the colored paste at step 2, and mix for 5 minutes.
4. Pass items 1 and 2 through a 1200-μm sieve using a sifter. Collect in an s.s. drum. Load to a mixer. Mix at a high speed for 10 minutes.
5. Add colored starch paste from step 3 to the dry powder in the mixer. When the addition is over, mix at medium speed to get the satisfactory wet mass.
6. Add item 10 if required. Record extra quantity if used.
7. Pass the wet mass through a FitzMill using sieve 24250, knives forward, at medium speed.
8. Collect and spread the granules onto the trays, one-third the thickness of the tray, and dry the granules at 55°C for 16 hours. After 4 hours of drying, stir the granules in the trays, and change the positions of the trays for uniform drying. *Note:* Stirring is a very important step to avoid migration of color. Migration leads to mottling of the tablet.
9. Check the moisture of dried granules. The limit is not more than 1.5%. Dry further if required to get a moisture content of 1.5%.
10. Pass the granules through a 1.25-mm sieve using a granulator at medium speed. Do not fill the hopper completely. This increases excess fines.
11. Pass item 8 through a 500-μm sieve using a sifter. Collect in a polyethylene bag, and add to the blender. Mix for 5 minutes
12. Pass item 9 through a 250-μm sieve using a sifter. Collect in a polyethylene bag, and add 4.4 to 6.7 g powder from the bulk. Mix it, and then add it to the blender. Mix for 1 minute.
13. Check temperature and humidity before starting compression. The limits are as follows: temperature 25°C to 27°C; RH 45% to 55%.
14. Compress the granules using round concave punches. The weight of 10 tablets is 2.80 g ± 2%.
15. Coat tablets. (See the details in the Appendix.)

Ciprofloxacin Tablets (500 mg) Cipro

Cipro film-coated tablets are available in 100-, 250-, 500-, and 750-mg (ciprofloxacin equivalent) strengths. The inactive ingredients are starch, microcrystalline cellulose, silicon dioxide, crospovidone, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and water.

Ciprofloxacin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00, 582.19	1	Ciprofloxacin Ciprofloxacin HCl·H_2O	582.19
10.00	2	Crospovidone (Kollidon CL)	10.00
60.00	3	Sodium starch glycolate (Primojel)	60.00
9.50	4	Povidone (PVP K-30)	9.50
54.37	5	Microcrystalline cellulose (Avicel PH 101)	54.37
20.00	6	Crospovidone (Kollidon CL)	20.00
20.00	7	Sodium starch glycolate (Primojel)	20.00
6.00	8	Magnesium stearate	6.00
3.46	9	Colloidal silicon dioxide (Aerosil 200)	3.46
–	10	Absolute alcohol (ethanol, dehydrated alcohol)	268.00

Manufacturing Directions

Note: It is important to note the following:

- Avoid overmixing lubricants because this could reduce hardness.
- Process the products in an explosion-proof area. Relative humidity should not be more than 50%, and the temperature should be not more than 27°C.

1. Granulating solution: Dissolve item 4 in item 10 under slow stirring by stirrer.
2. Dry powder mixing: Sift items 1, 3, and 2 through a stainless steel sieve (900-μm) in sifter. Load into a mixer. Mix and chop for 3 minutes at low speed.
3. Kneading
   a. Knead the mixed powder with granulating solution for 2 minutes while mixing at low speed. Then mix and chop at high speed for 2 minutes.
   b. If required, add more absolute alcohol, and mix and chop at low speed to get to the end point of granulation. Record the additional quantity of absolute alcohol. Unload the wet mass in a stainless steel tray for drying.
4. Drying
   a. Dry the wet mass in the oven. Start air circulation without the heater "on" for 2 hours, keeping the door open. Then dry at 55°C for 5 hours.
   b. Check the LOD. The limit is 1.5% to 2.0%.
   c. If required, continue drying at 55°C for another half an hour to get the desired LOD.
5. Grinding: Pass the dried granules through a 1.25-mm sieve using a granulator at medium speed. Collect in stainless steel drums.
6. Lubrication
   a. Sift items 5, 7, 6, and 9 through a 500-μm sieve, and add it to the dry granules in the drum.
   b. Pass item 8 through a 250-μm sieve using a sifter. Add 40 to 60 g of granules from bulk. Mix in polyethylene bag for 1 minute. Add to a drum blender and mix for 1 minute.
7. Compression: Compress the granules using a rotary tabletting machine with 18 × 8 mm oblong concave punches. Compress into 770-mg tablets.
8. Coating: Coat using HPMC coating. (See Appendix.)

Ciprofloxacin Tablets (750 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
750.00, 900.00	1	Ciprofloxacin Ciprofloxacin HCl·H_2O	900.00
15.00	2	Crospovidone (Kollidon CL)	15.00
70.00	3	Sodium starch glycolate (Primojel)	70.00
11.00	4	Povidone (PVP K-30)	11.00
70.00	5	Microcrystalline cellulose (Avicel PH 101)	70.00
25.00	6	Crospovidone (Kollidon CL)	25.00
30.00	7	Sodium starch glycolate (Primojel)	30.00
7.50	8	Magnesium stearate	7.50
3.50	9	Colloidal silicon dioxide (Aerosil 200)	3.50
–	10	Absolute alcohol (ethanol, dehydrated alcohol)	400.00

Manufacturing Directions

See the manufacturing directions for the 500-mg tablet.

Cisapride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
52.92	1	Cirapride-(L)-tartarate	52.92
346.08	2	Lactose	346.08
66.000	3	Hydroxypropylmethylcellulose 2208	66.000
2.85	4	Magnesium stearate	2.85
5.70	5	Colloidal anhydrous silica	5.70
28.60	6	Talc	28.60

Cisapride Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Cisapride	5.20
80.90	2	Lactose monohydrate	80.90
10.80	3	Starch (maize)	10.80
3.00	4	Povidone (PVP K-30)	3.00
0.15	5	Polysorbate 20 (Tween 20)	0.15
19.40	6	Microcrystalline cellulose (Avicel PH 102)	19.40
0.60	7	Magnesium stearate	0.60
–	8	Purified water	18.00

Manufacturing Directions

Note: Avoid overmixing lubricants, otherwise hardness can be reduced.

1. Preparation of binding solution
   a. Dissolve item 4 in 16.0 g of item 8 (30°C), while mixing at slow speed by stirrer.
   b. Add item 5 to 2.0 g of item 8 (60–70°C). Stir manually with a spatula to make a clear solution.
   c. Add the previous step into step 1. Mix manually.
2. Sieving and mixing: Sift items 1 to 3 through a 500-μm sifter. Load into a mixer and mix for 5 minutes at low speed.

3. Kneading
   a. Add the binding solution to the dry powders, while mixing at speed I for 2 minutes. After the binding solution is added, mix further for 1 minute, using the mixer and chopper at low speed. Scrape sides and blade. Check for satisfactory granules with little or no lumps.
   b. If required, add extrapurified water, and record.
   c. Unload the granules into a stainless steel tray for drying.
4. Drying
   a. Dry the granules in an oven at 55°C for 10 hours. After 4 hours of drying, scrape the semidried granules to break the lumps for uniform drying.
   b. Check the LOD. The limit is 0.7% to 1.0%.
   c. Transfer the dried granules into stainless steel drums.
5. Grinding
   a. Pass the dried granules through a 1-mm sieve at medium speed. Collect in stainless steel drums.
   b. Load granules into the drum blender.
6. Lubrication
   a. Sift item 6 through a 500-μm sieve using a sifter. Add to step 2, in a drum blender. Mix for 5 minutes.
   b. Sift item 7 through a 500-μm stainless steel sieve in sifter. Add 4- to 6-g granules in a polyethylene bag to sieve item. Mix manually for 1 minute. Add to drum blender, and blend for 1 minute.
   c. Unload in stainless steel drums.
7. Compression: Compress the granules using a rotary tabletting machine with 7-mm round punches and a compression weight of 120 mg.

Cisapride Tartarate Mini Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6	1	Cisapride tartarate	6
3.54	2	Explotab	3.55
25.36	3	Avicel PH 101	25.36
3.54	4	Aerosil 200	3.54
3.54	5	Magnesium stearate	3.54

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6	1	Cisapride tartarate	6
6.92	2	Methocel K100M	6.92
3.45	3	Klucel LF	3.45
17.68	4	Avicel pH 101	17.68
3.45	5	Aerosil 200	3.45
3.45	6	Magnesium stearate	3.45

Manufacturing Directions

1. The ingredients (1–5), with the exception of magnesium stearate, are blended for 45 minutes.
2. Magnesium stearate is then added and blending continued for 5 minutes.
3. The blend is then tabletted in a 3.8-mm round deep concave punches with fill weight of 35.48 mg in the first formula and 34.54 in the second formula.
4. Coat the tablets using the following formulation: Eudragit L 12.5, 49.87%; talc 2.47%; diethyl phthalate 1.27%; isopropyl alcohol 43.33%; purified water 3.07%. Coat to provide 12.5% weight gain.

Citalopram Hydrobromide Tablets Celexa

Celexa is a film-coated, oval-scored tablet containing citalopram HBr in strengths equivalent to a 20- or 40-mg citalopram base. The inactive ingredients are copolyvidone, cornstarch, croscarmellose sodium, glycerin, lactose, monohydrate, magnesium stearate, hydroxypropyl methyl cellulose, microcrystalline cellulose, polyethylene glycol, titanium dioxide, and iron oxides are used as coloring agents in the pink 20-mg tablets.

Clarithromycin Tablets (250 mg/500 mg) Biaxin

Each yellow oval film-coated Biaxin tablet contains 250 or 500 mg of clarithromycin and the following inactive ingredients: cellulosic polymers, cros-carmellose sodium, D&C Yellow No. 10, FD&C Blue No. 1, magnesium stearate, povidone, propylene glycol, silicon dioxide, sorbic acid, sorbitan monooleate, stearic acid, talc, titanium dioxide, and vanillin. The 250-mg tablet also contains pregelatinized starch.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Clarithromycin[a]	256.00
80.90	2	Microcrystalline cellulose (Avicel PH 102)	80.90
8.00	3	Croscarmellose sodium (Ac-Di-Sol)	8.00
9.00	4	Povidone (PVP K-30)	9.00
1.10	5	Polysorbate 80 (Tween 80)	1.10
51.50	6	Microcrystalline cellulose (Avicel PH 102)	51.50
10.00	7	Croscarmellose sodium (Ac-Di-Sol)	10.00
22.00	8	Pregelatinized starch (starch 1500)	22.00
2.25	9	Magnesium stearate	2.25
4.50	10	Talc (fine powder)	4.50
3.00	11	Stearic acid	3.00
1.75	12	Colloidal silicon dioxide (Aerosil 200)	1.75
–	13	Alcohol (ethanol 95%)	88.00

[a]Clarithromycin 6.0 mg/tablet is added as an excess to compensate for the water content and assay of the material. The weight of clarithromycin is factored based on potency. The weight of microcrystalline cellulose (Avicel PH 101) is then adjusted to compensate for the factored potency of clarithromycin. Adjust the fill weight and formula for a 500-mg tablet.

Manufacturing Directions

Precautions: Avoid overmixing lubricants, otherwise hardness can be reduced. Process the products in an explosion-proof area, with relative humidity of not more than 50%, and a room temperature of not more than 27°C.

1. Screen, if necessary, through an approximately 710-µm screen, the following: clarithromycin, croscarmellose sodium, microcrystalline cellulose (Avicel PH 101), and silicon dioxide. Blend together in suitable massing equipment.
2. Dissolve povidone in approximately 240 mL of ethanol—a complete solution must be achieved.
3. While mixing the blended powders from step 1, add the povidone solution from step 2.
4. Continue mixing to ensure an even distribution of the solution, and then add extra ethanol until a characteristic granule mass is obtained.
5. If necessary, pass the wet mass through a 3- to 4-mm screen. Dry at approximately 50°C to 55°C until the LOD is not more than 3%.
6. Sift dried granule over a 1.4-mm (approximately) screen. Pass the oversized granules through a 1.7-mm (approximately) screen, using a suitable mill. Alternate screening and milling systems may be used to yield suitable sized granules.
7. Load a portion of the granule from step 6 into a suitable blender. Add microcrystalline cellulose (Avicel PH 102) and croscarmellose sodium, blend, add talc, purify, and blend until uniform.
8. Mix together stearic acid and magnesium stearate with a small portion of granule. If necessary, pass through a 0.5-mm (approximate) screen.
9. Add the steps above, mix, then add the balance of granule. Mix until uniform.
10. Compress tablets to the following parameters: tablet weight 8.5 g/10 tablets ± 3%.
11. Coat using an HPMC coating solution.

Clarithromycin Dispersible Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Clarithromycin base	250.00
22.50	2	Crospovidone	22.50
62.50	3	Croscarmellose sodium	62.50
3.80	4	Polysorbate	3.80
566.20	5	Microcrystalline cellulose	566.20
40.00	6	Aspartame	40.00
20.00	7	Saccharin sodium	20.00
20.00	8	Mint flavor	20.00
5.00	9	Colloidal silica	5.00
10.00	10	Magnesium stearate	10.00

Clarithromycin Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Clarithromycin	500.00
200.00	2	Methocel K100 LV Premium CR Grade	200.00
260.00	3	Lactose monohydrate	260.00
30.00	4	Talc	30.00
	5	Magnesium stearte	

Manufacturing Directions

1. Methocel (K 100 LV) is loaded into a mixer, and dry blended with clarithromycin.
2. The mixture is granulated using water until proper granulation is obtained. The granulation is then dried, sifted, and ground to appropriate size.
3. Talc and magnesium stearate are screened and blended with dry granulation. The granulation is then loaded into hopper and compressed into tablets. The tablets are then coated with an aqueous coating.

Clarithromycin Controlled-Release Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Clarithromycin	1000.000
25.00	2	Methocel K15 MCR	25.00
12.50	3	Methocel K4 MCR	12.50
12.50	4	Lactose	12.50
20.00	5	Sodium stearyl fumarate	20.00
12.50	6	Magnesium stearate	12.50
10.00	7	Talc	10.00
0.50	8	Colloidal silicon dioxide	0.50

Manufacturing Directions

1. Clarithromycin is blended with the two polymers and lactose and wet granulated with water. The granules are dried, sized, lubricated, and compressed to tablets (1161.5 mg).
2. The tablets thus obtained are optionally film coated.

Clenbuterol Tablets (20 mcg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.02	1	Clenbuterol hydrochloride	0.02
99.00	2	Ludipress	99.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components in a Turbula mixer, and press to tablets with a compression force of 20 kN.
2. Compress into 100-mg tablets, using 8-mm punches.
3. If the content uniformity does not meet the requirements, prepare a premix of clenbuterol hydrochloride with a small part of the Ludipress before mixing with the other components of the tabletting mixture.

Clindamycin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Clindamycin, use clindamycin hydrochloride	22.70
265.00	2	Lactose dihydrate	265.00
33.33	4	Starch (maize)	33.30
2.00	5	Hydroxypropyl cellulose (Klucel EF)	2.00
30.00	6	Calcium lactate. 5H20	30.00
41.00	7	Lactic acid	41.00
128.00	8	Microcrystalline cellulose (Avicel PH 102)	128.00
12.00	9	Kollidon CL	12.00
7.00	10	Aerosil 200	7.00

Manufacturing Directions

1. Clindamycin HCl, lactose, one-half of the cornstarch, HPC, calcium lactate, and lactic acid are granulated in a fluidized-bed granulator.
2. The resulting granules and the remainder of the cornstarch, Kollidon, microcrystalline cellulose, magnesium stearate, and Aerosil are passed through a forced sieve (1.25 mm) and homogenized in a container mixture.
3. The resulting mixture is tabletted on a rotary tabletting machine.

Clobazam Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Clobazam	10.00
135.00	2	Dicalcium phosphate	135.00
7.00	3	Kollidon VA64	7.00
7.00	4	Kollidon CL	7.00
1.50	5	Magnesium stearate	1.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force (15 kN).
2. Compress into 165-mg tablets, using 8-mm biplanar punches.

Clomifen Citrate Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Clomifen citrate	50.00
100.00	2	Ludipress	100.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, sieve, and press with low-compression force.
2. Compress into 154-mg tablets, using 8-mm biplanar punches.

Clomipramine Hydrochloride Tablets, Buccal (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Clomipramine hydrochloride	10.00
90.00	2	Gelatin	90.00
20.00	3	Glycerin, anhydrous	20.00
10.00	4	Lactose, anhydrous	10.00
20.00	5	Mannitol	20.00

Manufacturing Directions

1. Clomipramine hydrochloride (10 g) and 90 g of gelatin are mixed and pulverized in a mill.
2. After mixing, 20 g of glycerin, 10 g of lactose, and 20 g of mannitol are added, and the components are mixed until uniform.
3. Compress 150 mg to provide a buccal dosage unit. Each buccal unit contains 10 mg of clomipramine hydrochloride.

Clomipramine Hydrochloride Tablets, Effervescent (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Clomipramine hydrochloride	300.00
1985.00	2	Sodium bicarbonate	1985.00
1000	3	Citric acid	1000

Manufacturing Directions

1. The components (i.e., clomipramine hydrochloride, sodium bicarbonate, and citric acid, as set forth in the preceding table) are thoroughly mixed.
2. An effervescent tablet is produced by placing the mixture in a die, following with compression with an appropriate punch. Relatively little compression force is used (e.g., about 3000 to about 20000 pounds of force).

Clonazepam Tablets (1 mg/2 mg)

Klonopin, a benzodiazepine, is available as scored tablets with a K-shaped perforation containing 0.5 mgf and 1 or 2 mg of clonazepam, and unscored tablets with a K-shaped perforation containing 1 or 2 mg of clonazepam. Each tablet also contains lactose, magnesium stearate, microcrystalline cellulose, and cornstarch, with the following colorants: 0.5 mg of FD&C Yellow No. 6 Lake; 1 mg of FD&C Blue No. 1 Lake and of FD&C Blue No. 2 Lake.

Clonidine Tablets (0.1 mg/0.2 mg/0.3 mg) Plavix

Plavix for oral administration is available as pink, round, biconvex, engraved film-coated tablets containing 97.875 mg of clopidogrel bisulfate, which is the molar equivalent of 75 mg of clopidogrel base. Each tablet contains anhydrous lactose, hydrogenated castor oil, microcrystalline cellulose, polyethylene glycol 6000, and pregelatinized starch as inactive ingredients. The pink film coating contains ferric oxide (red), hydroxypropyl methylcellulose 2910, polyethylene glycol 6000, and titanium dioxide. The tablets are polished with carnauba wax.

Codeine, Acetaminophen, and Pentobarbital Tablets (15 mg/300 mg/30 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Codeine phosphate, 2.5% excess	15.375
300.00	2	Acetaminophen	300.00
30.00	3	Pentobarbital sodium, use pentobarbital	27.50
40.00	4	Calcium carbonate, precipitated	40.00
58.66	5	Lactose monohydrate	58.66
20.00	6	Povidone K 29–32	20.00
20.00	7	Starch (corn)	20.00
2.00	8	Polyethylene glycol, milled	2.00
0.066	9	Red dye	0.066
0.054	10	Yellow dye	0.054
0.018	11	Scarlet dye	0.018
25.79	14	Polacrillin potassium (Amberlite IRP-88)	25.79
10.40	15	Magnesium steareate	10.40

Manufacturing Directions

1. Mixing
   a. Add codeine phosphate to acetaminophen in the presence of an authorized person.
   b. Pass step a through a micropulverizer fitted with a 6.35-mm aperture or similar screen at high speed, with the hammers forward if the acetaminophen has a bulk density above 0.4 g/cc. After micropulverizing, the bulk density should be checked and should not exceed 0.4 g/cc. Add this to the mixer.
   c. Pass pentobarbital and calcium carbonate through an 840-μm aperture screen, and then add to the mixer.
   d. Add lactose, povidone, cornstarch, and polyethylene G 8000 NF (milled) to the mixer, and mix for 5 minutes.
   e. Dissolve the dyes in water and add alcohol.
   f. Add the dye solution to the powders in the mixer, and mix until the color is evenly dispersed.
   g. Screen the wet granulation through a 9.52-mm aperture screen.
   h. Oven dry for 2 to 3 hours at 43°C, or use a fluid-bed dryer at room temperature for 12 minutes or until the LOD is 1% to 2% (1 hour at 105°C on an Ohaus, Brabender, or equivalent balance).
   i. Mill the dried granulation through a 1.2-mm aperture screen (FitzMill or similar, medium speed, knives forward), and then add to a suitable mixer (V or similar).
   j. Pass the amberlite and magnesium stearate through a 595-μm aperture screen on a suitable shaker (Russel or similar), and add to the mixer (V or similar).
   k. Blend for 30 minutes.
   l. Discharge the blended material into polyethylene-lined containers. Seal and deliver this to the compression area.
2. Compression
   a. Compress on an 11.90-mm standard concave punch.
   b. The weight of 10 tablets is 5.2 g.

Conjugated Estrogens and Medroxyprogeste Tablets, Prempro

Prempro 2.5 mg—Each peach tablet for oral administration contains 0.625 mg conjugated estrogens, 2.5 mg of medroxyprogesterone acetate, and the following inactive ingredients: calcium phosphate tribasic, calcium sulfate, carnauba wax, cellulose, glyceryl monooleate, lactose, magnesium stearate, methylcellulose, pharmaceutical glaze, polyethylene glycol, sucrose, povidone, titanium dioxide, and red ferric oxide.

Prempro 5 mg—Each light-blue tablet for oral administration contains 0.625 mg of conjugated estrogens, 5 mg of medroxyprogesterone acetate, and the following inactive ingredients: calcium phosphate tribasic, calcium sulfate, carnauba wax, cellulose, glyceryl monooleate, lactose, magnesium stearate, methylcellulose, pharmaceutical glaze, polyethylene glycol, sucrose, povidone, titanium dioxide, and FD&C Blue No. 2.

Premphase—Each maroon Premarin tablet for oral administration contains 0.625 mg of conjugated estrogens and the following inactive ingredients: calcium phosphate tribasic, calcium sulfate, carnauba wax, cellulose, glyceryl monooleate, lactose, magnesium stearate, methylcellulose, pharmaceutical glaze, polyethylene glycol, stearic acid, sucrose, titanium dioxide, FD&C Blue No. 2, D&C Red No. 27, FD&C Red No. 40. These tablets comply with USP Drug Release Test 1. Each light-blue tablet for oral administration contains 0.625 mg of conjugated estrogens and 5 mg of medroxyprogesterone acetate and the following inactive ingredients: calcium phosphate tribasic, calcium sulfate, carnauba wax, cellulose, glyceryl monooleate, lactose, magnesium stearate, methylcellulose, pharmaceutical glaze, polyethylene glycol, sucrose, povidone, titanium dioxide, and FD&C Blue No. 2.

Conjugated Estrogens (0.3–2.50 mg) Prematin

Tablets are available in 0.3-, 0.625-, 0.9-, 1.25-, and 2.5-mg strengths of conjugated estrogens. Premarin tablets contain the following inactive ingredients: calcium phosphate tribasic, calcium sulfate anhydrous (white tablet), calcium sulfate, carnauba wax, cellulose, glyceryl monooleate, lactose, magnesium stearate, methylcellulose, pharmaceutical glaze, polyethylene glycol, stearic acid, sucrose, talc, and titanium dioxide. The 0.3-mg tablets also contain D&C Yellow No. 10, FD&C Blue No. 1, FD&C Blue No. 2, FD&C Yellow No. 6. The 0.625-mg tablets also contain FD&C Blue No. 2, D&C Red No. 27, and FD&C Red No. 40. The 0.9-mg tablets also contain D&C Red No. 6, D&C Red No. 7. The 1.25-mg tablets contain black iron oxide, D&C Yellow No. 10, and FD&C Yellow No. 6. The 2.5-mg tablets contain: FD&C Blue No. 2 and D&C Red No. 7.

Coumadin Tablets

Coumadin tablets also contain (all strengths) lactose, starch, and magnesium stearate; 1 mg of D&C Red No. 6; 2 mg of FD&C Blue No. 2 and FD&C Red No. 40; 2 1/2 mg of FD&C Blue No. 1, and D&C Yellow No. 10; 4 mg of FD&C Blue No. 1 Lake; 5 mg of FD&C Yellow No. 6; 7 1/2 mg of D&C Yellow No. 10, and FD&C Yellow No. 6; 10 mg of dye free.

Crospovidone Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Crospovidone (micronized)	1000.00
150.00	2	Citric acid	150.00
25.00	3	Aerosil® 200	25.00
100.00	4	Sucrose (crystalline)	100.00
1.00	5	Saccharin sodium	1.00
QS	6	Water	QS
5.00	7	Magnesium stearate	5.00
125.00	8	Sodium bicarbonate	125.00
65.00	9	Flavor mixture	65.00

Manufacturing Directions

1. Granulate mixture of items 1 to 5 with item 6, dry, and pass through a sieve.
2. Mix the dry granules with items 7 to 9, and press with medium-compression force.
3. The dosage may be increased to 2000 mg crospovidone by increasing the tablet weight to 3200 mg.
4. Compress 1590-mg tablets, using 20-mm-diameter biplanar punches.

Cyclobenzaprine Hydrochloride Tablets (10 mg)

Cyclobenzaprine HCl is supplied as 10-mg tablets for oral administration. The inactive ingredients are hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxide, lactose, magnesium stearate, starch, and titanium dioxide.

Cyclobenzaprine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Cyclobenzaprine	10.00
74.00	2	Lactose anhydrous	74.00
35.00	3	Starch (maize)	35.00
1.00	4	Magnesium stearate	1.00
25.00	5	Starch (maize)	25.00
–	6	Water, purified	30.00 mL

Manufacturing Directions

1. Charge the active ingredient (cyclobenzaprine) and lactose in a suitable mixer.
2. Blend until a uniform mix is obtained.
3. Add item 5 to item 6 to make a paste.
4. Add step 3 into step 2 to form a suitable mass.
5. Add item 3 to step 4, and mix until granules are formed.
6. Screen granules through a suitable milling machine, using a 1/4-in. stainless steel screen.
7. Dry the milled granules in a suitable drying oven until the desired moisture of less than 2% is obtained.
8. Mill the dried granules through a suitable milling machine using a 1/4-in. mesh stainless steel screen, and transfer to a blender.
9. Add the magnesium stearate to the blender after passing through a 250-μm sieve. Then blend for 3 minutes.
10. Compress the tablets.
11. Coat the tablets using an aqueous or nonaqueous coating. (See Appendix.) For example, 2.5 mg of hydroxypropymethylcellulose can be dissolved in 25 mg of deionized water. An aqueous (10 mg) suspension of 1.88 mg of talc, 0.5 mg of titanium dioxide, 0.1 mg of yellow iron oxide, and 0.02 mg of red iron oxide is stirred into this solution. The coating suspension is sprayed on the tablets. The coated tablets are dried overnight at 45°C.

Cyproheptadine Tablets (4 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Cyproheptadine	4.00
194.00	2	Ludipress	194.00
2.00	3	Magnesium stearate	12.00

Manufacturing Directions

1. Pass all ingredients through an 0.8-mm sieve.
2. Mix and press with very low-compression force (4 kN).
3. Compress into 202-mg tablets, using 8-mm biplanar punches. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

Dapsone Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Dapsone	50.00
80.00	2	Starch (maize)	80.00
50.00	3	Dicalcium phosphate	50.00
20.00	4	Lactose monohydrate	20.00
8.00	5	Starch (maize)	8.00
0.12	6	Methyl paraben	0.12
0.02	7	Propyl paraben	0.03
1.50	8	Talc	1.50
1.00	9	Magnesium stearate	1.00
–	10	Water, purified	QS

Manufacturing Directions

1. Charge items 1 to 4 in a suitable vessel, after passing them through a #40-mesh screen. Mix at medium speed for 15 minutes.
2. In a separate vessel, take a sufficient quantity of item 10, and heat it to 80°C; add items 5 and 6, and dissolve. Allow the mixture to cool to 50°C, and then add item 7. Stir and mix this to obtain a smooth paste.
3. Add the wet mass in step 2 to step 1, and mix well. Pass the wet mass through an 8-mm screen, and collect on paper-lined trays.
4. Dry the wet mass at 50°C overnight to an LOD of not more than 2%.
5. Pass dried granules through an 18-mm sieve, and collect them in a tumble mixer.
6. Pass item 8 through a 500-μm and item 9 through a 250-μm sieve screen, and add to step 5. Blend for 1 minute.
7. Compress into 200-mg tablets, using 8-mm round punches.

Delavirdine Mesylate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Delavirdine mesylate	200.00
198.76	2	Microsrystalline cellulose	198.76
71.29	3	Coarse powder lactose monohydrate spray	71.29
75.00	4	Hydroxypropyl methylcellulose 2910 3 cps	75.00
110.00	5	Croscarmellose sodium Type A	110.00
1.50	6	Colloidal silicon dioxide	1.50
5.00	7	Magnesium stearate	5.00

Manufacturing Directions

1. The above tablets are manufactured by intensely mixing the delavirdine mesylate and the microcrystalline cellulose in a high-shear mixer.
2. Then add and mix the hydroxypropyl methylcellulose, croscarmellose, lactose, and screened colloidal silicon dioxide in a high-shear mixer. Finally add screened magnesium stearate and lubricate in a high-shear mixer. The resulting mixture is compressed and film coated, and polished to give tablets that have about 200 mg of delavirdine mesylate/tablet.

Desloratidine Tablets (5 mg), Clarinex

Clarinex® (desloratadine) tablets are light blue, round, film-coated tablets containing 5 mg of desloratadine, an antihistamine, to be administered orally. The tablet also contains the following excipients: dibasic calcium phosphate dihydrate USP, microcrystalline cellulose NF, cornstarch NF, talc USP, carnauba wax NF, white wax NF, coating material consisting of lactose monohydrate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and FD&C Blue #2 Aluminum Lake.

Desogestrel and Ethinyl Estradiol Tablets (0.15 mg/0.03 mg), Ortho-Cept

Ortho-Cept 21 and Ortho-Cept 28 tablets provide an oral contraceptive regimen of 21 orange, round tablets, each containing 0.15 mg of desogestrel (13-ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol) and 0.03 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17, diol). Inactive ingredients include vitamin E, cornstarch, povidone, stearic acid, colloidal silicon dioxide, lactose, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, talc, and ferric oxide. Ortho-Cept 28 also contains seven green tablets containing the following inactive ingredients: lactose, pregelatinized starch, magnesium stearate, FD&C Blue No. 1 Aluminum Lake, ferric oxide, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, and talc.

Diazepam Tablet (10 mg)

Formulation: Diazepam,10 g; Ludipress,100 to 480 g; magnesium stearate, 0.5 to 2.0 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with medium compaction force 11 to 490 mg based on label required.

Diazepam Tablets (2 mg/5 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Diazepam	10.00
70.00	2	Potato starch	70.00
150.00	3	Lactose	150.00
1.50	4	Potato starch, cold swelling	1.50
0.076	5	Polysorbate 80	0.076
48.00	6	Microcrystalline cellulose	48.00
0.75	7	Magnesium stearate	0.75
QS	8	Talc, QS	300.00

Manufacturing Directions

1. Granulation
   a. Weigh and mix for 10 minutes potato starch, lactose, potato starch (cold swelling), and diazepam in a suitable mixer.
   b. Pass the mixture through a FitzMill at highspeed impact forward.
   c. Separately dissolve polysorbate 80 in purified water.
   d. Wet the mixture from step 1b with the solution from step 1c, adding more water if necessary.
   e. Pass the wet mass through a FitzMill sieve #24192, and dry in a drying oven at 35°C for 20 hours.
   f. Pass the dried granulation through a FitzMill.
   g. Separately pass through a FitzMill sieve (0.3-mm screen) the following: microcrystalline cellulose, magnesium stearate, and talc.
   h. Add the granules from step 1f, and mix for 15 minutes.
2. Compression: Compress using round, flat punches with beveled edges and a break line on one side. Theoretical weight of 300 mg (290–310 mg); thickness 3.2 mm (range: 3.1–3.3 mm); diameter 9.5 mm (range 9.3–9.7 mm). For 2-mg and 5-mg tablets, adjust fill weight accordingly; for larger tablet size, adjust proportionally with lactose and starch.

Diclofenac Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Diclofenac sodium	25.00
85.00	2	Lactose, monohydrate	85.00
10.00	3	Sodium starch glycolate (pH 5.5–7.5)	10.00
3.00	4	Povidone (K 29–32)	3.00
3.00	5	Starch (corn)	3.00
58.00 mL	6	Alcohol isopropyl, anhydrous	58.00 mL
5.00	7	Sodium starch glycolate (pH 5.5–7.5)	5.00
1.50	8	Magnesium stearate	1.50

Manufacturing Directions

1. Granulation
   a. Dry mix together diclofenac sodium, lactose, sodium starch glycolate, and starch in a suitable planetary mixer for 10 to 15 minutes.
   b. Dissolve povidone in 44 mL of alcohol and ensure complete solution.
   c. While mixing, add povidone solution to step 1a, and add the remaining alcohol to obtain suitable mass. Add an extra quantity of alcohol, if required.
   d. Pass the wet mass through a #4 mesh (4.8-mm aperture) screen, and spread on paper-lined oven trays.
   e. Dry the granules at 40°C to an LOD of not more than 2% (3 hours at 60°C under vacuum).
   f. Request samples.
   Note: The balance of manufacturing in the "Granulation" process should be done at not more than 45% relative humidity and at a temperature not exceeding 26.5°C.
   g. Mill the dried granule through a FitzMill fitted with a 1.19-mm aperture screen at slow speed and with knives forward.
   h. Store the material in clean, polyethylene-lined containers that are sealed.
2. Lubrication
   a. Charge one-half of the screened granule from step 1h into a suitable blender. Add sodium starch glycolate and magnesium stearate to the blender, and then add the balance of screened granule from step 1h. Blend for 15 to 20 minutes.
   b. Store in clean, tared polyethylene-lined containers, and seal and weigh for yield.
3. Compression
   a. Compress on a suitable tablet machine equipped with a dedusting unit, using 1/4-in.-diameter concave punches with both sides plain.
   b. The theoretical weight of 10 tablets is 1.325 g (range 1.295–1.355 g), with a thickness of 3.7 to 4.1 mm.
4. Coating: Use a subcoat, an enteric color coat, and a finishing coat. (See Appendix.)

Diclofenac Sodium Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Diclofenac sodium	50.00
85.00	2	Lactose, monohydrate	85.00
15.00	3	Sodium starch glycolate (pH 5.5–7.5)	15.00
5.00	4	Povidone (K 29–32)	5.00
4.00	5	Starch (corn)	5.00
0.073 mL	6	Alcohol isopropyl, anhydrous refined	73.00 mL
7.00	7	Sodium starch glycolate (pH 5.5–7.5)	7.00
2.00	8	Magnesium stearate impalpable powder	2.00

Manufacturing Directions

Follow the manufacturing directions in the previous formulation. The theoretical weight of 10 tablets is 1.68 g (range: 1.64–1.72), with a thickness of 4.60 to 5.0 mm. Apply an enteric coat. (See Appendix.)

Diclofenac Sodium Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Diclofenac sodium	100.00
15.00	2	Eudragit® RSPN, 5% (methyl methacrylate copolymer)	15.00
6.00	3	Dibutyl phthalate (2%)	6.00
176.00	4	Dicalcium phosphate dihydrate	176.00
3.00	5	Magnesium stearate	3.00
–	6	Isopropyl alcohol	QS

Manufacturing Directions

1. Charge items 1, 2, and 4 in a planetary blender, and mix for 10 minutes.
2. In a separate container, add items 3 and 6 until homogenous. Add to step 1 slowly to form loose aggregates of blend.
3. Pass the aggregates through a #8 mesh sieve onto paper-lined trays.
4. Dry the granules in a room with low humidity.
5. Pass the dried granules through a #20-mesh screen into a blending vessel.
6. Add item 5 after passing through a 250-μm sieve to step 5, and blend for 2 minutes.
7. Compress into 300-mg tablets, using a suitable punch.
8. Coat using an enteric coating. (See Appendix.)

Diclofenac Sodium Dispersable Tablets (50 mg)

Formulation: Diclofenac Na, 50.0 mg; Avicel® PH 102, 143.8 mg; Kollidon® CL, 50.0 mg; Aerosil® 200, 5.0 mg; Magnesium stearate, 1.0 mg.

Manufacturing Directions

Mix the ingredients together, pass through a 0.8-mm sieve, and compress into tablets with a force of about 10 kN at 248 mg.

Diclofenac Sodium Tablets (25 mg) Voltaren, Cataflam

Diclofenac potassium is available as Cataflam® immediate-release tablets of 50 mg for oral administration. Cataflam inactive ingredients include calcium phosphate, colloidal silicon dioxide, iron oxides, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, sodium starch glycolate, starch, sucrose, talc, and titanium dioxide.

Diclofenac sodium is available as Voltaren delayed-release (enteric-coated) tablets of 25, 50, and 75 mg for oral administration, as well as Voltaren-XR extended-release tablets of 100 mg. Voltaren inactive ingredients are hydroxypropyl methylcellulose, iron oxide, lactose, magnesium stearate, methacrylic acid copolymer, microcrystalline cellulose, polyethylene glycol, povidone, propylene glycol, sodium hydroxide, sodium starch glycolate, talc, titanium dioxide, D&C Yellow No. 10 Aluminum Lake (25-mg tablet only), and FD&C Blue No. 1 Aluminum Lake (50-mg tablet only). Voltaren-XR inactive ingredients are cetyl alcohol, hydroxypropyl methylcellulose, iron oxide, magnesium stearate, polyethylene glycol, polysorbate, povidone, silicon dioxide, sucrose, talc, and titanium dioxide.

Diclofenac Sustained-Release Tablets (100 mg)

Formulation: Diclofenac sodium (Ivotec), 100.0 g; Kollidon SR, 100.0 g; silicon dioxide, colloidal, 3.4 g; magnesium stearate, 3.4 g.

Manufacturing Directions

All ingredients are passed through a 0.8-mm sieve, blended for 10 minutes in a Turbula mixer, and then compressed with medium-compression force at 206.40 mg.

Diclofenac Tablets (50 mg)

Formulation: Diclofenac sodium, 50.0 g; Ludipress, 150.0 g; magnesium stearate, 1.5 g; polyethylene glycol 6000, powder, 15.0 g; Kollidon CL, 10.0 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve and press with low-compression force at 226 mg.

Didanosine Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Didanosine	50.00
17.00	2	Microcrystalline cellulose	17.00
2.10	3	Sodium starch glycolate	2.10
0.60	3	Magnesium stearate (for compaction)	0.60
0.40	4	Magnesium stearate (for tabletting)	0.30

Manufacturing Directions

1. Sift items 1 to 4 through a 250-μm mesh, mix well, and dry compress.
2. Pass granules through a large mesh and blend with item 4. Finally, compress into 70-mg tablets, using 8-mm punches.
3. Coat using Eudragit L-30D-55 coating solution. (See Appendix.)

Diethylcarbamazine Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Diethylcarbamazine citrate	102.00
100.00	2	Dicalcium phosphate	100.00
3.50	3	Gelatin	3.50
130.00	4	Lactose monohydrate	130.00
35.00	5	Starch (maize)	35.00
10.00	6	Talc	10.00
3.50	7	Magnesium stearate	3.50
–	8	Water, purified	QS

Manufacturing Directions

1. Sift items 1, 2, and 4 through a 500-μm sieve, and charge them in a suitable blender. Blend for 5 minutes.
2. In a separate vessel, charge items 3 and 5; add sufficient hot item 8 to dissolve and disperse into a smooth slurry.
3. Add step 2 into step 1, make a suitable wet mass, and pass through a 2.38-mm sieve onto paper-lined trays. Dry overnight at 60°C to an LOD of not more than 2.5%.
4. Pass the dried granules through a #16-mesh sieve into a blending vessel.
5. Sift items 6 and 7 through a 250-μm sieve, add to step 4, and blend for 1 minute.
6. Compress into 350-mg tablets, using 9.7-mm punches.

Difenoxin and Atropine Tablets (0.5 mg/0.025 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	Difenoxin hydrochloride	0.50
0.025	2	Atropine sulfate	0.025
88.00	3	Lactose monohydrate	88.00
23.00	4	Starch (corn)	23.00
2.50	5	Starch (corn)	2.50
5.00	6	Talc	5.00
1.00	7	Magnesium stearate	1.00
–	8	Water, purified	QS

Manufacturing Directions

1. Blending
   a. Prepare a blend of lactose, starch (item 4), and talc.
   b. Blend difenoxin hydrochloride and atropine sulfate with a small quantity of blend from step 1a.
   c. Blend this premix with the remainder of step 1. Pass through a #40-mesh (420-μm aperture or similar) screen.
   d. Slurry the starch (item 5) in 5 mL of cold purified water. Add the slurry to 20 mL of boiling purified water.
   e. Mass blend with starch paste from step 1d, adding more hot purified water, if necessary.
   f. Pass the mass through a #8 mesh (2.38-mm aperture or similar) screen.
   g. Dry the granules at 35°C (95°F) until the LOD is not greater than 5%.
   h. Screen the dried granules through a #20-mesh (840-μm aperture or similar) screen and lubricate with magnesium stearate.
2. Compression: Compress on a rotary tablet machine using 6.35-mm circular punches.

Digoxin Tablets (0.125 mg/0.25 mg), Lanoxin

Lanoxin is supplied as 125-mcg (0.125-mg) or 250-mcg (0.25-mg) tablets for oral administration. Each tablet contains the labeled amount of digoxin and the following inactive ingredients: corn and potato starches, lactose, and magnesium stearate. In addition, the dyes used in the 125-mcg (0.125-mg) tablets are D&C Yellow No. 10 and FD&C Yellow No. 6.

Digoxin Tablets

Manufacturing Directions

1. 12.5 g digoxin and 50.5 g polyvinyl pyrrolidone (MGW: 25000) in 1500 g of an isopropanol–water mixture (7+3) are added to the pot of a planetary agitator of a volume of 20 L.
2. 437 g of amorphous, porous silica is added in portions to this solution while stirring with a blade agitator.
3. After silica has combined with the liquid phase and the batch has taken on a gel type, completely lump-free structure, 4500 g of lactose is added in portions and the batch is mixed vigorously.
4. The pasty mass is then spread evenly on drying trays and dried for 3 hours at 80°C. Thereafter the dry material is passed through a 0.75-mm screen, provided with an addition of 15 wt.% of pelletizing aids, and compacted to tablets in the usual manner.

Dihydroxyaluminum Sodium Carbonate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
31.00	1	Dihydroxyaluminum sodium carbonate (Giulini A 265)	31.00
61.50	2	Sugar	61.50
2.00	3	Magnesium stearate	2.00
15.00	4	Starch	15.00
QS	5	Flavor, sweetener	0.50

Manufacturing Directions

Blend to mix and compress into 110-mg tablets, using 6-mm punch.

Diltiazem Hydrochloride Tablets (60 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Diltiazem hydrochloride	60.00
100.00	2	Lactose monohydrates	100.00
66.00	3	Oil castor hydrogenated (Cutina HR)	66.00
20.00	4	Polyethylene glycol 8000, milled	20.00
0.06 mL	5	Alcohol isopropyl anhydrous	60.00 mL
4.00	6	Magnesium stearate	4.00

Manufacturing Directions

1. Mill castor oil hydrogenated through a #120-mesh (125-μm aperture) screen at medium speed with knives forward.
2. Charge milled castor oil hydrogenated from step 1, lactose (item 2), and diltiazem hydrochloride into a suitable planetary mixer and dry blend for 10 to 15 minutes.
3. Dissolve the polyethylene glycol in the isopropyl alcohol (warm to 40–45°C, if necessary).
4. Gradually add the warm solution from above step 3 to powder blend, and mix until a suitable mass is obtained.
5. Pass the mass through a #4 mesh (4.8-mm aperture) screen, and spread on paper-lined oven trays.
6. Dry the granules at 45°C to 50°C to an LOD of not more than 1% (at 60°C under vacuum for 3 hours). Allow to cool.
7. Mill the dried granule through a #16-mesh (1.19-mm aperture) screen, with knives forward at medium speed. As an alternative, pass the dried granule through a 1.19-mm aperture screen fitted to an oscillating granulator.
8. Charge the screened granule into a suitable blender, add magnesium stearate, and blend for 5 to 10 minutes.
9. Compress on a suitable rotary machine, using 3/8-in. standard concave punches. The theoretical weight of 10 tablets is 250 mg/tablet, with hardness not less than 4 kPa.

Diltiazem Tablets 60 mg Caradizem

Cardizem direct-compression tablets: Each tablet contains 30, 60, 90, or 120 mg of diltiazem HCl. It also contains D&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake (60 and 120 mg), or FD&C Blue No. 1 Aluminum Lake (30 and 90 mg), hydroxypropyl methylcellulose, lactose, magnesium stearate, methylparaben, microcrystalline cellulose, silicon dioxide, and other ingredients.

Diltiazem Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Diltiazem	60.00
141.00	2	Ludipress	141.00
5.00	3	Polyethylene glycol 6000 powder	5.00
1.00	4	Aerosil 200	1.00
1.00	5	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with low-compression force.
2. Compress into 215-mg tablets, using 8-mm biplanar punches.

Dimenhydrinate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Dimenhydrinate	50.00
245.00	2	Ludipress®	245.00
5.00	3	Magnesium stearate	5.00

Manufacturing Directions

1. Mix all components, sieve, and press with low-compression force.
2. Compress into 300-mg tablets, using 8-mm biplanar punches.

Dimenhydrinate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Dimenhydrinate	50.00
50.00	2	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
125.00	3	Lactose	125.00
2.29	4	Croscarmellose sodium (Ac-Di-Sol, SD-711)	2.29
1.00	5	Fumed silicon dioxide	1.00
0.50	6	Stearic acid	0.50
0.50	7	Magnesium stearate	0.50

Manufacturing Directions

1. Screen items 1, 5, and 6 separately through a 40-mesh sieve.
2. Blend items 1, 2, 4, and 5 in a V-blender for 3 minutes.
3. Add item 3 in the blender, and mix for 17 minutes.
4. Add item 6, and blend for 3 minutes.
5. Add item 7 to the blender, and mix for 5 minutes.
6. Compress using 3/8-in., flat, beveled-edge punches to a hardness of 6 kPa and average tablet weight of 228 mg.

Dimenhydrinate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Dimenhydrinate	100.00
40.00	2	Lactose monohydrate	40.00
40.00	3	Cornstarch	40.00
6.00	4	Kollidon® 90F	6.00
30.00	5	Isopropanol	30.00
14.00	6	Kollidon® CL	14.00
16.00	7	Talc	16.00
2.00	8	Aerosil® 200	2.00
2.00	9	Calcium arachinate	2.00

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with item 5, dry, pass through an 0.8-mm sieve, mix with items 6 to 9, and press with low-compression force.
2. Compress into 210-mg tablets, using 9-mm biconvex punches.

Dimenhydrinate Tablets (50 mg), DC

Formulation: Dimenhydrinate, 50 g; Aerosil 200, 4.0 g; Ludipress, 140 g; Kollidon CL, 2.0 g; magnesium stearate, 1.5 g.

Manufacturing Directions

1. Mix dimenhydrinate with Aerosil 200, add other components, and then sieve.
2. Press with low-compression force at 202 mg.

Diphenhydramine and Psuedoephedrine Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Diphenhydramine Hydrochloride	25.00
60.00	2	Pseudoephedrine Hydrochloride	60.00
415.00	3	Cab-o-sil	415.00
200.00	4	Water	200.00

Manufacturing Directions

1. Diphenhydramine hydrochloride and pseudoephedrine hydrochloride are mixed in the water until thoroughly dissolved.
2. Cab-o-sil M5 (silicon dioxide) is poured into a planetary mixer to which the dissolved drug solution is added and mixed at slow speed.
3. This is continued for 5 minutes until the solution and Cab-o-sil are completely mixed.
4. The entire composition is dried in a forced hot air oven for 7 hours at 50°C.
5. The composition is dried to an LOD of 1.0%.
6. The dried material is then screened through a No. 30 U.S. standard mesh screen and compressed to give average weight of 1.0 g containing 50 mg of diphenhydramine hydrochloride and 120 mg of pseudoephedrine hydrochloride.

Diphenhydramine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Diphenhydramine hydrochloride	25.00
150.00	2	Calcium phosphate (dibasic)	150.00
20.00	3	Starch (StaRX 1500)	20.00
QS	4	Polyvinylpyrrolidone (PVP)	QS
QS	5	Alcohol, USP	QS
75.00	6	Stearic acid (fine powder)	75.00
25.00	7	Cellulose (microcrystalline)	25.00
QS	8	Purified water, USP	QS

Manufacturing Directions

1. In a planetary mixer, charge the diphenhydramine hydrochloride, calcium phosphate dibasic and starch.
2. Mix for 5 to 10 minutes.
3. In a separate mixer, charge polyvinylpyrrolidone, alcohol, and water in a : 1:50:40 ratio.
4. Moisten this mixture with solution from the previous step to granulate.
5. Record the volume used.
6. Pass the wet mass through a #14-mesh screen on dryer trays.
7. Dry the granulation at 120°F to 130°F or use a fluid-bed dryer.
8. Pass the dried granules through a #20-mesh screen.
9. Charge dried granules to twin-shell blender, and add stearic acid (previously passed through #30-mesh screen) and microcrytalline cellulose.
10. Mix for 5 to 7 minutes.
11. Compress into 300-mg tablets, using a rotary press with 5/16-in. standard concave punches.

Diphenoxylate Hydrochloride and Atropine Sulfate Tablets (2.5 mg/0.025 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Diphenoxylate hydrochloride	2.50
0.025	2	Atropine sulfate	0.025
11.40	3	Starch (maize)	11.40
54.00	4	Lactose monohydrate	54.00
2.50	5	Starch (maize)	2.50
0.60	6	Magnesium stearate	0.60
QS	7	Water, purified, ca	11.00

Manufacturing Directions

1. Sieve item 5 and disperse into 2.50 g of cold item 7. Then add the balance of item 7 at 70°C and heat to 80°C until completely gelatinized. Prepare a smooth slurry without lumps.
2. Leave the starch paste to cool to 40°C to 50°C.
3. Sieve item 4 and item 3 through a 250-μm sieve. Load items 1 and 2 into the mixer, and mix the items for 5 minutes at medium speed.
4. Add a starch paste cooled to 40°C to 50°C, and mix for 3 minutes at slow speed until a satisfactory mass is obtained. Add extra item 7 if required.
5. Spread the wet granules onto trays, and dry at 55°C for 12 hours.
6. Pass the dried granules through a 1-mm sieve.
7. Sieve item 6 through a 250-μm sieve, add to granules, and mix for 1 minute.
8. Compress into 71-mg tablets, using 5.5-mm punches.

Divalproate Sodium Tablets (125 mg), Depakote

Depakote tablets are supplied in three dosage strengths containing divalproex sodium equivalent to 125, 250, or 500 mg of valproic acid. The inactive ingredients are cellulosic polymers, diacetylated monoglycerides, povidone, pregelatinized starch (contains cornstarch), silica gel, talc, titanium dioxide, and vanillin. In addition, individual tablets contain the following: *125-mg tablets:* FD&C Blue No. 1 and FD&C Red No. 40; *250-mg tablets:* FD&C Yellow No. 6 and iron oxide; and *500-mg tablets*: D&C Red No. 30, FD&C Blue No. 2, and iron oxide.

Divalproate Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.25	1	Povidone K 29–32	6.25
125.00	2	Valproic acid, use divalproex sodium	134.55
25.00	3	Cornstarch	25.00
6.25	4	Povidone K 29–32	6.25
35.00	5	Silicon dioxide	35.00
QS	6	Alcohol SD 3A 200 proof, ca	38 mL
7.50	7	Silicon dioxide	7.50

Manufacturing Directions

Caution: Avoid inhaling or making skin contact with sodium hydrogen divalproate. Wear dust respirator and eye protection during the processing of granulating, lubricating, and compressing sections.

1. Granulation
   a. Dissolve povidone (item 1) in approximately 33 mL of alcohol.
      Caution: Sodium divalproate melts under excessive shear. Ensure adequate lubrication during the milling step.
   b. Cross-feed sodium hydrogen divalproate, pregelatinized starch, povidone (item 4), and approximately one-half of the silicon dioxide (item 5) through a comminuting mill, fitted with a 686-μm aperture screen at high speed, hammers forward.
      Note: To permit easy milling, it is advantageous to premix sodium hydrogen divalproate with one-third of silicon dioxide (item 5) for 5 minutes in a suitable mixer before passing through the comminuting mill.
   c. Charge the milled materials from step 2 and the remaining silicon dioxide (item 5) into a suitable mixer. Blend for 5 to 10 minutes. Add povidone solution (step 1a) to the contents of the mixer to obtain a suitable mass. The materials do not wet easily, but they overmass rapidly. If necessary, add extra alcohol, up to 15 mL. Another method, if using high-shear mixers is to charge the milled materials from step 2 and the

remaining silicon dioxide into the mixer bowl. Blend at fast mixer/fast chopper conditions for 2 minutes. Add the povidone solution (step 1) over a period of 20 to 30 seconds using fast mixer/fast chopper conditions. Discharge from the mixer at a motor current of 35 to 40 amps. If necessary, add extra alcohol, portion wise, up to 8 mL, allowing for sufficient time between additions to ensure that the motor current does not exceed 40 amps.

d. Pass the wet mass through an oscillating granulator fitted with a 4.0-mm aperture screen and spread on paper-lined oven trays. As an alternative, pass the wet mass through a 9.53-mm aperture screen fitted to a comminuting mill, at slow speed, with knives forward, and spread on paper-lined oven trays. Dry at 49°C to an LOD of not more than 2% (3 hours, 60°C, vacuum).
Note: The balance of manufacturing in the "Granulation" process should be done at not more than 45% relative humidity and at temperatures of not more than 30°C.

e. Pass the dried granule through a 1.18-mm or 1.40-mm aperture screen fitted to an oscillating granulator, or screen the dry granules on a 1.4-mm aperture screen fitted to a suitable sieve shaker. Pass coarse granule through either a 1.18-mm or 1.40-mm aperture screen fitted to an oscillating granulator.

2. Lubrication
Note: The balance of manufacturing in the "Lubrication" stage should be done at not more than 40% relative humidity and at not more than 30°C.
   a. Charge one-half of the screened granule from step 1d into a suitable blender. Add silicon dioxide (item 7) via a 1.7-mm aperture screen to the blender followed by the balance of the screened granule from step 1d.
   b. Blend for 20 minutes, ensuring that no pockets or agglomerations of lubricant silicon dioxide remain.
   c. Discharge into tared polythene-lined drums.
3. Compression: Compress into 215-mg tablets, using 6.24 × 11.90-mm punches. For higher-strength 250- and 500-mg tablets, use proportional amounts and larger-sized punches.
Note: The balance of manufacturing in the "Compression" stage must be done at not more than 40% relative humidity and at not more than 26.5°C.
   a. Coating: Apply a PVP subcoat, an enteric opaque methocel coating, and a finishing coat. (See Appendix for details.)

Divalproex Sodium Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Valproic acid, use divalproex sodium, milled	538.20
80.00	2	Hydroxypropyl methylcellulose (Methocel K 15M), CR	80.00
180.00	3	Methyl cellulose (Methocel K100 L), CR	180.00
121.80	4	Lactose, anhydrous	121.80
50.00	5	Microcrystalline cellulose (Avicel PH 101)	50.00
30.00	6	Colloidal silicon dioxide	30.00

Note: Item 3 can be replaced by item 4. Note that this is a once-daily use formulation.

Manufacturing Directions

1. Pass item 1 through a #40-mesh sieve (0.42-mm nominal mesh opening) and charge in a suitable mixing vessel.
2. Pass items 2 to 5 through a 250-μm mesh, add to step 1, and mix for 20 minutes.
3. Add item 6 to step 2, and blend for an additional 5 minutes.
4. Compress into 1000-mg tablets, using a suitable punch.

Doxazosin Mesylate Tablets (1 mg/2 mg/4 mg/8 mg)

Doxazosin mesylate is available as colored tablets for oral use and contains 1 mg (white), 2 mg (yellow), 4 mg (orange), and 8 mg (green) of doxazosin as the free base. The inactive ingredients for all tablets are microcrystalline cellulose, lactose, sodium starch glycolate, magnesium stearate, and sodium lauryl sulfate. The 2-mg tablet contains FD&C Yellow No. 10 and FD&C Yellow No. 6; the 4-mg tablet contains FD&C Yellow No. 6; the 8-mg tablet contains FD&C Blue No. 10 and FD&C Yellow No. 10.

Doxycycline Hydrochloride Tablets (100 mg)

Inert ingredients for the tablet formulation are ethylcellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, talc, titanium dioxide, and FD&C Yellow No. 6 Lake. Inert ingredients for the coated pellets are lactose, NF; microcrystalline cellulose, NF; and povidone, USP. Each shell and band contains FD&C Blue No. 1; FD&C Yellow No. 6, D&C Yellow No. 10; gelatin, NF; silicon dioxide; sodium laurel sulfate, NF; and titanium dioxide, USP.

Doxycycline Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Doxycycline hydrochloride	100.00
40.00	2	Microcrystalline cellulose PH102	40.00
3.00	3	Aerosil 200	3.00
13.00	4	Sodium starch glycolate	13.00
1.75	5	Magnesium stearate	1.75
2.00	6	Talc	2.00

Manufacturing Directions

1. Charge items 1 to 6 in a suitable blender after passing them through a #60 sieve.
2. Mix the items for 10 minutes.
3. Compress into 160-mg tablets, using 12 × 5-mm punches.
4. Coat using HPMC coating. (See Appendix.)

Doxycycline Monohydrate Tablets

Manufacturing Directions

1. Doxycycline monohydrate (105.8 g) and microcrystalline cellulose (45 g) are mixed for 15 minutes in a planetary mixer.
2. The mixture is then granulated with 60 mL of water. After 10 minutes of kneading, the obtained wet mass is passed through a 2-mm sieve and the wet granulation dried at about 40°C until its water content is below 2% by weight.
3. The granulate is then passed through a 0.71-mm sieve and is mixed for 20 minutes with low-substituted hydroxypropylcellulose LHll (18 g), hydroxypropyl methylcellulose 5 cps viscosity(4 g), saccharin (10 g), colloidal silica (0.6 g), and enough lactose to bring the total weight of the mixture to 248 g. Then magnesium stearate (2 g) is added and the mixing is continued for an additional 2 minutes.
4. The resulting mixture is compressed into tablets, each of about 250 mg, about 9-mm diameter and hardness of 70 to 100 N, or into tablets, each of about 125 mg having a hardness of 60 to 90 N. The tablets disintegrate completely in water at room temperature within 30 to 45 seconds.

Efavirenz Tablets

Manufacturing Directions

1. Core tablet: Efavirenz, 950 g; microcrystalline cellulose NF, 380 g; hydroxypropyl cellulose LF NF, 60.8 g; croscarmellose sodium, 95 g; sodium lauryl sulfate, 19 g; lactose hydrous spray dried, 19.8% w/w; magnesium stearate, 1% w/w; water, 1.045 L.
2. Film coating material per tablet: 3.3% by wt of tablet hydroxypropyl cellulose LF NF 8.54 mg (2.5%), hydroxypropyl methylcellulose USP 6CPS 8.54 mg (2.5%), titanium dioxide USP 3.42 mg (1%), and water (94%).
3. Efavirenz (950 g) is blended with microcrystalline cellulose (380 g), sodium lauryl sulfate (19 g), hydroxypropyl cellulose (60.8 g), and croscarmellose sodium (95 g) in a Fielder 10 L high-shear granulator mixer for 4 minutes.
4. At least about 1.1 wt% water per weight of efavirenz (1.045 L) is added to wet granulate the blended mixture over about 6 minutes to about 8 minutes to agglomerate the mixture using an appropriate spray nozzle.
5. The granulated mixture is dried to a moisture content of about 2% to about 5% in a Glatt WST-15 fluid-bed dryer .
6. The dried mixture is milled using a 40 G round screen in a Comil. The milled mixture is blended in a V-blender with lactose for 4 minutes (calculated amount is the amount needed to make the final composition contain 19.8% lactose by weight).
7. The blended mixture is lubricated with magnesium stearate (calculated amount is the amount needed to make the final composition contain 1% magnesium stearate by weight) in the V-blender for 3 minutes.
8. The lubricated mixture is compressed.
9. The compressed tablets are film coated with an aqueous coating suspension that contains 2.5% hydroxypropyl cellulose (HPC); 2.5% hydroxymethylcellulose (HPMC); and 1% titanium dioxide and 94% water by weight percent in a pan coater to a coat weight of about 3.3% per tablet. Note that the coat is the dried form of the suspension.

Eletriptan-Coated Fast-Crumbling Granule Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
98.50	1	Eletpritan (salt)	98.50
4.90	2	AGG sodium croscarmellose	4.90
20.40	3	Ethylcellulose	20.40
4.00	4	Polyoxyethylene glycol 6000	4.00
3.70	5	AGM Sodium croscarmellose precipitated	3.70
1.40	6	Precipitated silica	1.40
3.90	7	Aspartame	3.90
3.50	8	AcDiSol	3.50

Manufacturing Directions

1. A granulation solution is first prepared by dissolving 48 g of ethylcellulose in 273 g of ethyl alcohol.
2. A coating suspension is then prepared by mixing 97 g of ethylcellulose, 28.5 g of polyethylene glycol 6000, 26 g of sodium croscarmellose, 10 g of precipitated silica, and 27.5 g of aspartame in 1900 g of ethyl alcohol, until a homogeneous suspension is obtained.
3. The powder mixture consisting of 700 g of eletriptan and 35 g of Acdisol is then fluidized.
4. Granulation process is then started by spraying the granulation solution for about 15 to 20 minutes at a spraying rate of 25 g/min and a suspension atomization pressure of 0.8 bar.
5. The actual coating is then performed, by spraying the coating suspension for about 1.5 hours at a spraying rate of about 15 to 20 g/min and a suspension spraying pressure of 1.5 bar.
6. The coated granules thus obtained are then formulated as fast-crumbling multiparticulate tablets, the composition of which is as follows:
   a. Coated granules Eletriptan, 136.8 mg (salt) (equivalent to 80 g of base active principle); Mannitol, 575.20 mg; sodium croscarmellose, 24 mg; aspartame 30 mg; mint liquorice, 10 mg; magnesium stearate, 8 mg.
   b. The tablets are manufactured by screening all the excipients, followed by homogenization of the granules coated with the mixture of excipients in a plowshare granulator. The granules obtained are then distributed and shaped on a rotary tabletting machine. The hardness of the tablets obtained is about 30 N.

Enalapril Maleate Tablets (2.5 mg/5 mg/10 mg/20 mg) Vasotec

Enalapril maleate is supplied as 2.5-, 5-, 10-, and 20-mg tablets for oral administration. In addition to the active ingredient enalapril maleate, each tablet contains the following inactive ingredients: lactose, magnesium stearate, starch, and other ingredients. The 2.5-, 10-, and 20-mg tablets also contain iron oxides.

Enalapril Maleate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Enalapril maleate	20.00
10.00	2	Sodium carbonate powder	10.00
146.72	3	Lactose hydrous powder	146.72
22.00	4	Starch (corn)	22.00
1.10	5	Magnesium stearate	1.10
0.050	6	Iron oxide red	0.050
0.130	7	Iron oxide yellow	0.130

Manufacturing Directions

Note: Use goggles, and wear dust protection. Also, process under low-humidity conditions.

1. Granulation: Mix the ingredients with the excipients in a planetary mixer. Pass through a FitzMill equipped with a stainless steel screen, and remix in the planetary mixer. Wet the granulate with starch paste. Pass the wet mass through FitzMill. Dry the granules in hot air, and pass the dried granules through a FitzMill. Collect in polyethylene-lined containers.
2. Lubrication: Transfer the dried, milled granules into the planetary mixer, and magnesium stearate, and mix. Collect in polyethylene-lined drums.
3. Compression: Compress into 200-mg tablets, using round punches.

Enalapril Maleate Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Enalapril maleate	20.00
5.00	2	Sodium carbonate powder	5.00
160.50	3	Lactose hydrous powder	160.50
22.00	4	Starch (corn)	22.00
1.10	5	Magnesium stearate	1.10
0.050	6	Iron oxide red	0.050

Manufacturing Directions

Follow the instructions listed for the 20-mg strength.

Enoxacin Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Enoxacin, use enoxacin sesquihydrate	434.00
80.00	2	Calcium carboxymethyl cellulose	80.00
6.00	3	Hydroxypropylmethyl cellulose	6.00
60.00	4	Cellulose microcrystalline (Avicel PH 101)	60.00
6.00	5	Silicon dioxide colloidal	6.00
14.00	6	Magnesium stearate	14.00
QS	7	Water, purified, ca	200 mL

Manufacturing Directions

1. Granulation
   a. If necessary, mill the enoxacin using a comminuting mill fitted with a 3-mm screen or sift through a 425-μm (40-mesh) screen.
   b. Load the Enoxacin and calcium carboxymethylcellulose into a suitable mixer, and blend for 10 minutes.
   c. Dissolve the hydroxypropyl cellulose in 200 mL of hot (80°C) water and allow to cool to below 40°C.
   d. Add the solution from step 3 to the powder blend from step 2. Mix to produce a satisfactory mass. If necessary, add more purified water.
   e. If necessary, pass the wet mass through a 4-mm screen, and load onto paper-lined trays.
   f. Dry at 55°C to give an LOD of 6.5% to 7.5% (140°C, 2 hours).
   g. Pass the dried granulation through a 1.00- mm screen using a suitable granulator, adding Avicel, silicon dioxide, colloidal, and magnesium stearate, simultaneously.
   h. Blend for 5 minutes in a suitable mixer.
2. Compression: Compress using 16.00 × 8.00 mm ovaloid punches.
3. Coating: Coat using aqueous Methocel* coating. (See Appendix.)

Entacapone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Entacapone	200.00
50.00	2	Microcrystalline Cellulose	50.00
400.00	3	Mannitol	400.00
10.00	4	Magnesium stearate	10.00

Eplerenone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Eplerenone	50.00
71.40	2	Lactose monohydrate	71.40
26.14	3	Microcrystalline cellulose intra granular PH101	26.14
18.00	4	Microcrystalline cellulose extragranular	18.00
5.10	5	Hydroxypropylmethyl cellulose 2910	5.10
8.50	6	Croscarmellose sodium (Acdisol)	8.50
1.70	7	Sodium lauryl sulfate	1.70
1.70	8	Talc	1.70
0.85	9	Magnesium stearate	0.85

Manufacturing Directions

1. Mix and granulate by wet method and compress into 50 mg dose immediate-release tablet (tablet diameter of 9/32 in.') or 25 mg dose immediate-release tablet (tablet diameter of 7/32 in.') using appropriate fill weight.
2. Coat tablets using Opadry White YS-1–18027A at 3% or alternately Opadry Yellow YS-1–12524-A at 4% gain.

Ergotamine Tartrate Fast-Melt Tablets

1. Ergotamine tartrate, 10%; sodium bicarbonate, 27%; citric acid anhydrous, 22%; Avicel PH113, 15%; xylitol, 15%; L-HPC LH-11, 5%; Fujicalin SG, 4%; Crodesta F160, 2%.
2. Dry the above ingredients to significantly reduce the moisture content of each material.
3. Blend for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix EGT-EGF (20–80 mesh), 55%; microcrystalline cellulose, 26%; Mannitol 10%; AcDiSol, 2.5%; L-HPC LH-11, 2.5%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; fumed silicon dioxide, 0.1%.
5. Pass the above granules through a #20 screen and then blend for 5 minutes prior to compression.
6. Ergotamine tartrate tablets are then compressed to a hardness of approximately 1 to 5 kPa and tablets disintegrate in water in approximately 15 to 35 seconds.

Erythromycin and Sulfamethoxazole Tablets

Manufacturing Directions

1. 500 g of sulfamethoxazole and 10 g of a starch derivative are charged into a mass mixer. 10 grams of cornstarch are added along with sufficient water to make a starch paste. This starch paste is used to make a standard granulation tableting, which is dried and sized.
2. Separately, 275 g of erythromycin and 10 g of conventional cellulosic binder are charged into a mass mixer. A solution of 10 g povidone in water is added, and the mixture is granulated. The granulation is dried and sized in similar fashion to the sulfamethoxazole granulation, to yield particles of 10 to 40 mesh. Oversize and undersize particles are recycled.
3. Separately, 80 g of a cellulose phthalate enteric coating polymer, and 8 g of an alkyl citrate plasticizer are dispersed in a sufficient quantity of acetone and ethanol to make a solution. 0.3 g of blue dye lake are added, and the dispersion is stirred to mix.
4. The erythromycin granulation is coated with this solution in a particle coater and the resulting coated particles are sized.
5. Separately, a portion of the sulfamethoxazole granulation is charged into a blender. The dried erythromycin-coated particles sized to 10 to 40 mesh are added, as well as 200 g of microcrystalline cellulose, NF and 4 g of conventional lubricants and glidants. The remainder of the sulfamethoxazole granulation is added and the mixture is blended. This blended material is compressed in a conventional tablet press at applied force of 1500 to 6000 lbs/in.^{2}, into tablets having a weight per 10 tablets of approximately 12 g.

Erythromycin Ethylsuccinate Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Erythromycin, use erythromycin ethylsuccinate, citrate, washed[a]	470.58
200.00	2	Sucrose	200.00
200.00	3	Sodium citrate	200.00
50.00	4	Starch (maize)	50.00
2.50	5	Dye (optional)	2.50
—	6	Water, purified, ca	90.00
40.00	7	Polarcillin potassium (Amberlite IRP-88)	40.00
6.00	8	Magnesium stearate	6.00

[a]Adjust for potency; taken as 850 mcg/g for the amount given.

Manufacturing Directions

Caution: Protect face and hands; relative humidity in the working area should not exceed 50%.

1. Granulation
   a. Pass the following items through a 0.5-mm aperture stainless steel screen: erythromycin ethylsuccinate, sucrose, sodium citrate, starch (maize), and dye (if used). Transfer the screened items to a suitable planetary mixer, and mix for 10 minutes.
   b. While mixing, add purified water to the powders from step 1 until a suitable mass is formed. If necessary, add more purified water to complete the granulation.
   c. Pass the wet mass from step 1b through a suitable granulator fitted with a 2.0-mm aperture stainless steel screen. Collect the granules on paper-lined trays.
   d. Dry the granules in an oven at 50°C until the LOD content is in the range of 1% to 1.5%.
   e. Pass the dried granules through a suitable granulator fitted with a 1.0-mm aperture screen. Collect the granules, and store in securely closed, double polyethylene-lined drums.
2. Lubrication
   a. Place into a suitable blender the dried, screened granules from step 1e.
   b. Pass the amberlite and magnesium stearate through a 0.5-mm aperture stainless steel screen. Add the screened powders to the blender.
   c. Blend for 10 minutes.
   d. Discharge the blended granules into double polyethylene-lined drums. Close securely, and store until ready for compression.
3. Compression: Compress using 9 × 19 mm ovaloid punches. Compress 967 mg. If using dye, compress 969 mg per tablet.
4. Coating: Apply Methocel*, opaque methocel, and Celar glass Methocel* coatings. (See Appendix.)

Erythromycin Particle-Coated Tablets (150 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Cellulose microcrystalline (Avicel PH 101)	150.00
12.00	2	Sodium starch glycolate	12.00
12.00	3	Hydroxypropyl cellulose	12.00
150.00	4	Lactose monohydrate powder	150.00
QS	5	Alcohol SD 3A 200 proof, ca	200 mL
333.00	6	Erythromycin, use erythromycin particle coated*	530.25
1.25	7	Stearic acid	1.25
1.25	8	Wax hydrogenated vegetable (Sterotex K)	1.25
1.25	9	Magnesium stearate powder	1.25
1.25	10	Silicon dioxide	1.25

Note: Adjust weight of erythromycin-coated particles to allow for variable potency: (333 × 1000)/potency = G required for 1000 tablets. Adjust the weight of cellulose and microcrystalline NF (7) to compensate for variable potency of erythromycin. The amount required is 770.75; the factor weight of item 6 is G, required for 1000 tablets.

Manufacturing Directions

Caution: Protect face and hands from erythromycin because some individuals may be sensitive and reactions may occur. Take a shower after excessive exposure during manufacture.

1. Granulating
   a. Charge cellulose microcrystalline (item 1), sodium starch glycolate, hydroxypropyl cellulose, and lactose into a suitable mixer. Mix for approximately 20 minutes.
   b. Granulate by adding approximately 200 mL of alcohol while mixing.
   c. Pass wet granulation through a 5/8-in. band in rotary granulator or a similar granulator.
   d. Spread on paper-lined trays, and dry at 49°C until reaching an LOD of not more than 2% (60°C, 3 hours vacuum).
   e. Pass dried granulation through 1.2-mm aperture screen. Mill oversize material through a 1.2-mm screen, knives forward, medium speed using a FitzMill.
   f. Charge into polyethylene-lined drums.
2. Lubricating
   a. Charge ingredients from step 1f into the blender.
   b. Add erythromycin-coated particles.
   c. Mix and mill approximately 12.5 g of cellulose microcrystalline (item 7), stearic acid, hydrogenated vegetable oil wax, magnesium stearate, and colloidal silicon dioxide through 595-μm aperture screen, knives forward, at high speed, using a FitzMill into a blender.
   d. Charge the balance of the cellulose microcrystalline (item 7) into the blender, and blend for 10 minutes.
   e. Discharge into polyethylene-lined drums.
3. Compression
   a. Compress the product using ovaloid 8.6 × 18.9-mm punches.
   b. Do not grind tablets or rework culls. Use a compressing machine with a force feeder.
   c. The weight of 10 tablets is 11 g, the thickness is 7.7 to 8.6 mm, and the hardness is 18 to 25 kPa.
4. Coating: Use the HPMC clear coating solution. (See Appendix.)

Erythromycin Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Erythromycin, use erythromycin stearate (600 mcg/mg[a])	166.667
91.18	2	Sodium citrate dihydrate powder	91.180
3.287	3	Povidone K 29–32	3.287
11.51	4	Sodium carboxymethylcellulose, high viscosity	11.518
–	5	Alcohol denatured 200 proof	50.800 mL
8.68	6	Pollarcillin potassium (Amberlite IRP-88)	8.684

[a]Adjust for potency.

Manufacturing Directions

See below.

Erythromycin Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Erythromycin, use erythromycin stearate (600 mcg/mg[a])	166.66
100.00	2	Sodium citrate dihydrate powder	100.00
12.80	3	Povidone K 29—32	12.80
14.20	4	Sodium carboxymethylcellulose, high viscosity	14.20
—	5	Alcohol denatured 200 proof	50.80 mL

[a]Adjust for potency.

Manufacturing Directions

1. Granulation
   a. Sift the sodium citrate through a 600-μm aperture or similar screen.
   b. Charge erythromycin stearate, sodium citrate, povidone, starch, and sodium carboxymethylcellulose in a mixer, and mix for 15 minutes.
   c. Gradually add sufficient alcohol, while mixing, to produce a suitable mass.
   d. Dry the granulation at 49°C to less than 1.5% LOD or 7% moisture by Karl Fisher.
   e. Sift the dried granulation through a 1.19-mm aperture screen, or similar, and mill the oversized material through a #2 (1.59-mm aperture, or similar) band on the Hammer mill (FitzMill), or similar, at medium speed, knives forward, for 0 to 30 minutes.
   f. Load the granulation into the blender, add Amberlite IRP-88, if used, and blend for 20 to 30 minutes.
   g. Unload the contents of the blender into polyethylene-lined drums, and deliver to the compressing area.
2. Compression: Compress using 9.5-mm standard concave punches. Fill to appropriate amount.

Erythromycin Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Erythromycin, use erythromycin stearate (630 mcg/mg[a])	794.00
146.00	2	Starch (corn)	146.00
16.00	3	Povidone K 29–32	16.00
104.00	4	Magnesium hydroxide	104.00
—	5	Alcohol SD 3A 200 proof	210–250 mL
26.00	6	Polacrillin potassium (Amberlite IRP-88)	26.00

Note: During the drying step of granulation, starch has a water loss equivalent to approximately 6.2% of its weight. This enables a theoretical reduction in tablet weight of 9 mg. This may, however, be offset by a loss of active ingredient during the manufacturing process.
[a]Do not use erythromycin stearate with a potency less than 610 mcg/mg. Calculate the actual quantity of erythromycin stearate. Do not factor in any ingredient to compensate for erythromycin stearate potency change.

Manufacturing Directions

1. Granulation
   a. Load povidone, cornstarch, magnesium hydroxide, and approximately one-half of erythromycin stearate into a suitable blender, and blend for 10 minutes. Add the balance of the erythromycin stearate, and blend for 15 minutes.
   Note: Proceed to step 1d if only one wet granulation step is necessary.
   b. Empty the blender into tared, polyethylene-lined drums, and weigh for yield.
   c. Divide the blended powder into equal portions for massing. (The size of a massing "part" is predetermined from considering the capacity of the massing equipment.)
   d. Load preblended materials from step 1b into the mixer.
   e. Wet granulation, conventional method: Add 210 mL of alcohol slowly over a period of 10 minutes and mix for 5 minutes. If necessary, add additional alcohol (20–40 mL), and mix until a satisfactory mass is obtained. Do not overmix. Usually 5 minutes of mixing after the final addition of alcohol is sufficient. Record the total amount of alcohol used. Proceed to dry as in step 1g.
   f. Wet granulation, high-speed mixer method:
      i. Load preblended materials from step 1c into the mixer. Or if preblending is not required, load povidone, cornstarch, magnesium hydroxide, and erythromycin stearate into the high-speed mixer, and mix for 3 minutes with the agitator at slow speed and the granulator at fast speed.
      ii. Add 150 mL of alcohol while mixing with the agitator at a slow speed and the granulator at a fast speed over a period of 2 minutes. Continue to mix for another 4 minutes, adding additional alcohol, if necessary, to obtain a satisfactory granulation.
   g. Spread the wet mass onto paper-lined trays. Commence the drying setup immediately after this step has been completed. Do not air dry.

h. Load trays of granulation into a suitable drying oven, and dry at 50°C to 2% to 3.5% LOD, 3 hours in vacuum oven at 60°C, under 5-mm Hg vacuum. Under no circumstances must the Karl Fischer test method be used. Other LOD tests may be used for process control, provided equivalence can be demonstrated to the quoted vacuum oven method.
i. Alternative fluid-bed drying method: Charge granulate into fluid-bed dryer and dry at 40°C to 45°C.

Note: It is important not to dry the granulation below 2%. This loss is obtained after approximately 4 hours drying for oven loads from 70 to 130 kg, depending upon the amount loaded onto trays and the number of trays.

j. Repeat steps 1d through 1h if there is more than one part of blended powder from step 1b.
k. Allow the dried granule to cool, then screen through an 840-μm aperture screen using an oscillating granulator or through a 1.8-mm aperture screen using a comminuting mill with cutters forward at medium speed. Record the total weight of granulation.
l. Request samples.
m. Proceed to "Blending and Lubrication."

2. Lubrication
   a. If Amberlite is lumpy, screen through a 600- μm aperture screen before preblending.
   b. Preblend Amberlite with a small portion of the granule and the blend with approximately one-half of the bulk granule for 5 minutes.
   c. Add the balance of granule, and blend for a further 10 minutes.
   d. Empty the blender into tared, polyethylene-lined drums. Weigh.
3. Slugging (if required): Use a suitable compressing machine with either 19- or 12-mm flat punches.
   a. Compress the material into slugs having the following specifications: For 19 mm, weight is 1.7 to 1.75 g and hardness is 16 to 17 kPa; for 12 mm, weight is 0.8 to 0.85 g and hardness is 14 to 15 kPa.
   b. The slugs should show no signs of lamination, capping, or surface melting and should break with a distinct snap.
   c. Reduce slugs by passing slowly through a 0.107-in. (2.7-mm) perforated screen using cutters at medium speed.
   d. After reduction, lubricate as above.
4. Compression

   Note: Precompression may be used to meet hardness specifications.
5. Coating: Aqueous methocel. (See Appendix.)

Estazolam Tablets (1 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Estazolam	1.00
120.65	2	Lactose monohydrate	120.65
8.37	3	Starch (maize)	8.37
3.78	4	Starch (maize)	3.78
QS	5	Water, purified	19.00 mL
1.20	6	Stearic acid	1.20

Manufacturing Directions

Caution: Use a respirator and gloves throughout; shower after exposure.

1. Granulation
   a. Mix starch (item 5) together with approximately 10 mL water in a glass or stainless steel vessel; avoid formation of lumps.
   b. Boil the remaining 18 mL of water, and add it to the mix from step 1a, with continuous stirring until a gel is formed. Further heat may be necessary. A mix temperature of 95°C must be achieved before a gel is formed.
   c. Pass estazolam through a 0.7-mm aperture stainless steel screen.
   d. Pass through a 1.19-mm aperture stainless steel screen lactose, starch (item 3), and hydroxypropylcellulose into a suitable planetary mixer. Add screened estazolam, and mix for 10 minutes.
   e. Add the starch gel from step 1b, and mix for 20 minutes or until a suitable mass is formed.
   f. Pass the wet mass through an oscillating granulator or similar, fitted with a 2.38-mm aperture stainless steel screen. Collect granules on paper-lined trays.
   g. Dry in an oven at 50°C until the LOD is less than 7%.
   h. Pass the dried granules through an oscillating granulator or a similar granulator, fitted with a 1.4-mm aperture stainless steel screen. Collect in a polyethylene-lined drum and close securely.
2. Lubrication
   a. Place the dried granules into a suitable planetary or ribbon filter.
   b. Pass starch (item 7) and magnesium stearate through a 0.25-mm stainless steel screen and mix. Add this blend to the granules, and mix for 5 minutes. Transfer to polyethylene-lined drums.
3. Compression: Compress in a suitable rotary machine using a 7-mm-diameter beveled edged, with weight of 10 tablets at 1.2 g (1.17–1.23 G) and thickness of 2.35 mm ± 0.12 mm.

Estazolam Tablets (2 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Estazolam	2.00
79.30	2	Lactose	79.30
24.30	3	Starch (maize), dried	27.10
2.40	4	Hydroxypropylcellulose	2.40
5.00	5	Starch (maize)	5.00
QS	6	Water, purified	28.00 mL
5.70	7	Starch (maize)	5.70
0.30	8	Magnesium stearate	0.30

Manufacturing Directions

See the manufacturing directions for 1-mg formulation of estazolam.

Estradiol Tablets (0.5 mg/1 mg/2 mg), Estrace

Estrace tablets for oral administration contain 0.5, 1, or 2 mg of micronized estradiol per tablet. Estrace 0.5-mg tablets contain the following inactive ingredients: acacia, dibasic calcium phosphate, lactose, magnesium stearate, colloidal silicon dioxide, starch (corn), and talc. Estrace 1-mg tablets contain the following inactive ingredients: acacia, D&C Red No. 27 Aluminum Lake, dibasic calcium phosphate, FD&C Blue No. 1 Aluminum Lake, lactose, magnesium stearate, colloidal silicon dioxide, starch (corn), and talc. Estrace 2-mg tablets contain the following inactive ingredients: acacia, dibasic calcium phosphate, FD&C Blue No. 1 Aluminum Lake, FD&C Yellow No. 5 (tartrazine) (Aluminum Lake), lactose, magnesium stearate, colloidal silicon dioxide, starch (corn), and talc.

Estradiol Vaginal Tablets (25.8 mcg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
25.8 mcg	1	Estradiol hemihydrate equivalent to Estradiol 25 mcg	0.0258
101.974	2	Lactose Spray Dried	101.974
15.00	3	Maize starch	15.00
2.00	4	Hypromellose	2.00
1.00	5	Magnesium stearate	1.00
2.60	6	Hypromellose	2.60
0.50	7	Polyethylene glycol 4000	0.50
–	8	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 3, and 4 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 5% (=2.5 g) powder from step 1 to step 3 and mix well.
5. Add 10% (=5 g) powder from step 1 to step 4 and mix well.
6. Add 15% (=7.6 g) powder from step 1 to step 5 and mix well.
7. Transfer step 6 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 5 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 120-mg tablets, using a suitable punch (6 mm, round).
13. Charge item 8 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
14. Add item 7 to step 13 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Check that coating dispersion is clear and lump free.
15. Load core tablets from step 12 in coating pan and apply coating dispersion from step 14 to get 1.5% to 1.8% weight gain.

Estropipate Tablets (0.626 mg/1.25 mg/2.25 mg/5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.626	1	Estropipate, 25% excess	0.769
157.02	2	Lactose monohydrate	157.02
1.00	3	Yellow dye	1.00
0.007	4	Yellow dye	0.007
1.00	5	Dibasic potassium phosphate, anhydrous	1.00
1.20	6	TRIS (tromethamine)	1.20
7.00	7	Hydroxypropyl cellulose	7.00
10.00	8	Sodium starch glycolate	10.00
40.00	9	Cellulose microcrystalline	40.00
QS	10	Water, purified	QS
QS	11	Alcohol SD 3A 200 proof	QS
0.50	12	Colloidal silicon dioxide	0.50
1.25	13	Magnesium stearate	1.25
1.25	14	Wax, hydrogenated vegetable oil (Sterotex K)	1.5

Note: For 1.25-, 2.25-, and 5.0-mg tablets, adjust with item 2 and modify dyes.

Manufacturing Directions

1. Granulation
   a. Charge lactose cellulose microcrystalline, hydroxypropyl cellulose, dyes, or dye into mixer, and blend powders. If necessary, screen or mill powders to break up agglomerates. A portion of the cellulose microcrystalline may be added at the lubrication step.
   b. Dissolve the dibasic potassium phosphate in purified water. Use this solution to granulate powders in step 1a.
   c. Size wet granulation, dry, and pass through screen and mill.
   d. Dissolve tromethamine and estropipate in water or alcohol.
   e. Charge granulation from step 1c and sodium starch glycolate into mixer, and mass with step 1d. Size wet granulation and dry. Pass the dried granulation through screen and mill.
2. Lubrication
   a. Charge the portion of the dried granulation into the blender.
   b. Screen colloidal silicon dioxide, magnesium stearate, and hydrogenated vegetable oil wax, and charge into blender.
   c. Charge remainder of dried granulation into blender and blend.
3. Compression: Compress using a rotary machine using oval tooling. The theoretical weight is 221 mg.

Ethambutol Tablets (400 mg)

Formulation: Ethambutol, 400 g; Sorbitol, crystalline, 200 g; Kollidon VA 64, 20 g; Kollidon CL, 10 g; magnesium stearate, 10 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with medium/high-compression force at 620 mg.

Ethambutol Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Ethambutol hydrochloride	400.000
5.60	2	Silicon dioxide colloidal	5.600
68.00	3	Starch (corn) NF[a]	76.800
33.50	4	Mannitol	33.600
22.40	5	Starch (corn)	22.400
11.20	6	Corn oil hydrogenated	11.200
8.00	7	Magnesium stearate	8.000
11.20	8	Talc powder	11.200
QS	9	Water, purified	80.000

[a]The quantity of starch (corn) is based on a moisture content of 13% w/w. If the moisture content varies outside this range of 12.5% to 13.5%, then the amount used should be factored accordingly.

Manufacturing Directions

1. Massing
   a. Mix starch (item 5) with approximately 27.3 mL of purified water (item 9) in a glass or stainless steel vessel, avoiding the formation of lumps.
   b. Boil the remaining 52.8 mL of purified water (item 9), and add the mix from step 1a with continuous stirring until a gel is formed. Further heat may be necessary.
   Note: A mix temperature greater than 95°C must be exceeded before a gel is formed.
   c. Mill the ethambutol through a 1.59-mm aperture screen at medium speed with knives forward, then charge into a suitable mixer.
   d. Pass silicon dioxide, starch (corn) (item 3), and mannitol through a 1.00-mm aperture stainless steel screen and add to the mixer. Mix at 60 rpm for 10 minutes.
   e. Pass the mixed powders from step 1d through a 1-mm aperture stainless steel screen and return to the mixer.
   f. Add, in one charge, the starch gel from step 1b at 70°C to 80°C, and mix for 5 minutes at 60 rpm.
   g. Stop the mixer and inspect the mass. Add the extra 6.88 mL of purified water (item 10) at 50°C to complete the granulation while mixing. Mix for a further 5 minutes at 60 rpm.
2. Drying/granulation: Proceed to step 2a or 2b.
   a. Oven drying
      i. Pass the wet mass through an A granulator fitted with a 4.76-mm aperture stainless steel screen. Collect the granules on paper-lined trays.
      ii. Dry the granules in a hot-air oven at 50°C, turning over the granules every half hour. After 1 hour of drying, pass the granules through an A granulator fitted with a 2.38-mm aperture stainless steel screen. Collect the granules on paper-lined trays, and return to the hot-air oven at 50°C.
   b. Fluid-bed drying
      i. Pass the wet mass through an A granulator fitted with a 4.76-mm aperture stainless steel screen into the fluid-bed dryer bowl.
      ii. Dry the granules in the fluid-bed dryer at 50°C for 30 minutes, turning over after 15 minutes. Then, pass the granules through a granulator fitted with a 2.38-mm aperture stainless steel screen, and return to the fluid-bed dryer bowl with the air inlet and outlet fully open. Proceed to step 3.
   c. Continue drying the granules while turning them over every 30 minutes until the LOD is between 1.5% and 2%.
   d. Pass the dried granules through an A granulator fitted with a 1-mm aperture stainless steel screen. Collect the granules in a polyethylene-lined drum, and close securely.
   e. Request samples.
3. Lubrication
   a. Place the dried granules from step 2d in a suitable blender.
   b. Add oil castor hydrogenated, magnesium stearate, and talc via a 0.6-mm aperture stainless steel screen, and mix for 25 minutes.
   c. Transfer to a polyethylene-lined drum, and close securely until ready for compression.
4. Compression: Compress on a suitable tablet machine using ovaloid punches that are 15.5 × 7.7 mm or 14.6 × 7.8 mm, where the weight of 10 tablets is 5.6 g, hardness is more than 5 kPa, and the disintegration time is not more than 15 minutes. If using a coating, move to the next step.
5. Coating: Use an HPMC methylene chloride coating. (See Appendix.)

Ethambutol Tablets (800 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
800.00	1	Ethambutol	800.00
200.00	2	Dicalcium phosphate (Di-Tab)	100.00
30.00	3	Kollidon 30	30.00
–	4	Isopropyl alcohol	QS
50.00	5	Kollidon CL	50.00
15.00	6	Magnesium stearate	15.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4. Dry, pass through a 0.8-mm sieve, add items 5 and 6, and press with high-compression force.
2. Compress into 1.112-g tablets, using 20-mm oblong punches.

Etophylline and Theophylline Tablets (100 mg/22 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Etophylline powder (Knoll)	101.00
22.00	2	Theophylline, anhydrous	23.00
53.00	3	Ludipress	53.00
1.00	4	Magnesium stearate	1.00
2.00	5	Aerosil 200	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press into tablets with low-compression force.
2. Compress into 175-mg tablets, using 8-mm biplanar punches. To enhance the flowability of the tabletting mixture, the amount of Aerosil 200 can be increased.

Etophylline and Theophylline Tablets (100 mg/22 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Etophylline powder (Knoll)	100.00
22.00	2	Theophylline, anhydrous	23.00
50.00	3	Starch (maize)	50.00
3.00	4	Kollidon VA 64	3.00
4.00	5	Kollidon VA 64	4.00
–	6	Water, purified, ca	35.00
1.00	7	Magnesium stearate	1.00
5.00	8	Talc	5.00

Manufacturing Directions

1. Granulate a mixture of items 1 to 4 with solution of items 5 and 6. Pass through a 0.8-mm sieve, dry, mix with items 7 and 8, pass through a 0.5-mm sieve, and press with medium-compression force.
2. Compress into 183-mg tablets, using 8-mm biplanar punches.

Ezetimibe and Simvastatin Tablets (10 mg/40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Ezetimibe	10.00
40.00	2	Simvastatin	40.00
94.92	3	Lactose Monohydrate	94.92
40.00	4	Microcrystalline cellulose (Avicel PH102)	40.00
2.00	5	Hydroxylpropylmethyl cellulose	2.00
0.04	6	Butylated hydroxyanisole	0.04
3.00	7	Citric acid monohydrate	3.00
0.04	8	Propyl gallate	0.04
8.00	9	Croscarmellose sodium	8.00
2.00	10	Magnesium stearate	2.00
–	11	Water, purified	20.00
–	12	Ethanol 95%	10.00
4.00	13	Hydroxylpropylmethyl cellulose	4.00
–	14	Water, purified	35.00

Manufacturing Directions

1. Dissolve item 7 in half of item 11 (10 g) in a stainless steel container.
2. Dissolve item 5 in the mixture of remaining half quantity of item 11 and half quantity of item 12 (5 g) and add to step 1 and mix well.
3. Dissolve items 6 and 8 one by one in the remaining half quantity of item 12 in another stainless steel container.
4. Mix step 3 with step 2.
5. Pass items 3, 1, and 2 through 0.5-mm sieve and mix well.
6. Charge step 5 in a granulator.
7. Knead step 6 with solution of step 4 for 5 to 10 minutes until a loose, moist mass is obtained.
8. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
9. Spread step over paper-lined trays, and dry at 45°C to 50°C for 8 hours (the relative humidity over the granules should be 20–35%).
10. Pass the dried granules through a 1.25-mm sieve granulator.
11. Transfer the granules to a tumbler.
12. Pass 9 through 0.5-mm sieve and add to step 11 and mix for 15 minutes.
13. Pass item 10 through 0.250-mm sieve and add to step 12.
14. Mix step 13 for 2 minutes.
15. Compress into 200-mg tablets, using a suitable punch (8.5 mm, round).
16. Charge item 14 in a stainless steel vessel. Add item 13 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
17. Load core tablets from step 15 in coating pan and apply coating dispersion from step 16 to get 1.5% to 1.8% weight gain.

Ezetimibe and Simvastatin Tablets (10 mg/80 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Ezetimibe	10.00
80.00	2	Simvastatin	80.00
127.38	3	Lactose monohydrate	127.38
60.00	4	Microcrystalline cellulose (Avicel PH102)	60.00
3.00	5	Hydroxylpropylmethyl cellulose	3.00
0.06	6	Butylated hydroxyanisole	0.06
4.50	7	Citric acid monohydrate	4.50
0.06	8	Propyl gallate	0.06
12.00	9	Croscarmellose sodium	12.00
3.00	10	Magnesium stearate	3.00
–	11	Water, purified	30.00
–	12	Ethanol 95%	15.00
6.00	13	Hydroxylpropylmethyl cellulose	6.00
–	14	Water, purified	50.00

Manufacturing Directions

1. Dissolve item 7 in half quantity of item 11 (15 g) in a stainless steel container.
2. Dissolve item 5 in the mixture of remaining half quantity of item 11 and half quantity of item 12 (7.5 g) and add to step 1 and mix well.
3. Dissolve items 6 and 8 one by one in the remaining half quantity of item 12 in another stainless steel container.
4. Mix step 3 with step 2.
5. Pass items 3, 1, and 2 through 0.5-mm sieve and mix well.
6. Charge step 5 in a granulator.
7. Knead step 6 with solution of step 4 for 5 to 10 minutes until a loose, moist mass is obtained.
8. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
9. Spread step over paper-lined trays, and dry at 45°C to 50°C for 8 hours (the relative humidity over the granules should be 20–35%).
10. Pass the dried granules through a 1.25-mm sieve granulator.
11. Transfer the granules to a tumbler.
12. Pass item 9 through 0.5-mm sieve and add to step 11 and mix for 15 minutes.
13. Pass item 10 through 0.250-mm sieve and add to step 12.
14. Mix step 13 for 2 minutes.
15. Compress into 300-mg tablets, using a suitable punch (11.0 mm × 8.5 mm, modified oval).
16. Charge item 14 in a stainless steel vessel. Add item 13 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
17. Load core tablets from step 15 in coating pan and apply coating dispersion from step 16 to get 1.5% to 1.8% weight gain.

Ezetimibe Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
10.00	1	Ezetimibe	10.00
62.70	2	Lactose spray dried	62.70
20.00	3	Microcrystalline cellulose (Avicel PH102)	20.00
3.00	4	Povidone K30	3.00
1.00	5	Sodium lauryl sulfate	1.00
2.50	6	Croscarmellose sodium	2.50
0.80	7	Magnesium stearate	0.80

Manufacturing Directions

1. Pass item 2 through 1-mm sieve and collect in a tumbler.
2. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container and mix well for 5 minutes.
3. Transfer step 2 to step 1.
4. Pass item 6 and item 3 through 0.5-mm sieve and add to step 1.
5. Mix step 1 for 20 minutes using tumbler.
6. Pass item 7 through 0.250-mm sieve and add to step 5.
7. Mix step 6 for 2 minutes.
8. Compress into 100-mg tablets, using a suitable punch (5.0 mm × 5.5 mm, oval)

Famciclovir Tablets (125 mg/250 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
125.00	1	Famciclovir	125.00
165.00	2	Microcrystalline cellulose (Avicel) QS	165.00
4.00	3	Sodium starch glycolate (Primojel®)	4.00
0.50	4	Magnesium stearate	0.50

Manufacturing Directions

1. Sift Famciclovir, Avicel, and sodium starch glycolate through a 250-μm sieve into a mixer.
2. Mix for 5 minutes.
3. Sift magnesium stearate through a 250-μm sieve and add to step 1. Blend for 3 minutes.
4. Compress 295 mg in a suitable punch. For 250-mg strength, compress 590 mg.
5. Coat using a hypermellose coating. (See Appendix.)

Famotidine Tablets (20 mg), Pepcid

Each tablet for oral administration contains either 20 or 40 mg of famotidine. The inactive ingredients are hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxides, magnesium stearate, microcrystalline cellulose, starch, talc, and titanium dioxide. Each Pepcid RPD orally disintegrating tablet for oral administration contains either 20 mg or 40 mg of famotidine and the following inactive ingredients: aspartame, mint flavor, gelatin, mannitol, red ferric oxide, and xanthan gum.

Famotidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Famotidine	20.00
80.00	2	Microcrystalline cellulose (Avicel PH 102)	80.00
67.60	3	Pregelatinized starch (Starch 1500)	67.60
2.00	4	Povidone (PVP K-25)	2.00
–	5	Alcohol (ethanol 95%)	36.67
22.80	6	Microcrystalline cellulose (Avicel PH 102)	22.80
8.16	7	Pregelatinized starch (starch 1500)	8.16
2.00	8	Glyceryl behenate	2.00
2.41	9	Talc (fine powder)	2.41

Manufacturing Directions

1. Preparation of binding solution: Dissolve item 4 in item 5 to make a clear solution by using a stirrer at medium speed in a stainless steel container.
2. Dry mixing: Load items 1 to 3 into a mixer. Mix for 5 minutes with a mixer and chopper at low speed.
3. Wet massing
   a. Add the binding solution at a rate of 8.3 g/min to the dry powder in the mixer, while mixing at low speed. Mix and chop for a further 2 to 3 minutes at low speed.
   b. Check for a satisfactory wet mass. Add additional ethanol 95% if required to get a satisfactory wet mass.
4. Drying
   a. Spread the granules onto stainless steel trays to a thickness of one-quarter of the tray thickness. Load the trays on the trolley.
   b. Load the trolleys to the oven. Keep the doors open. Start the air circulation, heaters off, for 2 hours.
   c. Start the heaters of the dryer. Close the doors. Set the temperature at 55°C for 6 hours.
   d. Check the moisture contents of the dried granules (limit: not more than 3.5%). Dry further, if required, to get a moisture content of 3.5%.
5. Grinding: Pass the dried granules through a sifter using a 1250-μm sieve. Pass the retained granules through a granulator equipped with a 1.0-mm sieve.
6. Lubrication
   a. Pass items 6 and 7 through a 500-μm sieve using a sifter. Collect in a stainless steel container.
   b. Load the sized granules from step 5a along with sieved powder from step 6a into the blender. Blend for 3 minutes.
   c. Mix items 8 and 9 in a polythene bag for 1 minute. Pass this mixture through a 250-μm sieve into the sifter. Collect in a polythene bag. Add 3 to 5 g of granules from step 6b to it, and mix manually for 1 minute. Add this mixture to step 6b, and mix for 1 minute.
   d. Unload in stainless steel drums.
7. Compression: Compress the granules using a rotary tabletting machine. The dimension is 7.1 ± 0.1 mm concave plain. The weight of 10 tablets is 2.05 g ± 2%.
8. Tablet coating: Coat the tablet using an HPMC coating. (See Appendix.)

Famotidine Tablets (40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Famotidine	40.00
70.50	2	Microcrystalline cellulose (Avicel PH 102)	70.50
67.60	3	Pregelatinized starch (Starch 1500)	67.60
0.09	4	Ferric oxide (iron oxide red)	0.09
2.50	5	Povidone (PVP K-25)	2.50
—	6	Alcohol (ethanol 95%)	36.67
11.16	7	Microcrystalline cellulose (Avicel PH 102)	11.16
8.66	8	Pregelatinized starch (Starch 1500)	8.66
2.00	9	Glyceryl behenate	2.00
2.41	10	Talc (Fine powder)	2.41

Manufacturing Directions

See the manufacturing directions for the 20-mg formulation.

Fenoprofen Calcium Tablets

Manufacturing Directions

1. Mixture A: A Diosna mixer is charged with 17.5 kg of fenoprofen calcium, 2.64 kg of lactose, 1.75 kg of starch powder, and 656 g of pregelatinized starch through a #10-mesh screen. The mixture is blended for 5 minutes using a low-speed mixer and low-speed chopper settings.
2. While continuing to mix as described above, 4373 mL of a 15% wt/v aqueous povidone solution is added slowly.
3. The mixture is then agitated using a high-speed mixer and high-speed chopper settings for 3 minutes. During this time, purified water is added to the mixture in a quantity sufficient to produce a satisfactory granulation.
4. The granulation is then wet sieved through a #6 screen onto paper-lined trays. The granulation is dried at 110°F for 16 hours. The dried granulation is milled at 1400 rpm with a FitzMill into a clean, polyethylene lined drum yielding 22.32 kg of mixture A. The mill employed a 2AA plate with knives forward.
5. Mixture B: To a Diosna mixer is added 26.25 kg of fenoprofen calcium, 3.965 kg of lactose, 2.625 kg of starch powder, and 984.5 g of pregelatinized starch. The mixture is blended for 5 minutes using a low-speed mixer and low-speed chopper settings. While continuing to mix as described above, 6563 mL of a 15% wt/v aqueous povidone solution containing 495 g of Opaspray Butterscotch L-2701 (Manufactured by Colorcon, Inc.) is added slowly. The mixture is then agitated using a high-speed mixer and high-speed chopper settings for 3 minutes. During this time, purified water is added in a quantity sufficient to produce a satisfactory granulation. The wet granulation is sieved using a #6 screen onto paper-lined trays. The granulation is dried at 110°F for 16 hours.
6. A third mixture, mixture C, is prepared in the same manner as mixture B. After drying, this mixture is combined with mixture B and milled at 1400 rpm with a FitzMill into a clean polyethylene lined drum yielding 68.03 kg of mixture BC. The mill employed a 2AA plate with knives forward.
7. A ribbon mixer is charged with 11.6 kg of mixture A and 35.3 kg of mixture BC. To this mixture is added 1.5 kg of cellulose with sodium carboxymethylcellulose-591 (Avicel RC-591, FMC Corporation) and 120 g of sodium lauryl sulfate through a #30-mesh screen. The mixture is blended for 10 minutes. To the mixture is added 250 g of magnesium stearate and 500 g of stearic acid powder through a #30-mesh screen. Mixing is continued for an additional 5 minutes after which the granulation is discharged into a clean polyethylene lined drum, yielding 49.20 kg of material.
8. This is then compressed on a Manisty Express Tabletting Machine using appropriate tooling.
9. The resulting tablets are coated in a 48 in. Accela Cota with an aqueous film coating mixture consisting of hydroxypropyl methylcellulose 7% w/w, polyethylene glycol 2% w/w, propylene glycol 3% w/w, and benzyl alcohol 1% w/w. The tablets are then placed on paper-lined trays to dry.
10. The tablets prepared by the preceding method had the following per tablet unit formula: fenoprofen calcium, 700.0 mg; lactose, 105.7; starch powder, 70.0; pregelatinized starch, 26.25; povidone, 26.25; opaspray butterscotch, 9.9; cellulose with sodium CMC-591, 30.0; sodium lauryl sulfate, 2.4; magnesium stearate, 5.0; stearic acid powder, 10.0; clear film coat (theory) 19.32.

Ferrous Fumarate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ferrous fumarate	200
295.00	2	Ludipress®	295
5.00	3	Magnesium stearate	5

Manufacturing Directions

1. Mix all components, and pass through an 0.8-mm sieve.
2. Press with low-compression force.
3. Compress into 509-mg tablets, using 12-mm biplanar punches.

Ferrous Sulfate, Manganese Sulfate, and Copper Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
65.00	1	Anhydrous ferrous sulfate	65.00
3.50	2	Manganese sulfate	3.50
0.16	3	Copper sulfate	0.16
70.00	4	Ludipress®	70.00
10.00	5	Kollidon® 30	10.00
2.00	6	Magnesium stearate	2.00
3.00	7	Aerosil® 200	3.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with high-compression force.
2. Compress into 149-mg tablets, using 8-mm biplanar punches.

Ferrous Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Anhydrous ferrous sulfate	203.00
185.00	2	Ludipress®	185.00
15.00	3	Kollidon® VA 64	15.00
4.00	4	Magnesium stearate	4.00
4.00	5	Talc	4.00
3.00	6	Aerosil® 200	3.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press to tablets with medium-compression force.
2. Compress into 413-mg tablets, using 8-mm biplanar punches.

Fexofenadine and Pseudoephedrine Tablets (10 mg/240 mg), Allegra

Allegra-D® (fexofenadine HCl and pseudoephedrine HCl) extended-release tablets for oral administration contain 60 mg of fexofenadine HCl for immediate-release and 120 mg of pseudoephedrine HCl for extended release. Tablets also contain the following excipients: microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, magnesium stearate, carnauba wax, stearic acid, silicon dioxide, hydroxypropyl methylcellulose, and polyethylene glycol.

Fexofenadine and Pseudoephedrine Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
240.00	1	Pseudoephedrine sulfate	240.00
15.00	2	Microcrystalline cellulose (Avicel PH 101)	15.00
200.00	3	Xanthan gum Keltrol TF	200.00
80.00	4	Sodium alginate keltone HVCR	80.00
53.00	5	Calcium carbonate	53.00
6.00	6	Magnesium stearate	6.00
6.00	7	Aerosil 200	6.00
10.00	8	Fexofenadine	10.00
95.00	9	Lactose monohydrate	95.00
66.50	10	Microcrystalline cellulose (Avicel PH 101)	66.50
1.00	11	Yellow FD&C No. 10	1.00
20.00	12	Starch (maize)	20.00
6.00	13	Starch (maize)	6.00
1.50	14	Magnesium stearate	1.50
–	15	Water, purified	60.00

Manufacturing Directions

1. Charge pseudoephedrine sulfate, microcrystalline cellulose, xanthan gum, sodium alginate, calcium carbonate, and one-half of the lubricants in a suitable mixer, after sieving through a #44 sieve.
2. Pass the blend through a roll compactor.
3. Sieve the compact through a #22 sieve to obtain granules.
4. Mix the granules with the remaining lubricants (items 6 and 7), and compress into tablets (600 mg) to form the first tablet layer.
5. Charge items 8 to 12 after passing through a #100 sieve in a suitable mixer. Blend for 10 minutes.
6. Charge item 13 in a separate vessel, and make a paste (10%) using item 14.
7. Add step 6 into step 5, and granulate.
8. Dry the granules, and blend the sifted item 14.
9. Compress into 200-mg tablets (the second layer).
10. Use appropriate tabletting equipment for bilayer tabletting or core tabletting.

Fexofenadine Tablets (30 mg/60 mg/180 mg) Allegra

Each tablet contains 30, 60, or 180 mg of fexofenadine hydrochloride (depending on the dosage strength) and the following excipients: croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and pregelatinized starch. The aqueous tablet film coating is made from hydroxypropyl methylcellulose, iron oxide blends, polyethylene glycol, povidone, silicone dioxide, and titanium dioxide.

Finasteride Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Finasteride	5.00
56.70	2	Lactose monohydrate	56.70
5.00	3	Starch 1500 (pregelatinized starch)	5.00
20.00	4	Avicel PH 102 (microcrystalline cellulose)	20.00
27.00	5	Maize starch	27.00
5.50	6	Primojel (sodium starch glycolate)	5.50
0.60	7	Magnesium stearate	0.60
3.50	8	Hypromellose (hydroxypropyl methylcellulose)	3.50
0.60	9	Talc, fine powder, extra pure	0.60
0.60	10	Titanium dioxide	0.60
–	11	Purified water	QS
0.20	12	Disperse blue E132	0.20
0.10	13	Triacetin	0.10
–	14	Ethanol 95%	QS
–	15	Purified water	QS

Manufacturing Directions

1. Make a slurry of starch paste in purified water.
2. Mix finasteride, maize starch, and Primojel.
3. Add lactose monohydrate with step 2, and pass through a 0.5-mm sieve.
4. Knead the mixed powder from steps 2 and 3 with starch paste to make a suitable wet mass. Pass the wet mass through a #8 sieve onto drying trays.
5. Dry the granules for approximately 3.5 hours at 55°C to get the desired LOD of 2.5%.
6. Grind the dried granules from step 5, and blend with magnesium stearate, previously sieved (250 mm) in a drum blender. Blend for 2 minutes.
7. Lubricate the granules.
8. Compress into 120-mg tablets, using a suitable punch.
9. Disperse hypromellose and triacetin in purified water and ethanol. Keep it overnight. Disperse talc, titanium dioxide, and colorant, and homogenize.
10. Coat the core tablets with the coating dispersion in step 9. (See Appendix.)

Fluconazole Tablets (50 mg/100 mg/200 mg), Diflucan

Diflucan tablets: These tablets contain 50, 100, or 200 mg of fluconazole and the following inactive ingredients: microcrystalline cellulose, dibasic calcium phosphate anhydrous, povidone, croscarmellose sodium, FD&C Red No. 40 Aluminum Lake dye, and magnesium stearate.

Fluoxetine Tablets (20 mg)

Formulation: Fluoxetine HCl (BASF), 22.4 g; Ludipress, 176.0 g; magnesium stearate, 1.6 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press to tablets with low-compression force at 205 mg.

Fluoxetine Hydrochloride Tablets (10 mg/20 mg/40 mg), Prozac

Each Prozac® pulvule contains fluoxetine hydrochloride equivalent to 10 mg (32.3 mcmol), 20 mg (64.7 mcmol), or 40 mg (129.3 mmol) of fluoxetine. The pulvules also contain starch, gelatin, silicone, titanium dioxide, iron dioxide, and other inactive ingredients. The 10- and 20-mg pulvules also contain FD&C Blue No. 1, and the 40-mg pulvule also contains FD&C Blue No. 1 and FD&C Yellow No. 6.

Each Prozac tablet contains fluoxetine HCl equivalent to 10 mg (32.3 mmol) of fluoxetine. The tablets also contain microcrystalline cellulose, magnesium stearate, crospovidone, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and yellow iron oxide. In addition to the preceding ingredients, the 10-mg tablet contains FD&C Blue No. 1 Aluminum Lake and polysorbate 80.

Fluoxetine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Fluoxetine, use paroxetine hydrochloride	11.45
20.00	2	Microcrystalline cellulose	20.00
64.05	3	Lactose	64.05
4.00	4	Sodium starch glycolate	4.00
0.50	5	Magnesium stearate	0.50

Manufacturing Directions

1. Charge items 1 to 4 in a suitable blender, after passing through a 250-mm sieve.
2. Mix for 20 minutes.
3. Add item 5 after passing through a 250-μm mesh, and blend for 1 minute.
4. Compress.
5. Coat using HPMC coating, adding 6% to 10% tablet weight.
6. For a controlled-release formulation, use 5% to 12% of tablet core weight) %w/w of Eudragit RS 100 and 86.0; dibutyl phthalate 10.0; talc 4.0; FD&C Yellow No. 6 0.01; and triacetin 10.

Fluoxetine Hydrochloride Tablets (12.5 mg/25.0 mg), Controlled-Release Bilayer

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Fluoxetine, use paroxetine hydrochloride	28.59
15.00	2	Methocel K4M	15.00
62.00	3	Lactose monohydrate	62.00
3.00	4	Polyvinyl pyrrolidone	3.00
1.00	5	Magnesium stearate	1.00
1.00	6	Syloid 244	1.00
15.04	7	Compritol 888	15.04
29.32	8	Lactose monohydrate	29.32
4.00	9	Polyvinyl pyrrolidone	4.00
1.52	10	Magnesium stearate	1.52
–	11	Water, purified	QS
29.32	12	Methocel E5	29.32
0.08	13	Iron oxide	0.08

Manufacturing Directions

1. Two layers are made (items 1–6 and items 7–10, using item 11 as necessary for wet granulation).
2. Compress tablets on a Manesty triple-layer press.
3. Coat using items 12 and 13 on a Manesty triple-layer press.
4. Adjust item 3 for 12.5-mg strength.

Fluoxetine Hydrochloride Fast-Melt Tablets

Manufacturing Directions

1. Mix fluoxetine hydrochloride, 18%; sodium bicarbonate, 26%; citric acid anhydrous, 26%; microcrystalline cellulose, 4%; anhydrous lactose, 13%; xylitol, 10%; and Crodesta F160, 3%.
2. Dry above ingredients at an elevated temperature to significantly reduce the moisture content of each material.
3. Blend for 5 to 10 minutes and extruded in a hot melt extruder at approximately 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix FLX-EFG (20–80 mesh), 50%; anhydrous lactose, 31%; microcrystalline cellulose, 10%; L-HPC LH-11, 5%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; fumed silicon dioxide, 0.1%.
5. Screen the above granules and blend for 5 minutes prior to compression.
6. Fluoxethine HCl tablets are then compressed to a hardness of approximately 1 to 5 kPa (depending upon the dose of the active) and tablets disintegrate in water in approximately 15 to 40 seconds.

Fluvoxamine Maleate Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Fluvoxamine maleate	50.00
96.00	2	Mannitol	96.00
39.00	3	Maize starch	39.00
12.00	4	Pregelatinized starch (Starch 1500)	12.00
0.60	5	Colloidal silicone dioxide (Aerosil 200)	0.60
1.50	6	Sodium stearyl fumarate	1.50
QS	7	Purified water	QS

Manufacturing Directions

1. Make a slurry of starch paste in purified water.
2. Sift mannitol, fluvoxamine maleate, and the remaining part of maize starch through a 0.5-mm stainless steel sieve.
3. Knead the powder mix from step 2 with starch paste to get the desired wet mass. Then pass the mass through a #8 mesh to drying trays.
4. Dry at 50°C for 24 hours to reach an LOD of not more than 2%.
5. Pass the dried granules through a #16 mesh into a blending vessel.
6. Pass Starch 1500, Aerosil 200, and sodium stearyl fumarate through a 0.25-mm sieve into step 5. Blend for 2 minutes.
7. Compress into 200-mg tablets, using 12-mm punches.
8. Apply Eudragit L 100–55 coating. (See Appendix.)

Folic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Folic acid[a]	5.24
12.00	2	Maize starch (dried)[b]	12.00
5.26	3	Cellulose (microcrystalline) (Avicel™ PH102)	5.26
20.00	4	Cellulose (microcrystalline) (Avicel™ PH102)	20.00
1.50	5	Colloidal silicon dioxide (Aerosil® 200)	1.50
66.00	6	Lactose (spray-dried)[c]	66.00
2.50	7	Talc (fine powder)	2.50
2.50	8	Stearic acid (fine powder)	2.50

[a]Extra folic acid is added (0.08 mg/tablet) to compensate water (water NMT 8.0%).
[b]LOD: NMT 4.5% when dried at 120°C for 4 hours.
[c]Meets the USP NF, except particle size distribution, as follows: min 98%, 250 μm; 30% to 60%, 100 μm; max. 15%, 45 μm.

Manufacturing Directions

1. Folic acid must be protected from exposure to direct light.
2. Sift items 1 to 3 through a FitzMill (impact forward, high speed), and collect in a stainless steel drum.
3. Load the material into a blender, and mix for 3 minutes.
4. Sift items 4 to 8 through a 500-μm sieve using a sifter, and collect in a stainless steel drum.
5. Load this sieved material into a blender.
6. Mix for 5 minutes.
7. Unload the lubricated powder into a stainless steel drum. Check for small lumps or globules in the powder mix.
8. If required, pass the entire mass through a 500-μm sieve using a sifter, and mix for 1 minute in a blender.
9. Compress into 1.15-g tablets (hardness, 3–7 kPa), using 7-mm round flat punches.
10. For 1-mg tablets, compensate with lactose and compress as above.

Folic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Folic acid	5.00
195.00	2	Ludipress®	195.00
1.50	3	Magnesium stearate	1.50

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press into tablets using medium-compression force.
2. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.
3. Compress into 213-mg tablets, using 8-mm biplanar punches.

Fosinopril Tablets (20 mg), Monopril

Monopril is available for oral administration as 10-, 20-, and 40-mg tablets. Inactive ingredients include lactose, microcrystalline cellulose, crospovidone, povidone, and sodium stearyl fumarate.

Fosinopril Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Fosinopril sodium	20.00
134.50	2	Lactose monohydrate	134.50
40.00	3	Microcrystalline cellulose (Avicel PH 102)	40.00
7.00	4	Crospovidone	7.00
4.50	5	Povidone	4.50
4.00	6	Sodium stearyl fumarate	4.00
–	7	Alcohol	QS

Note: For 10- and 40-mg strength, adjust with item 2.

Manufacturing Directions

1. Charge items 1 and 2 in a suitable mixer, after sifting, and mix for 20 minutes.
2. In a separate vessel, charge item 5 with a suitable quantity of item 7, and make a binder solution.
3. Add step 2 into step 1 to make a wet mass.
4. Dry the mass at 45°C to 70°C in a tray oven or a fluid-bed dryer, until the LOD is less than 3%.
5. Pass the dried granules through a hammer mill fitted with 0.03- to 0.07-in. screen.
6. Transfer screened granules into a suitable blender, add items 3 and 4, and blend for 1 to 3 minutes.
7. Compress into 200-mg tablets.

Fucidine Tablets (125 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
125.00	1	Fucidine	125.00
63.00	2	Dicalcium phosphate (Di-Tab)	63.00
2.50	3	Kollidon 90C	2.50
–	4	Isopropyl alcohol	30 mL
6.20	5	Kollidon CL	6.20
1.30	6	Aerosil 200	1.30
3.00	7	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4. Dry and then pass the mixture through a 0.8-mm sieve.
2. Add the mixture of items 5 and 6, and press with low-compression force.
3. Compress into 200-mg tablets, using 9-mm punches. To accelerate the disintegration, the amount of Kollidon 90F should be reduced and Kollidon CL should be applied in intra- and extragranular forms.

Furazolidone Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Furazolidone	104.00
40.00	2	Lactose monohydrate	40.00
40.00	3	Dicalcium phosphate	30.00
2.00	4	Gelatin	2.00
2.00	5	Talc	2.00
2.00	6	Magnesium stearate	2.00
20.00	7	Starch (maize)	10.00
QS	9	Water, purified	QS

Manufacturing Directions

1. Sift items 1 to 3 through a 250-mm sieve, and charge into a suitable mixing vessel. Mix the items for 5 minutes.
2. Separately, charge a sufficient quantity of item 9. Add item 4, and dissolve it at 50°C. Add item 7, and mix until a smooth slurry is formed.
3. Add step 2 into step 1, and mix to form a wet mass suitable for granulation. Pass the mass through the sieve onto paper-lined trays, and dry at 60°C overnight to reach an LOD of not more than 2%.
4. Pass the dried granules through 1.19-mm mesh into a suitable blending vessel.
5. Sift items 5 and 6 through a 500-mm sieve, and blend for 2 minutes.
6. Compress into 200-mg tablets, using 8.3-mm punches.

Furosemide Tablets (40 mg), Lasix

Lasix is a diuretic that is an anthranilic acid derivative. Lasix for oral administration contains furosemide as the active ingredient. It also contains the following inactive ingredients: lactose, magnesium stearate, starch, and talc.

Furosemide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Furosemide	40.00
158.00	2	Ludipress	158.00
2.00	3	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through 0.8-mm sieve, and press with low-compression force.
2. Compress into 205-mg tablets, using 8-mm biplanar punches.

Furosemide Tablets (40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Furosemide	40.00
83.10	2	Starch (maize)	83.10
30.00	3	Lactose monohydrate	30.00
1.00	4	Colloidal silicon dioxide (Aerosil 200)	1.00
14.00	5	Starch (maize)	14.00
2.00	6	Talc (fine powder)	2.00
20.00	7	Starch 1500 (pregelatinized starch)	20.00
1.60	8	Stearic acid	1.60
8.00	9	Starch (maize, dried)	8.00
0.30	10	Magnesium stearate	0.30
–	11	Purified water	70.00

Manufacturing Directions

Note: Avoid overmixing lubricants, otherwise hardness can be reduced.

1. Preparing starch paste: Make a smooth slurry of item 5 in 14 g of item 11 (25–30°C). Transfer the slurry into 56 g of item 11 (80–90°C) preheated in a steam jacket vessel under continuous stirring to get a translucent paste. Cool to 45°C to 50°C.
2. Sieving and dry mixing: Sift items 1, 3, 2, and 4 through a stainless steel 630-mm sieve in sifter. Load into mixer. Mix for 5 minutes at low speed.
3. Kneading: Knead the powder mix in the mixer with starch paste at low mixer speed for 3 minutes. Scrape sides and blades. Mix and chop at low speed for 3 minutes. Check the end point of granulation. If required, add more purified water to separate the granules, freeing big lumps.
4. Drying
   a. Unload the wet mass in stainless steel trays for drying. Dry the wet mass in an oven at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break lumps for uniform drying.
   b. Check the LOD. The LOD limit is 2% to 2.5%.
   c. If required, dry further at 55°C to meet the LOD limit.
   d. Transfer the dried granules to stainless steel drums.
5. Grinding and lubricating
   a. Grind the dried granules through a 1.25-mm sieve using a granulator at medium speed. Collect in stainless steel drums. Load the granules into the blender.
   b. Sift items 7 and 9 through a 500-µm sieve, using a sifter, and add it into the blender. Mix for 2 minutes.
   c. Sift items 6, 8, and 10 through a 500-µm sieve. Add 2 to 4 g of granules from bulk (step 5a).
   d. Mix in a polythene bag for 1 minute, and add to blender. Blend the mixture for 1 minute.
   e. Unload in stainless steel drums.
6. Compression: Check temperature and humidity before starting compression. As a limit, the temperature should not exceed 27°C, and the recommended relative humidity is 55% to 60%. Compress the granules using a rotary tabletting machine. The diameter should be 8.0-mm round punches.

Furosemide Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Furosemide	200.00
388.00	2	Ludipress	388.00
6.00	3	Magnesium stearate	6.00
6.00	4	Aerosil 200	6.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 618-mg tablets, using 12-mm biplanar punches.

Gabapentin Tablets (600 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Gabapentin (10–125 mm)	600.00
24.00	2	Hydroxypropyl cellulose 75–150 cps (Klucel LF)	24.00
39.00	3	Corpovidone sodium (polyplasdone XL)	39.00
12.00	4	Calcium stearate	12.00
—	5	Alcohol	QS

Note: Compress 675 mg; for 800 mg, compress 900 mg.

Manufacturing Directions

1. Prepare a 7.5% solution of item 2 in item 5 by slowly adding item 2 to item 5 and mixing for 60 minutes at room temperature, until a clear homogenous solution is obtained
2. Charge item 1 in a fluid-bed dryer, and apply the solution in step 1 to granulate.
3. The process air volume is set to 100 cfm, and gabapentin is fluidized. When the product temperature reaches about 25°C to 28°C, the binder solution is applied. This solution is introduced through a pneumatically atomized nozzle positioned in the expansion chamber of the fluid-bed processor. The fluidized gabapentin particles are thus coated with the binder solution. While spraying, the process air volume is increased until the product temperature is stabilized between 12°C and 25°C. Once all the binder solution is applied, the process air volume is set to 150 cfm and the temperature to about 35°C to dry the coated particles. Drying is complete when the LOD, determined by a Computerized Moisture Analyzer Balance, is not more than 0.75%.
4. Pass the spray-coated particles through a comminuting mill.
5. Charge the sized particles in a V-blender with items 3 and 4. Blend these materials for 5 minutes.
6. Compress at a pressure of 12 to 14 kN. The hardness range of the 600-mg tablets is 13.3 to 14.9 kPa, with an average hardness of 14.2 kPa.
7. Optionally, coat the tablets with an aqueous dispersion such as an Opadry. (See Appendix.)

Galanthamine Hydrobromide Tablets (1 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Galanthamine hydrobromide	1.00
32.00	2	Calcium phosphate	3.20
5.00	3	Lactose	5.00
15.00	4	Microcrystalline cellulose	15.00
0.70	5	Talc	0.70
0.70	6	Magnesium stearate	0.70

Note: For 5-mg strength, fill a proportionate amount or adjust with item 2.

Manufacturing Directions

1. Pass items 1 to 4 through a 250-μm sieve, and charge in a blending vessel. Mix the materials for 10 minutes.
2. Pass items 5 and 6 through a 250-μm sieve, and add to step 1. Blend this mixture for 1 minute.
3. Compress.

Garlic Extract + Thyme Extract Tablets Cores with Vitamin C (300 mg + 25 mg + 100 mg)

Formulation: Garlic extract, granulated (Aflopa), 300 g; thyme extract, powder (Aflopa), 25 g; ascorbic acid, crystalline (BASF), 100 g; Kollidon CL, 14 g; Ludipress, 268 g; magnesium stearate, 7 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press to tablets with medium-compression force at 714 mg.

Garlic Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
95.00	1	Calcium phosphate, dibasic	95.00
94.00	2	Lactose monohydrate	94.00
9.00	3	Kollidon® 30	9.00
25.00	4	Water	25.00
100.00	5	Dried garlic powder	100.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, pass through an 0.8-mm sieve, add items 5 and 6, and press with low-compression force.
2. Compress into 312-mg tablets, using 9-mm biconvex punches.

Gemfibrozil Tablets (600 mg)

It is available in tablet form for oral administration. Each tablet contains 600 mg of gemfibrozil. Each tablet also contains calcium stearate; candelilla wax FCC; microcrystalline cellulose; hydroxypropyl cellulose; hydroxypropyl methylcellulose, USP; methylparaben, NF; Opaspray white; polyethylene glycol; polysorbate 80; propylparaben; colloidal silicon dioxide; and pregelatinized starch.

Gemfibrozil Tablets

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Gemfibrozil	600.00
120.00	2	Microcrystalline cellulose (Avicel PH 101)	120.00
40.00	3	Gelatin	40.00
2.00	4	Diotilan	2.00
16.00	5	Calcium stearate	16.00
54.00	6	Sodium carboxymethyl starch	54.00
24.00	7	Talc	24.00
8.00	8	Silicon dioxide colloidal	8.00
9.50	9	Hydroxypropylmethyl cellulose	9.50
4.00	10	Polyethylene glycol 4000	4.00
0.50	11	Simethicone	0.50
2.00	12	Titanium dioxide	2.00
–	13	Water, purified	QS
–	14	Alcohol	QS

Manufacturing Directions

1. Charge the gemfibrozil and microcrystalline cellulose in a suitable whirlpool mixer and homogenize.
2. Prepare an aqueous solution of item 3 and add to step 1.
3. Prepare an ethanolic solution of item 4, add to step 1, and granulate.
4. Dry the granules. Screen the granules through a 0.8-mm sieve screen, return to the mixer, and homogenize with the components of the external layer (calcium stearate, sodium carboxymethyl starch, talc, colloidal silicic acid).
5. Compress the homogenized mixture into oval biconvex tablets weighing 864 mg.
6. Coat the tablets to a final weight of 880 mg, using items 9 to 12. (See Appendix for details.)

Ginkgo Extract Tablets (40 mg)

Formulation: Ginkgo biloba extract, dry powder, 240 g; (Biogen) Aerosil 200, 1 g; Kollidon CL, 4 g; Ludipress, 203 g; magnesium stearate, 2 g.

Manufacturing Directions

Mix the Ginkgo extract with Aerosil 200, add the other components, pass through a 0.8-mm sieve, and press to tablets with low-compression force at 254 mg.

Glibenclamide Tablets (2.5 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Glibenclamide, micro (4.8% excess)	2.62
80.88	2	Lactose monohydrate	80.88
50.00	3	Starch (maize)	50.00
1.00	4	Colloidal silicon dioxide (Aerosil 200)	1.00
11.00	5	Starch (maize)	11.00
10.00	6	Starch (maize, dried)	10.00
3.00	7	Talc (fine powder)	3.00
0.50	8	Magnesium stearate	0.50
1.00	9	Colloidal silicon dioxide (Aerosil 200)	1.00
–	10	Purified water	55.00

Manufacturing Directions

Note: Glibenclamide is an oral hypoglycemic agent. During the processing of the batch, the person involved may take a glass full of 5% glucose solution, if required.

1. Preparing the binder
   a. Make a slurry of item 5 in 15 g of item 10 (40–45°C) in a stainless steel container. Check that it is free of lumps.
   b. Charge this slurry into 40 g of item 10 heated to 95°C into the vessel. Stir until there is complete gelatinization.
   c. Cool to 50°C.
2. Dry mixing: Load items 1 to 4 into the mixer (Diosna P 250). Mix and chop for 5 minutes at high speed.
3. Kneading
   a. Add starch paste to the mixer. Mix for 2 minutes, with the mixer at low speed and the chopper at high speed.
   b. Scrape the sides and blades. Mix and chop at low speed for 2 minutes. If required, add item 10.
   c. If required for breaking bigger lumps, pass the wet mass through a FitzMill, using sieve #24205 at medium speed, with knives forward.
4. Drying
   a. Spread the wet granules onto the trays. Load the trolleys onto the dryer. Dry the granules at 55°C for 10 hours or up to the moisture content limit. Scoop the granules after 4 hours of drying. Then rotate the trays—put the upper trays down and the down trays up—for uniform drying.
   b. Check the moisture content. Limit: not more than 2.5%.
5. Grinding: Pass the dried granules through a 1-mm sieve. Collect in a stainless steel drum and load in a blender.
6. Lubricating: Mix items 6, 7, and 9 in a polythene bag. Pass through a 250-μm sieve, using a sifter. Collect in a polythene bag. Add to the granules in the blender (step 5a). Mix this mixture for 5 minutes.
7. Pass item 8 through a 250-μm sieve. Collect in a polythene bag. Mix 2 g of granules with this, and add it to the blender in step 5a. Mix for 1 minute. Unload lubricated granules in a stainless steel drum.
8. Compressing: Compress the granules using a rotary tabletting machine. Toolings should be of length 10 mm × 5 mm. The weight of 10 tablets should be 1.6 g ± 3%.

Glibenclamide Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Glibenclamide, micro	5.00
78.50	2	Lactose monohydrate	78.50
50.00	3	Starch (maize)	50.00
1.00	4	Colloidal silicon dioxide (Aerosil 200)	1.00
10.00	5	Starch (maize)	10.00
11.00	6	Starch (maize, dried)[a]	11.00
3.00	7	Talc (fine powder)	3.00
0.50	8	Magnesium stearate	0.50
1.00	9	Colloidal silicon dioxide (Aerosil 200)	1.00
–	10	Purified water	55.00

[a]LOD: Not more than 4.5% when dried at 120°C for 4 hours.

Manufacturing Directions

Follow the manufacturing directions provided in the previous formulation.

Gliclazide Tablets (80 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
80.00	1	Gliclazide[a]	80.00
30.00	2	Starch (maize)	30.00
40.00	3	Lactose monohydrate	40.00
23.00	4	Dicalcium phosphate	23.00
4.00	5	Starch maize	40.00
1.80	6	Gelatin	1.80
0.06	7	Propyl paraben	0.06
0.06	8	Methyl paraben	0.06
1.00	9	Talc	1.00
1.00	10	Magnesium stearate	1.00
1.00	11	Sodium croscarmellose	1.00
1.00	12	Aerosil 200	1.00
1.00	13	Sodium starch glycolate	1.00
–	14	Water, purified, ca	50 mL

[a]Untapped bulk density of 0.69 to 0.70.

Manufacturing Directions

1. Screen items 1 to 4 through a 250-µm sieve.
2. Charge items 1 to 4 in a suitable vessel, and mix for 30 minutes.
3. In a separate vessel, heat item 14 to boiling, and add to it items 7 and 8 at 90°C to dissolve. Add item 6, and stir and mix to dissolve completely. Then allow the mixture to cool to room temperature.
4. Add item 5 to step 3, and stir and mix to obtain a lump-free slurry. Stop heating, and mix for another 5 minutes.
5. Add the slurry in step 4 to step 2. Stir at a high speed for 30 minutes to obtain a uniform wet mass.
6. Pass the wet mass through an 8-mm size sieve, and dry the mass in a fluid-bed dryer for 50 minutes at 50°C.
7. Pass the dried granules through #20 mesh (grind larger size), and transfer to a tumbler.
8. Sift items 11 to 13 through a 500-µm sieve, and sift item 10 through a 250-µm sieve. Then add these items to step 7, and blend for 10 minutes.
9. Compress into 180-mg tablets, using 3-mm punches.

Glimepiride Tablets (1 mg/2 mg), Amaryl

Amaryl® tablets contain the active ingredient glimepiride and the following inactive ingredients: lactose (hydrous), sodium starch glycolate, povidone, microcrystalline cellulose, and magnesium stearate. In addition, Amaryl 1-mg tablets contain ferric oxide red. Amaryl 2-mg tablets contain ferric oxide yellow and FD&C Blue No. 2 Aluminum Lake. Amaryl 4-mg tablets contain FD&C Blue No. 2 Aluminum Lake.

Glimepiride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Glimepiride	2.00
109.90	2	Lactose monohydrate	109.90
35.00	3	Avicel PH 102 (microcrystalline cellulose PH 102)	35.00
8.00	4	Primojel (sodium starch glycolate)	8.00
0.75	5	Iron oxide yellow	0.75
0.85	6	Dispersed FD&C Blue No. 2	0.85
3.00	7	Polyvinyl pyrrolidone K-30 (PVP K-30)	3.00
0.50	8	Magnesium stearate	0.50
QS	9	Purified water	QS

Manufacturing Directions

1. Dissolve color in water and homogenize it. Then make a binding solution with PVP K-30.
2. Mix glimepiride with Primojel, iron oxide yellow, and dispersed blue E 132 (FD&C Blue No. 2), and pass through a 0.710-mm sieve.
3. Mix Avicel PH 102 with powder from step 2, and pass through a 0.710-mm sieve.
4. Mix lactose monohydrate with powder from step 3, and pass through a 0.710-mm sieve.
5. Knead the powder with binding solution to get the desired granules.
6. Dry the granules at 60°C for 12 hours to obtain an LOD of not more than 3%.
7. Pass the dried granules in a Frewitt granulator using a 1.25-mm sieve.
8. Compress into 160-mg tablets, using 12-mm punches. For 1-mg and 3-mg strengths, compress the same weight and adjust with lactose.

Glipizide Tablets (5 mg), Glucotrol

Immediate-release tablets—Each immediate-release tablet for oral administration contains glipizide, 5 or 10 mg, and the following inactive ingredients: cornstarch, anhydrous lactose, microcrystalline cellulose, colloidal silicon dioxide, and stearic acid.

Extended-release tablets—Inert ingredients in the formulations are as follows: polyethylene oxide, hydroxypropyl methylcellulose, magnesium stearate, sodium chloride, red ferric oxide, cellulose acetate, polyethylene glycol, and Opadry white and black ink. Glucotrol XL extended-release tablets are similar in appearance to conventional tablets. Each tablet, however, consists of an osmotically active drug core surrounded by a semipermeable membrane.

The core is divided into two layers: an "active" layer containing the drug and a "push" layer containing pharmacologically inert (but osmotically active) components. The membrane surrounding the tablet is permeable to water but not to drug or osmotic excipients. As water from the gastrointestinal tract enters the tablet, pressure increases in the osmotic layer and "pushes" against the drug layer, resulting in the release of drug through a small, laser-drilled orifice in the membrane on the drug side of the tablet. The Glucotrol XL extended-release tablet is designed to provide a controlled rate of delivery of glipizide into the GI lumen, which is independent of pH or GI motility. The function of the Glucotrol XL extended-release tablet depends upon the existence of an osmotic gradient between the contents of the bilayer core and fluid in the GI tract. Drug delivery is essentially constant as long as the osmotic gradient remains constant and then gradually falls to zero. The biologically inert components of the tablet remain intact during drug GI transit and are eliminated in the feces as an insoluble shell.

Glipizide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Glipizide, 10% excess	6.00
43.00	2	Starch (maize)	43.00
50.00	3	Lactose monohydrate	50.00
28.00	4	Dicalcium phosphate	28.00
2.00	5	Gelatin	2.00
0.075	6	Propyl paraben	0.075
0.075	7	Methyl paraben	0.075
2.00	8	Magnesium stearate	2.00
2.00	9	Sodium starch glycolate	2.00
–	10	Water, purified, ca	50 mL

Manufacturing Directions

1. Pass items 1 to 4 through a 250-μm sieve, and charge in a suitable blender. Mix these items for 30 minutes.
2. In a separate vessel, charge item 10 and bring to boil by heating. Add items 6 and 7, and stir to dissolve at 90°C. Allow to cool to 50°C.
3. Add items 4 and 5 to step 2. Stir and mix vigorously at 50°C to obtain a smooth paste without lumps. Allow the mixture to cool to room temperature.
4. Transfer step 3 to step 1, and mix to obtain a wet mass.
5. Transfer the wet mass onto trays, and dry in an oven at 60°C overnight to an LOD of not more than 2.5%.
6. Pass dried granules through #20 mesh, and collect in a tumble blender.
7. Pass item 9 through a 500-μm sieve and item 8 through a 250-μm sieve. Add to step 8. Blend for 2 minutes.
8. Compress into 120-mg tablets, using 6-mm punches.

Glipizide Tablets CR (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Xanthan gum	20.00
30.00	2	Locust bean gum	30.00
108.00	3	Dextrose	108.00
8.30	4	Surelease®	8.30
–	5	Water, purified	–
5.00	6	Glipizide	5.00
3.30	7	Sodium stearyl fumarate	3.30
43.70	8	Dextrose powder, anhydrous	43.70

Manufacturing Directions

1. Charge items 1 to 3 in a mixer, and mix at high speed for 3 minutes using a chopper blade.
2. In a separate vessel, add and mix item 4 with item 5, and spray the mixture gradually into step 1 while mixing at high speed to provide even distribution and to produce a suitable wet mass.
3. Dry the wet mass in a fluid-bed dryer to an LOD of less than 10% (preferably less than 5%).
4. Pass the dried granules through a 20-mesh screen, and transfer them to a mixing vessel (V-blender). Blend for 10 minutes.
5. Add items 6 and 8 to step 4 after passing through a 250-μm sieve. Blend the mixture for 15 minutes.
6. Add item 7, and blend for 3 minutes.
7. Compress into 220-mg tablets, using a suitable punch at 5-kPa hardness.

Glyburide and Metformin Tablets (250 mg/500 mg; 1.25 mg/2.50 mg), Glucovance

The glyburide used in Glucovance has a particle size distribution of 25%, with an undersize value not more than 6 mm, a 50% undersize value not more than 7 to 10 mm, and a 75% undersize value not more than 21 μm. Glucovance is available for oral administration in tablets containing 1.25 mg glyburide with 250 mg metformin hydrochloride, 2.5 mg glyburide with 500 mg metformin hydrochloride, and 5 mg glyburide with 500 mg metformin hydrochloride. In addition, each tablet contains the following inactive ingredients: microcrystalline cellulose, povidone, croscarmellose sodium, and magnesium stearate. The tablets are film coated, which provides color differentiation.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Metformin hydrochloride	250.00
1.25	2	Glyburide	1.25
7.00	3	Croscarmellose sodium	7.00
10.00	4	Povidone	10.00
28.25	5	Microcrystalline cellulose (Avicel PH 101)	28.25
2.25	6	Magnesium stearate	2.25
—	7	Water, purified	QS

Note: For 2.5/500 strength, increase the fill volume to double.

Manufacturing Directions

1. Charge croscarmellose sodium and glyburide in a suitable blender, and blend for 10 minutes.
2. In a separate vessel, charge metformin hydrochloride and magnesium stearate (99.5%:0.5% w/w) using high shear force.
3. In a separate container, add item 4 and an appropriate quantity of item 7 (1:10 ratio) to make paste.
4. Add the paste in step 3 to steps 1 and 2 combined and mixed prior to the addition of the paste.
5. Granulate using a high-shear mixer. Dry the granules in a fluid-bed dryer at approximately 60°C to achieve a moisture content of not more than 2%.
6. Size the dried granules with a screening mill, and mix with the microcrystalline cellulose using a tumble mixer.
7. Incorporate magnesium stearate as a lubricant, using a tumble mixer (step 6) to produce the final compression blend.
8. Compress 300 mg for 250/1.25 and 600 mg for 500/2.5 tablets.
9. Coat the tablets using an HPMC-based film-coating system, until the required amount of film coat is applied. The typical level of a film coat applied to the tablets is 2% w/w. (See Appendix for details.)

Glyburide Tablets (5 mg), Micronase

Micronase® tablets (standard glyburide)—mmase tablets contain glyburide, which is an oral blood-glucose-lowering drug of the sulfonylurea class. Glyburide is a white, crystalline compound, formulated as mmase tablets of 1.25-, 2.5-, and 5-mg strengths for oral administration. The inactive ingredients of the compound are colloidal silicon dioxide, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, sodium alginate, and talc. In addition, the 2.5-mg tablet contains aluminum oxide and FD&C Red No. 40. The 5-mg tablet contains aluminum oxide and FD&C Blue No. 1.

Glynase® PresTab® tablets (micronized glyburide)—Glynase PresTab tablets contain micronized (smaller particle size) glyburide, which is an oral blood-glucose-lowering drug of the sulfonylurea class. Glyburide is a white, crystalline compound, formulated as Glynase PresTab tablets of 1.5-, 3-, and 6-mg strengths for oral administration. The inactive ingredients of the compound are colloidal silicon dioxide, cornstarch, lactose, and magnesium stearate. In addition, the 3-mg strength contains FD&C Blue No. 1 Aluminum Lake, and the 6-mg tablet contains D&C Yellow No. 10 Aluminum Lake.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Glyburide, micronized (ca 5 m^2/g)	5.25
140.00	2	Lactose spray dried (foremost spray-dried lactose #315 or #316)	140.00
28.60	3	Starch (maize)	28.60
0.75	4	Magnesium stearate	0.75

Manufacturing Directions

1. Charge items 1 to 3 in a suitable mixing vessel. Mix for 20 minutes, until a homogenous mixture is reached.
2. Sift item 4 through a 250-μm mesh and add to step 1. Blend slowly for 2 minutes.
3. Compress into ca 175-mg tablets, using a suitable punch.

Griseofulvin Tablets (125 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
125.00	1	Griseofulvin, micronized	125.00
250.00	2	Ludipress	250.00
10.00	3	Polyethylene glycol 6000 powder	10.00
19.00	4	Aerosil 200	19.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, and mix.
2. Press with low-compression force, applying a vibrating hopper.
3. Compress into 367-mg tablets, using 12-mm biplanar punches.
4. The flowability of the tabletting mixture can be increased by adding higher amounts of Ludipress and Aerosil 200.

Griseofulvin Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Griseofulvin	500.00
100.00	2	Kollidon VA 64	100.00
–	3	Dimethylformamide	7500.00
75.00	4	Kollidon CL	75.00
75.00	5	Lactose monohydrate	75.00
5.00	6	Magnesium stearate	5.00
5.00	7	Aerosil 200	5.00

Manufacturing Directions

1. Dissolve the mixture of items 1 and 2 in item 3.
2. Evaporate to dryness.
3. Pass the obtained coprecipitate through a 0.5-mm sieve.
4. Mix with items 4 to 7 and press with low-compression force.
5. Compress into 751-mg tablets, using 12-mm biplanar punches.

Guaifenesin Tablets

Manufacturing Directions

1. Inner tablet: Guaifenesin, 175.0 mg; microcrystalline cellulose, 35.1 mg; crosspovidone, 35.0 mg; polyvinylpyrrolidone, 7.3 mg; talc, 2.3 mg; zinc stearate, 2.3 mg. Total 257.0 mg.
2. Outer Tablet: Guaifenesin, 425.0 mg; hydroxypropyl-methylcellulose K4M, 139.9 mg; stearic acid, 30.0 mg; zinc stearate, 5.4 mg. Total 600.3 mg.
3. The inner tablet is made by oscillating guaifenesin and half of the polyvinylpyrrolidone through a 30-mesh screen.
4. The blend is then transferred to a pharmaceutical-grade blender and mixed until it is of uniform consistency.
5. It is then granulated with polyvinylpyrrolidone that had been previously dissolved in a sufficient amount of purified water to make a solution of about 8% to about 12% of polyvinylpyrrolidone.
6. This mixture is discharged and dried in a forced air oven at 40°C until the water content is less than 1%.
7. The dried granulation is then oscillated through a 12-mesh screen and returned to the blender.
8. The remaining polyvinylpyrrolidone, microcrystalline cellulose, and talc are added to this dried granulation and mixed until it is of uniform consistency.
9. Finally, zinc stearate is added and the mixture is mixed until it is of uniform consistency.
10. This mixture is then compressed into inner tablets, using a standard tabletting press.
11. The outer tablet is made by first passing guaifenesin through an oscillator equipped with a 30-mesh screen.
12. After this step, guaifenesin is transferred to a blender and hydroxypropyl methylcellulose K4M and stearic acid are added to it. It is mixed until uniform.
13. Zinc stearate is added and the mixture is blended until uniform.
14. The mixture of ingredients that comprise the outer tablet is compressed around the already formed inner tablet, on a standard compression coating tablet press.

Guaifenesin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Percent (w/w) ((w/w)Quantity/1000 Tablets (g)
69.77	1	Guaifenesin USP	69.77
16.00	2	Starch 1500	16.00
9.48	3	Microcrystalline Cellulose NF	9.48
4.00	4	Starch 1500	4.00
0.50	5	Stearic Acid NF	0.50
0.25	6	Magnesium stearate	0.25
100.00	7	Total	100.00

Manufacturing Directions

1. Granulation: items 1 and 2 are preblended for 2 minutes prior to granulating with water to appropriate moisture.
2. Wet mass for 3 minutes.
3. Size the granulation.
4. Lubricant passed through a 60-mesh screen prior to blending.
5. Colloidal silicon dioxide is passed through a 30-mesh screen along with the MCC.
6. All the ingredients except the lubricant are blended for 10 minutes.

Heparin Tablets*

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.08	1	Heparin (low molecular weight)	0.08
0.40	2	Water	0.40
0.92	3	Monoglyceride	0.92
1.24	4	CPL-Galactolipid	1.24
1.40	5	Palm kernel stearin	1.40

*Other proportions may include heparin 0.18, 0.21 and proportionally increased excipients. Lipid materials Trade name and source Galactolipids from oats (CPL-Galactolipid; Lipid Technologies Provider AB, Karlshamn, Sweden) Medium chain monoglyceride (Akoline MCM; Karlshamns AB, Karlshamn Sweden) Palmkernel stearin (fraction of palmkernel oil; Karlshamns AB, Karlshamn Sweden) Heparin (low molecular weight; Calbiochem, p. no. 375097 Hydrogenated cotton seed oil (Akofine NF; Karlshamns AB, Karlshamn Sweden)

Manufacturing Directions

1. The ingredients are blended and the mixture melted by heating to a temperature of 60°C and stirred at this temperature for 5 hours when all heparin had dissolved.
2. Aliquots (0.24 g) of the melted phase are cast in a mould covered with hydrogenated triglyceride (Akofine NF) powder. The mould is cooled in a freezer and the tablets recovered.

Herbal Hemorrhoid Tablets

Manufacturing Directions

1. Initially genera Glycyrrhizae Radix, Rhei Rhizoma, Ephedrae Herba, Moutan Radicis Cortex, Menthae Herba, Pinelliae Rhizoma, Pasoniae Radix, Acontii Tuber, Corni Fructus, Gypsum, Ginseng Radix and Pelladendri Radix, respectively, are washed with water to remove sand, clay, dust and the like.
2. These natural substances are cleaned and dried to a moisture content of approximately 5%.
3. 168 g of Glycyrrhizae Radix, 104 g of Rhei Rhizoma, 104 g of Ephedrae Herba, 168 g of Moutan Radicis Cortex, 104 g of Menthae Herba, 168 g of Pinelliae Rhizoma, 56 g of Pasoniae Radix, 56 g of Acontii Tuber, 56 g of Corni Fructus, 168 g of Ginseng Radix, and 104 g of Pelladendri Radix are cut into a particle size of about 1 cm and mixed together.
4. To the mixture mentioned above are added, 104 g of Testidinis Carapax, 56 g of Natrii Sulfas, 168 g of Gypsum, 56 g of Cinnabaris, and 256 g of Talcum.
5. Thereafter, this mixture is placed in an extractor having an aromatic vapor collector.
6. 12 L of water is added to approximately 2 kg of the mixture in the extractor.
7. The mixture in the extractor is heated up to about 80°C for 1 hour and then extracted.
8. The aqueous mixture is filtered first in a centrifugal separator and is then filtered again in a microfilter.
9. The aromatic vapor distilled from the aqueous mixture is condensed and added as an aromatic liquid to the filtrate.
10. The filtrate is evaporated through an automatic vacuum evaporator to a moisture content of about 30% to produce an extract that is useful as an antihemorrhoidal composition in extract form.
11. At this time, the concentrated liquid is dried through a dry sprayer to produce a granulated formulation, a tablet formulation, a pill formulation, an ointment formulation, or the like, for use as an antihemorrhoid medicine.

Horsetail Extract Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
450.00	1	Horsetail extract (powder)	456.00
14.00	2	Kollidon® VA 64	14.00
5.00	3	Lutrol F 68	5.00
QS	4	Isopropanol	~120.00
14.00 g	5	Kollidon® CL	14.00
QS	6	Magnesium stearate	QS

Manufacturing Directions

1. Granulate the extract (item 1) with solution of items 2 to 4, then dry, pass through an 0.8-mm sieve, mix with items 5 and 6 and press with high-compression force.
2. Compress into 489-mg tablets, using 12-mm biplanar punches.

Hydrochlorothiazide and Potassium Chloride (50 mg/300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Hydrochlorothiazide	50.00
300.00	2	Potassium chloride	300.00
15.00	3	Kollidon CL	15.00
2.00	4	Aerosil 200	2.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve. Mix the components, and press.
2. Compress into 369-mg tablets, using 9-mm punches.

Hydrochlorothiazide Fast-Melt Tablets

Manufacturing Directions

1. Mix hydrochlorothiazide, 20%; sodium bicarbonate, 25%; citric acid anhydrous, 25%; Avicel PH113, 18%; xylitol, 10%; Crodesta F160, 2%.
2. Dry at elevated temperatures to significantly reduce the moisture content of each material.
3. Blend for 10 minutes and extrude in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix HYD-EFG (30–60 mesh), 50%; microcrystalline cellulose, 31%; anhydrous lactose, 10%; AcDiSol, 2.5%; L-HPC LH-11, 2.5%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; Cab-O-Sil M5P 0.1%.
5. The above granules are then screened and blended with the ingredients for 5 minutes prior to compression.
6. Hydrochlorothiazide tablets are then compressed to a hardness of approximately 1 to 3 kPa and tablets disintegrate in water in approximately 15 to 35 seconds.

Hydrochlorothiazide Tablets (50 mg)

Hydrochlorothiazide is supplied as 25-, 50-, and 100-mg tablets for oral use. Each tablet contains the following inactive ingredients: calcium phosphate, FD&C Yellow No. 6, gelatin, lactose, magnesium stearate, starch, and talc.

Hydrochlorothiazide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Hydrochlorothiazide	50.00
280.00	2	Ludipress	280.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, and pass through a 0.8-mm sieve.
2. Compress with a low-compression force. Compress into 328-mg tablets, using 8-mm punches.

Hydrochlorothiazide Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Hydrochlorothiazide	50.00
422.00	2	Lactose monohydrate	422.00
8.00	3	Kollidon 90F	8.00
—	4	2-Propanol	38 mL
15.00	5	Kollidon CI	15.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with item 2, Pass through a 0.8-mm sieve, add items 5 and 6, and press with low-compression force.
2. Compress into 495-mg tablets, using 12-mm biplanar punches.

Hydrochlorothiazide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Hydrochlorothiazide	50.00
64.76	2	Dicalcium phosphate	64.76
64.76	3	Lactose	64.76
20.00	4	Starch 1500	20.00
0.50	5	Magnesium stearate	0.50

Manufacturing Directions

1. All the materials (except magnesium stearate) are blended for 15 minutes.
2. Magnesium stearate is then added and blended for 5 additional minutes.
3. Compress 200 mg tablets; for 25.00-mg strength, compress 100 mg.

Hydrocodone and Acetaminophen Tablets (5.0 mg/500 mg; 7.50 mg/750 mg)

Each tablet contains hydrocodone bitartrate (5 mg) and acetaminophen (500 mg). Other ingredients include colloidal silicon dioxide, cornstarch, croscarmellose sodium, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, povidone, and stearic acid. Each extra-strength tablet contains hydrocodone bitartrate (7.5 mg) and acetaminophen (750 mg). Other ingredients include colloidal silicon dioxide, cornstarch, croscarmellose sodium, magnesium stearate, povidone, and stearic acid.

Hydrocodone and Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
750.00	1	Acetaminophen powder	750.00
7.50	2	Hydrocodone bitartrate	7.50
12.00	3	Colloidal silicon dioxide	12.00
154.40	4	Microcrystalline cellulose	154.40
64.00	5	Croscarmellose sodium	64.00
26.00	6	Hydroxypropyl methylcellulose	26.00
124.80	7	Starch (maize)	124.80
4.00	8	Magnesium stearate	4.00
–	9	Water, purified	QS

Note: For 500 mg item 1 and 5.0 mg item 2 formulation, adjust fill volume.

Manufacturing Directions

1. Pass hydrocodone bitartrate through a #20 mesh. Pass acetaminophen and colloidal silicon dioxide (50%) through a Frewitt SG Turbo Sieve equipped with a 1.0-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum at speed setting 5 (approximately 1030 rpm).
2. Pass microcrystalline cellulose (50%), croscarmellose sodium (50%), cornstarch (66%), and hydroxypropyl methylcellulose through the Turbo Sieve at the same settings as in step 1. Charge the screened powders into a Lodige MGT-600 mixer, and mix for 5 minutes with the plow speed at approximately 103 rpm and no choppers.
3. Add water to the mixer over a 10-minute period, using a stainless steel transfer container with a valve, while mixing with the plows at about 103 rpm and the choppers at slow speed.
4. Mix the wet mass for another 15 minutes, until a wattmeter reading of 15 to 16 MkW is reached.
5. Dry the material. Preheat a Glatt fluid-bed dryer by running it for 2.5 minutes at 60°C inlet air temperature at 3500 m^3/h. Set the exhaust blower bypass speed at about 40%, the filter shaking interval for about 2 minutes, and the filter shaking duration for 5 seconds. Transfer the material in the dryer for drying. Decrease the inlet air to 2500 m^3/h and the inlet air temperature to 55°C after 30 minutes. Dry the material until an LOD of less than 0.5% is reached.
6. Pass the dried granulation through a FitzMill using a #20 mesh wire screen with knives forward, at medium speed.
7. Pass the remaining microcrystalline cellulose and the colloidal silicon dioxide through a Frewitt SG Turbo Sieve equipped with a 1-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum. The speed setting is at approximately 1030 rpm.
8. Add magnesium stearate, and mix for 3 minutes.
9. Compress using a 13/32-in. round tooling.

Hydrocodone and Ibuprofen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Ibuprofen	400.00
15.00	2	Hydrocodone bitartrate	15.00
12.00	3	Colloidal silicon dioxide	12.00
154.40	4	Microcrystalline cellulose	154.40
64.00	5	Croscarmellose sodium	64.00
26.00	6	Hydroxypropyl methylcellulose	26.00
124.80	7	Starch (maize)	124.80
4.00	8	Magnesium stearate	4.00
–	9	Water, purified	QS

Manufacturing Directions

1. Pass hydrocodone bitartrate through a #20 mesh. Pass ibuprofen and colloidal silicon dioxide (50%) through a Frewitt SG Turbo Sieve equipped with a 1.0-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum at speed setting 5 (approximately 1030 rpm).
2. Pass microcrystalline cellulose (50%), croscarmellose sodium (50%), cornstarch (66%), and hydroxypropyl methylcellulose through the Turbo Sieve at the same settings as in step 1. Charge screened powders into a Lodige MGT-600 mixer, and mix for 5 minutes with the plow speed at approximately 103 rpm and no choppers.
3. Add water to the mixer over a 10-min period, using a stainless steel transfer container with a valve while mixing with the plows at about 103 rpm and the choppers at slow speed.
4. Mix the wet mass for another 15 minutes until a wattmeter reading of 15 to 16 MkW is reached.
5. Dry the material using a preheated Glatt fluid-bed dryer; preheat by running the dryer for 2.5 minutes at 60°C inlet air temperature at 3500 m^3/h. Set the exhaust blower bypass speed at about 40%, the filter shaking interval for about 2 minutes, and the filter shaking duration for 5 seconds. Transfer the material in the dryer for drying. Decrease the inlet air to 2500 m^3/h and the inlet air temperature to 55°C after 30 minutes. Dry the material until an LOD of less than 0.5% is reached.
6. Pass the dried granulation through a FitzMill using a #20 mesh wire screen, with knives forward, at medium speed.
7. Pass the remaining microcrystalline cellulose and the colloidal silicon dioxide through a Frewitt SG Turbo Sieve equipped with a 1-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum. The speed setting is at approximately 1030 rpm.
8. Add magnesium stearate, and mix for 3 minutes.
9. Compress using a 13/32-in. round tooling.

Hydromorphone Hydrochloride Fast-Melt Tablets

Manufacturing Directions

1. Mix hydromorphine hydrochloride 15%, sodium bicarbonate 28%, citric acid anhydrous 24%, microcrystalline cellulose 10%, anhydrous lactose 11%, xylitol 10%, sucrose stearate 2%.
2. Mix the above ingredients and dry at elevated temperatures to significantly reduce the moisture content of the material.
3. Blend for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix HDM-EGF (30–60 mesh), 50%; microcrystalline cellulose, 18%; anhydrous lactose, 18%; cross povidone, 5%; L-HPC LH-11, 5%; aspartame, 3.25%; natural orange powder, 0.15%; magnesium stearate, 0.45%; fumed silicon dioxide, 0.15%.
5. Screen the above granules and blend for 5 minutes prior to compression.
6. Hydromorphone tablets are compressed to a hardness of approximately 1 to 5 kPa (depending upon the dose of the active) and tablets disintegrate in water in approximately 15 to 35 seconds.

Hydroxyzine Tablets

Inert ingredients for the tablets are acacia, carnauba wax, dibasic calcium phosphate, gelatin, lactose, magnesium stearate, precipitated calcium carbonate, shellac, sucrose, talc, and white wax. The 10-mg tablets also contain sodium hydroxide, starch, titanium dioxide, and FD&C Yellow No. 6 Lake. The 25-mg tablets also contain starch and velo dark green. The 50-mg tablets also contain starch and velo yellow. The 100-mg tablets also contain alginic acid, FD&C Blue No. 1, polyethylene glycol, and FD&C Red No. 3.

Hyoscine Butylbromide Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.000	1	Hyoscine butyl bromide	10.000
16.500	2	Lactose monohydrate	16.500
28.000	3	Lactose monohydrate, dense	28.000
17.930	4	Starch (maize)	19.720
2.240	5	Povidone (PVP K-30)	2.240
–	6	Purified water	5.080
0.400	7	Magnesium stearate	0.400
2.740	8	Pregelatinized starch (Starch 1500)	2.740

Manufacturing Directions

Caution: Hyoscine butylbromide is a potent smooth muscle relaxant. Inhalation can produce toxic effects. Strictly adhere to the usage of mask, gloves, and goggles.

1. Preparation of binding solution: Dissolve item 5 in item 6 by stirring to make a clear solution. Use the stirrer at medium speed in a stainless steel container.
2. Dry mixing: Check to see if hyoscine butyl bromide is in fine powder form. If not, pass through a 630-μm sieve using a sifter. Load items 1, 2, 4, and 3 into the mixer, and mix for 5 minutes with the mixer and chopper at low speed.
3. Wet massing
   a. Add the binding solution to the dry powder in the mixer while mixing at low speed. When the addition is over, mix and chop for a further 2 minutes at high speed.
   b. Scrape the lid and blade, and check for a satisfactory wet mass. Add more item 6 if required to get a satisfactory wet mass.
4. Drying
   a. Spread the granules onto stainless steel trays to a thickness of one-third of the tray thickness, and load the trays on the trolley.
   b. Load the trolleys into the oven. Dry at 60°C for 16 hours. Turn the granules after 3 to 4 hours so as to ensure uniform drying of the granules.
   c. Check the moisture content of the dried granules, keeping in mind the limit of 1.0% to 1.5%.
5. Grinding: Pass the dried granules through a granulator equipped with a 1.0-mm sieve.
6. Lubricating
   a. Mix items 7 and 8 in a polythene bag, and pass through a 250-μm sieve using a sifter. Collect the material in a stainless steel container.
   b. Load the sized granules from step 5a along with sieved powder from step 6a into the drum mixer. Mix these items for 3 minutes.
   c. Unload into stainless steel drums.
7. Compression: Compress the granules using a rotary tabletting machine (with dies and punches: 6 mm, concave, plain punches with fill weights of 780 mg).
8. Coating: Sugar coat the tablets. (See Appendix.)

Ibuprofen and Domperidone Maleate Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
7.50	2	Domperidone maleate	7.50
750.00	3	Sucrose	750.00
50.00	4	Sorbitol	50.00
1.12	5	Silica fumed	1.12
6.75	6	Stearic acid	6.75

Manufacturing Directions

1. Combine items 1 to 6 to form a homogeneous blend.
2. Compress by direct compression to form a chewable tablet containing 200 mg of ibuprofen and 7.5 mg of domperidone maleate.
3. Compression weight approximately 1015 mg per tablet.

Ibuprofen and Domperidone Maleate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
5.00	2	Domperidone maleate	5.00
20.00	3	Microcrystalline cellulose	20.00
30.00	4	Croscarmellose sodium	30.00
2.00	5	Magnesium stearate	2.00
2.00	6	Hydrogenated cottonseed oil	2.00
60.00	7	Tricalcium phosphate	60.00
10.00	8	Hydroxypropyl cellulose	10.00
10.00	9	Hydroxypropylmethyl cellulose	10.00
112.00	10	Sorbitol	112.00

Manufacturing Directions

1. Ibuprofen, domperidone maleate, tricalcium phosphate, hydroxypropyl cellulose, croscarmellose sodium, and microcrystalline cellulose are sieved and blended to form a homogeneous mixture
2. The mixture is granulated to a suitable end point with water and dried.
3. The dried granules are blended with magnesium stearate
4. The lubricated granules are compressed to form tablet cores each containing 200 mg of ibuprofen and 5 mg of domperidone or each containing 400 mg of ibuprofen and 10 mg of domperidone.
5. The tablet cores are coated with a conventional film coating.

Ibuprofen and Domperidone Sustained-Release Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Ibuprofen	400.00
20.00	2	Domperidone maleate	20.00
100.00	3	Xanthan gum	100.00
12.00	4	Hydroxypropyl methylcellulose	12.00
6.00	5	Stearic acid	6.00
2.00	6	Colloidal silicon dioxide	2.00

Manufacturing Directions

1. Granulate the hydroxypropyl methylcellulose and ibuprofen with approximately 20% of the total content of xanthan gum using water as the granulating agent.
2. The ibuprofen granule is combined with the remainder of the xanthan gum and the other ingredients and compressed into tablets containing 400 mg of ibuprofen and 20 mg of domperidone.

Ibuprofen and Hydrocodone Bitartarate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
7.52	2	Hydrocodone Bitartarate	7.52
6.00	3	Colloidal silicon dioxide	6.00
77.20	4	Microcrystalline cellulose	77.20
32.00	5	Sodium croscarmellose	32.00
13.00	6	Hydroxypropyl methylcellulose	13.00
62.40	7	Corn startch	62.40
2.00	8	Magnesium stearate	2.00

Manufacturing Directions

1. Hydrocodone bitartrate is passed through a #20 mesh handscreen.
2. Ibuprofen (50%) and colloidal silicon dioxide (0.75%) are passed through a Frewitt SG Turbo Sieve equipped with a 1.0-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-line collecting drum at speed setting 5 (approximately 1030 rpm).
3. Microcrystalline cellulose (9.5%), croscarmellose sodium (4.0%), cornstarch (10.6%), and hydroxypropyl methylcellulose (3.3%) are passed through the turbosieve at the same settings.
4. The screened powders are introduced into a Lodige MGT-600 mixer and mixed for 5 minutes with plow speed at approximately 103 rpm and NO choppers.
5. Water is added to the mixer over a 10-minute period using a stainless steel transfer container with a valve while mixing with plows at about 103 rpm and choppers at slow speed.
6. The wet material is mixed for another 15 minutes until a Wattmeter of 15 to 16 kW is reached.
7. To dry the material, a Glatt fluid-bed dryer is preheated by running it for 2.5 minutes at 60°C, with inlet air temperature at 3500 m^3/h. The exhaust blower bypass speed is set at about 40%, the filter shaking interval for about 2 minutes, and the filter shaking duration is for 5 seconds. The material is placed in the dryer for drying. The inlet air is decreased to 2500 m^3/h and the inlet air temperature to 55°C. after 30 minutes. The material is dried until an LOD of less than 0.5% is reached.
8. The dried granulation is passed through a FitzMill using a #20 mesh wire screen 1536-0200 with knives forward at medium speed.
9. The remaining microcrystalline cellulose and the colloidal silicon dioxide is passed, alternatively, through a Frewitt SG Turbo Sieve equipped with a 10-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum. The speed setting is set at approximately 1030 rpm.
10. The milled granulation, the remaining croscarmellose, the screened colloidal silicon dioxide, the microcrystalline cellulose, and the cornstarch are introduced into a Littleford FKM-3000 mixer through a chute and mixed for 3 minutes at fast speed.
11. Magnesium stearate is passed through a Frewitt Turbo Sieve equipped with a 1.0-mm round-hold screen, an angle bar, a cloth skirt and a polyethylene line collecting drum. The speed setting is at about 1030 rpm.
12. Magnesium stearate is then added to the mixture and mixed for 3 minutes at fast speed. The final blend is discharged through a cloth sleeve into tared totes with inserts with minimum jogging.
13. The composition is compressed into tablets by using a Kilian TX-32 tablet press and 13/32 in. round tooling and filmed coated.

Ibuprofen Chewable Tablets

Manufacturing Directions

1. PVAP and PVP-K90, equivalent to a 2:1 weight ratio, are dissolved in minimum volumes of an aqueous ammonium hydroxide solution (28% v/v) and water, respectively, and then mixed.
2. To the resulting mixture, ibuprofen, equal to the amount of PVAP used, is dissolved and then 0.1N HCl solution is added drop wise until the pH of the solution is 1.0.
3. The white solid precipitate is filtered, washed with water, and then vacuum dried.
4. The entrapped granules containing 39.06% ibuprofen are used in the preparation of tablets.
5. Appropriate amounts of the granules and the cherry vehicle, corresponding to 200 mg of ibuprofen per 668 mg of tablet, are accurately weighed and then mixed and tablets compressed.

Ibuprofen Coated Fast-Crumbling Granule Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
16.00	2	Sodium croscarmellose (AGG)	16.00
27.50	3	Aspartame	27.50
12.20	4	Precipitated silica	12.20
35.00	5	Ethylcellulose	35.00
8.00	6	Hypermellose	8.00
1.33	7	Sodium (AGM) croscarmellose	1.33
	8	Pharmacoat 606	

Manufacturing Directions

1. A suspension is obtained by mixing ethylcellulose, 80% precipitated silica, and 30% aspartame in ethyl alcohol, until a homogeneous suspension is obtained.
2. The powder mixture consisting of ibuprofen, item 7, 70% aspartame, and 20% precipitated silica is then fluidized.
3. Granulation is then started by spraying the mixture for about 15 to 20 minutes at a spraying rate of 25 g/min and a suspension atomization pressure of 0.8 bar.
4. The actual coating is then performed by spraying the remainder of the mixture over about 1.5 hours at a spraying rate of 15 to 20 g/min and a suspension atomization pressure of 1.5 bar.
5. 15% of the mixture is sprayed during the granulation step, and the remainder to 100% is sprayed during the coating step.
6. The granules obtained are then formulated as fast-crumbling multiparticulate tablets, with the following composition: coated granules, 300 mg; Mannitol, 344 mg; sodium croscarmellose, 21 mg; precipitated silica, 7 mg; aspartame, 20 mg; mint flavoring, 4 mg; magnesium stearate, 4 mg.

Ibuprofen Fast-Dissolve Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
121.90	1	Ibuprofen coated	121.90
11.00	2	Citric acid	11.00
3.90	3	Magnasweet 135	3.90
6.50	4	Aspartame	6.50
7.80	5	Cherry flavor	7.80
39.00	6	Croscarmellose sodium	39.00
1.95	7	Silicon dioxide	1.95
3.25	8	Magnesium stearate	3.25
457.90	9	Fast-dissolving granulation (see below)	457.90

Manufacturing Directions

1. Fast-dissolving granulation is made by combining 400 g of melted PEG 900 with fructose powder (100 g) in a planetary mixer (low-shear mixer) and mixed until granules are formed.
2. The granulations are allowed to cool, and then screened.
3. Ingredients are screened, and then mixed in a V-blender.
4. Tablets are compressed (653.7 mg) at 600 lb (about 2.7 kN).
5. The tablets have hardness of 0.2 to 0.5 kPa and disintegrate in less than 15 seconds.

Ibuprofen Sustained-Release Bi-Layer Tablet

Manufacturing Directions

1. Immediate-release layer composition
   a. Part I: Ibuprofen USP 160.0 mg; microcrystalline cellulose NF, 32.0 mg; (Avicel PH 101) starch NF, 32.0 mg; pregelatinized starch NF, 16.0 mg; (Starch 1500) sodium starch glycolate NF, 6.4 mg.
   b. Part II: Hydroxypropyl methylcellulose, 1.6 mg; 2910 USP (Methocel E-5) Purified Water USP q.s.
   c. Part III: Sodium starch glycolate NF, 1.6 mg (Explotab); colloidal silicon dioxide NF, 0.8 mg. Total 250.4 mg.
   d. Weigh the components of Part I and preblend them in a high-shear mixer (fielder: impeller speed of approximately 118 RPM for 3 minutes).
   e. Prepare the granulating agent (Part II) by dissolving hydroxypropyl methylcellulose 2910 USP into purified water USP (a ratio of 3.2 g of hydroxypropyl methylcellulose to 200 g water).
   f. Deliver the granulating agent to the powders of Part I, in the high-shear mixer.
   g. Granulate the mixture for 20 minutes (fielder: impeller speed of approximately 118 rpm).
   h. Remove the completed wet granulation from the high-shear mixer and load into the product bowl of a fluid-bed apparatus (e.g., Aeromatic or Glatt).
   i. With an inlet air temperature of approximately 60°C, dry the granulation to a moisture level of 0.5% to 1.1% as determined by loss on drying (e.g. Computrac). The wet granulation can also be dried on trays in drying ovens.
   j. Sieve the dried granulation (e.g. Glatt Quick Sieve: Stator No. 3, Screen No. 1.5 mm, 1000 rpm). Other machines such as a Fitzpatrick Comminution Mill can also be used.
   k. Blend the sieved and dried granulation with the powders of Part III using a suitable mixer such as a twin-shell, ribbon, or planetary mixer.
2. Sustained-release layer
   a. Povidone USP, 14.7 mg (Plasdone K 29/32); alcohol USP 1:1 mixture q.s. purified water USP
   b. Part III: Pregelatinized starch NF, 8.0 mg (Starch 1500 LM); microcrystalline cellulose NF, 7.3 mg (Avicel PH 101); magnesium stearate NF, 5.0 mg; colloidal silicon dioxide, NF 5.0 mg (Cab-O-Sil). Total = 523.3 mg; total tablet weight = 773.7 mg.
   c. Weigh the components of Part I and preblend them in a high-shear mixer (fielder: impeller speed of approximately 250 Rpm for 1 minute).
   d. Prepare the granulating agent (Part II) by dissolving the Povidone USP in a 1:1 mixture of alcohol USP and purified water USP (a ratio of 12.25 g of povidone to 100 g of alcohol/water).
   e. Spray the granulating agent at a rate of 600 mL/min onto Part I in the high-shear mixer.
   f. Granulate the mixture for 1 minute after the addition of Part II (fielder: impeller speed of approximately 250 rpm).
   g. Remove the completed wet granulation from the high-shear mixer and load it into the product bowl of a fluid-bed apparatus (e.g., Aeromatic or Glatt).
   h. With an inlet air temperature of approximately 60°C, dry the granulation to a moisture level of 0.3% to 0.8% as determined by loss on drying (e.g., Computrac).
   i. The wet granulation can also be dried on trays in drying ovens.
   j. Sieve the dried granulation (Fitzpatrick Comminution Mill, Model D6: medium speed, knives forward, 0.093 screen). Other machines such as Glatt Quick Sieve can also be used.
   k. Blend the sieved and dried granulation with the powders of Part III by using a suitable mixer such as a twin-shell, ribbon, or planetary mixer.
3. Compression of tablets or caplets
   a. Load the granulation of the immediate-release layer into one hopper and the granulation of the sustained-release layer into the second hopper of a bilayer tabletting machine (e.g., Stokes Versapress).
   b. Compress tablets using 0.749 × 0.281 × 0.060 extra deep concave capsule shaped tooling. (Tablet tooling of other shapes such as oval or round can also be used).
   c. The sustained-release layer has a target weight of 523.3 mg and the immediate-release layer has a target weight of 250.4 mg. Ideal tablet hardness immediately after compression is 11 to 12 kPa.

Ibuprofen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
88.00	2	Maize starch	88.00
30.00	3	Maize starch	30.00
12.80	4	Maize starch (dried)[a]	12.80
1.60	5	Stearic acid (fine powder)	1.60
–	6	Purified water	144.00

[a]Loss on drying: NMT 4.5% when dried at 120°C for 4 hours.

Manufacturing Directions

1. Pass item 3 through a 250-μm sieve using a sifter.
2. Prepare a slurry of item 3 with 10.67 g of cold item 6 (25–30°C) in a stainless steel container.
3. Pour the slurry into a vessel containing 37.33 g of hot item 6 (70–90°C).
4. Heat to 80°C to 90°C and mix until mixture swells and becomes translucent.
5. Cool to 50°C.

6. Check weight (theoretical weight, 58.00 g). If required, adjust with hot purified water. Record the quantity of extra water added.
7. Pass items 1 and 2 through sifter using 250-μm sieve.
8. Load it into a mixer (if required, grind item 1 through a 1-mm sieve).
9. Mix the powder for 15 minutes at high speed.
10. Add binding solution to the dry powder in the mixer and mix for 15 minutes at high speed. Check for satisfactory wet mass.
11. Pass the wet mass through a FitzMill using sieve 24207, knives forward, and medium speed.
12. Collect and spread the granules onto the trays, one third the thickness of the tray.
13. Load the trolleys into the oven and dry the granules at 55°C for 36 hours.
14. After 12 hours of drying, stir the granules in the trays and change the position of the trays for uniform drying.
15. Check the moisture of the dried granules. The limit NMT is 2.5%. Dry further if required to obtain moisture content of 2.5%.
16. Check the weight of dried granules (theoretical weight = 318.00 g).
17. Pass the dried granules through a 1.5-mm sieve using a granulator. Collect in a stainless steel drum and add it to the blender.
18. Pass items 4 and 5 through a 250-μm sieve using a sifter.
19. Add the sieved material to the granules in a blender and mix for 5 minutes.
20. Compress into 330-mg tablets, using 10-mm convex punches at 4 to 9 kPa.
21. Coat the tablets using one of the polyvinylpyrrolidone (PVP) coating solutions provided in the Appendix or use the following sugar-coating formulation:

Bill of Materials: Sugar Coating			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
7.06	1	Sandrac varnish (WMR)	7.06
3.33	2	Povidone (PVP K-25)	3.33
1.86	3	Povidone (PVP K-25)	1.86
175.85	4	Sucrose	175.85
0.16	5	Titanium dioxide	0.16
1.20	6	Polishing emulsion*	1.20
1.33	7	Talc (fine powder)	1.33
–	8	Purified water	87.10

*See appendix for polishing emulsion formulation.

22. Load the tablets into the pan.
23. Start the tablets rolling with the exhaust on and air supply off.
24. Pour the item 1 solution onto the rolling tablets and allow the tablets to roll, using hand agitation if required, permitting the solution to spread well over the tablet bed.
25. Permit the tablets to roll until tack develops, at which point item 7 should be quickly sprinkled over the tablets.
26. Allow to roll freely for 2 minutes at 45°C.
27. Do not roll too long, as the seal may be worn from the tablet edges.
28. After 2 minutes of rolling, jog the tablets every 1 minute over a period of 15 minutes with exhaust and drying air on at 45°C.
29. Continue jogging for a further 15 minutes. Jog every 3 minutes with exhaust and drying air temperature on at 45°C.
30. Dissolve 2.40 g of item 2 in 28.80 g of item 8.
31. Apply a half quantity of it to the tablets over 5 minutes; allow to dry and apply the remainder over a 15-minute period.
32. Heat 11.52 g of item 8 to boiling, dissolve 26.88 g of item 4, and cool down to 25°C.
33. Check weight (theoretical weight, 38.40 g). If less, adjust weight to 38.40 g with purified water.
34. Apply sugar coat over a 30-minute period.
35. Dry the tablets in the coating pan at 30°C, jogging every 1 hour for 6 hours.
36. Heat 72.0 g of item 8 in mixer to boiling.
37. Dissolve 168.0 g of item 4 and then cool to 25°C.
38. Filter the syrup through a 180-μm stainless steel sieve.
39. Dissolve item 3 in 3.68 g of item 8.
40. Dissolve 4.53 g of item 4 in item 6.
41. Disperse item 5 in about 10.67 g of sugar syrup from the previous step and homogenize.
42. Mix these steps with sugar syrup. Check for evenness of the dispersion.
43. Apply sugar coating.

Bill of Materials: Polishing Coat			
Scale (mg/tablet)	Item	Material Name	Quantity/kg (g)
28.75	1	Bee's wax, bleached (white bee's wax)	28.75
70.00	2	Polyethylene glycol (PEG-6000)	70.00
57.50	3	Carnauba wax	57.50
125.00	4	Talc (fine powder)	125.00
718.75	5	Ethanol, 95%	718.75

44. Melt items 1 to 3 in a steam-heated vessel by gentle heating to 70°C or in a stainless steel container on a hotplate heater.
45. Add item 4 to the vessel or stainless steel container and stir manually.
46. Add item 5 to the vessel or stainless steel container and stir manually.
47. Pass the mixture through a homogenizer.
48. Store the polishing emulsion in a closed container at room temperature.
49. Apply gloss solution.
50. Add item 6 without air to the tablet bed carefully to get a uniform distribution while rolling.
51. After 5 minutes of distribution, turn on the cold air and roll further until a shine appears.
52. Once the desired polish appears, stop rolling the pan.
53. Dry the tablets in the pan at 30°C for 30 minutes. Final tablet weight should be 480 mg.

Ibuprofen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
115.00	1	Lactose	115.00
11.30	2	Povidone	11.30
QS	3	Water, purified	QS
23.00	4	Starch (maize)	23.00
40.00	5	Starch pregelatinized	40.00
11.00	6	French chalk	11.30
1.10	7	Magnesium stearate	1.10
6.80	8	Explotab	6.80
400.00	9	Ibuprofen	400.00

Manufacturing Directions

1. Granulation
   a. Charge the following into a planetary mixer: ibuprofen, starch pregelatinized, and polyvinylpyrrolidone. Mix all for 15 minutes.
   b. Pass the powder through a #40-mesh screen.
   c. Add a sufficient quantity of purified water to form a desirable mass.
   d. Pass the mass through #40 mesh on a dryer tray.
   e. Dry the granules in a fluid-bed dryer or use a fan-forced oven at 50°C to 60°C for 24 hours to dry granules to an LOD of not more than 1%.
   f. Pass the granules through a #40 sieve mesh.
2. Blending
   a. Charge the granules in a planetary mixer. Add maize starch, French chalk (item 6), magnesium stearate, and Explotab, and mix for 20 minutes.
3. Compressing: Compress using a rotary press in round punches. The average weight is 610 mg (± 5%).
4. Coating: Apply a sugar coating. (See Appendix.)

Ibuprofen Tablets (400 mg), Motrin

Ibuprofen, a nonsteroidal antiinflammatory agent, is available in 400-,600-, and 800-mg tablets for oral administration. The inactive ingredients are carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, and titanium dioxide.

Ibuprofen Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Ibuprofen	400.00
43.70	2	Starch (maize)	48.45
18.00	3	Povidone (PVP K-30)	18.00
105.00	4	Starch (maize)	108.13
40.00	5	Starch (maize, dried)	40.00
4.00	6	Colloidal silicon dioxide (Aerosil 200)	4.00
3.45	7	Colloidal silicon dioxide (Aerosil 200)	3.45
1.50	8	Stearic acid	1.50
4.50	9	Magnesium stearate	4.50
–	10	Purified water	163.97

Manufacturing Directions

1. Preparing the paste
   a. Pass item 2 through a sifter using a 630-μm sieve. Prepare a slurry of item 2, with 51.78 g of item 10 (30°C). Pour the slurry into a vessel containing 112.19 g of item 10 (70°C). Heat to 80°C to 90°C, and mix until the material swells and becomes translucent.
   b. Cool to 50°C. Check the weight. The theoretical weight is 212.43 g.
   c. If required, adjust with item 10 (70°C). Record the quantity of extra water added.
2. Mixing: Load items 1, 4, and 3 to the mixer. Mix for 5 minutes at high speed.
3. Wet massing:
   a. Add two-thirds of the starch paste quantity (preparing the paste, step 1b) to the dry powder in the mixer (Diosna). Mix for 4 minutes at low speed. Scrape the sides and blades.
   b. Add the remaining quantity, and mix for 3 minutes at low speed. Scrape the sides and blades.
   c. Mix and chop for a further 2 minutes. Check for a satisfactory wet mass. If required, add additional purified water to obtain a satisfactory wet mass.
4. Drying
   a. Dry the granules in a fluid-bed dryer at 55°C for 3 hours. Keep just enough air pressure in order to bounce the granules. After 1 hour of drying, scrape the semidried granules to break the lumps for uniform drying. Unload in a stainless steel drum. Keep overnight for curing.
   b. Check the moisture content of the dried granules. The limit is not more than 2.5%
5. Grinding: Pass the granules through a 1.25-mm sieve using a granulator. Collect the granules in a stainless steel drum, and add to the blender.
6. Lubricating
   a. Mix items 6 and 8 in a stainless steel drum, and pass through a 500-μm sieve using a sifter. Collect in a stainless steel drum, and add to the blender.
   b. Pass items 5 and 9 through a 250-μm sieve in a sifter. Collect the sieved items in a stainless steel drum, and add to the blender. Mix the materials for 2 minutes.
   c. Unload the result in stainless steel drums.
7. Compressing
   a. Compress the tablets after slugging.
   b. Check the temperature and humidity before starting slugging and compression.
   c. The recommended relative humidity is 45% to 55% at temperatures 25°C to 27°C.
8. Slugging: Slug the granules using a rotary tabletting machine with 16-mm punches.
9. Grinding: Grind the slugs through a 6.0-mm sieve followed by a 1.25-mm sieve. Keep 5.40 g of the granules aside. Load the rest of the ground granules in a blender.
10. Sift 5.4 g of the ground granules from step 9 through a 630-μm sieve using a sifter. Add the retained granules to the blender.
11. Add item 7 into the sieved granules from step 10. Mix in a polythene bag. Sift through a 630-μm sieve using a sifter. Add to the blender, and mix for 2 minutes.
12. Compress the granules using a rotary tabletting machine (12.7-mm concave punches; compress 620 mg).
13. Tablet coating: Coat using Opadry and HPMC coatings. (See Appendix.)

Ibuprofen Tablets (400 mg)

Formulations: Ibuprofen (Francis), 400 g; Aerosil 200, 4 g; Ludipress, 342 g; Kollidon CL, 8 g; magnesium stearate, 8 g.

Manufacturing Directions

1. Pass ibuprofen and magnesium stearate through a 200-μm sieve.
2. Mix with the other components and press with medium-compression force at 752 mg.

Ibuprofen Tablets (600 mg)

Formulations: Ibuprofen 50 (BASF), 600 g; Aerosil 200, 9 g; Avicel PH 200, 108 g; Kollidon VA 64, 50 g; Kollidon CL, 27 g; Macrogol 6000 powder, 6 g.

Manufacturing Directions

1. Mix ibuprofen with Aerosil 200, and add the other components.
2. Press with low-compression force at 793 mg.

Ibuprofen Tablets (600 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
600.00	1	Ibuprofen	600.00
129.80	2	Starch (maize)	144.22
1.15	3	Colloidal silicon dioxide (Aerosil 200)	1.15
70.00	4	Starch (maize)	70.00
5.00	5	Colloidal silicon dioxide (Aerosil 200)	5.00
8.07	6	Stearic acid	8.07
41.15	7	Pregelatinized starch (Starch 1500)	41.15
10.00	8	Magnesium stearate	10.00
–	9	Purified water	469.00

Manufacturing Directions

See the manufacturing directions for 400-mg strength tablet.

Imipramine Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Imipramine hydrochloride	26.00
1.40	2	Polyvinyl pyrroidone	1.40
1.40	3	Magnesium stearate	1.40
1.40	4	Talc	1.40
50.00	5	Lactose monohydrate	50.00
50.00	6	Dicalcium phosphate	50.00
14.00	7	Starch (maize)	14.00
–	8	Isopropyl alcohol, ca	20 mL

Manufacturing Directions

1. Sift through a 250-μm sieve, and charge items 1 and 5 to 7 in a suitable mixing vessel. Mix the items for 10 minutes.
2. In a separate vessel, charge item 2 and a suitable quantity of item 8 to dissolve it.
3. Add step 2 into step 1, and make a suitable wet mass; pass through a 2.38-mm sieve and dry in a dehumidified room overnight.
4. Pass the dried granules through #18 mesh into a blending vessel.
5. Sift items 3 and 4 through a 250-μm sieve, and add to step 4. Blend for 1 minute.
6. Compress into 140-mg tablets, using 7.2-mm punches.

Indomethacin Sustained-Release Tablets (75 mg)

Formulation: Indomethacin (Synopharm), 75 g; Kollidon SR, 125 g; Ludipress LCE, 100 g; silicon dioxide, colloidal, 1.5 g; magnesium stearate, 1.5 g.

Manufacturing Directions

All ingredients are passed through a 0.8-mm sieve, blended for 10 minutes in a mixer, and then compressed with medium-compression force at 303 mg.

Indomethacin Tablets (50 mg), DC

Formulation: Indomethacin, 50 g; Ludipress, 227 g; Kollidon CL, 20 g; magnesium stearate, 3 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force at 303 mg.

Indomethacin Tablets (100 mg)

Formulation: Indomethacin, 100 g; Ludipress, 397 g; magnesium stearate, 3 g.

Manufacturing Directions

1. Mix all components, and pass through a 0.8-mm sieve.
2. Press with low-compression force at 500 mg.
3. If the flowability of indomethacin is not good, it should be mixed with a low percentage of Aerosil 200.

Inosin Tablets

Bill of Materials			
Scale (g/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Inosin (Ribaxin, Russia)	200.00
51.00	2	Lactose monohydrate	51.00
6.00	3	Kollidon® 90F	6.00
QS	4	Isopropanol	60.00 mL
10.00	5	Kollidon® CL	10.00
3.00	6	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with the solvent mixture of items 4.
2. Dry and pass through an 0.8-mm sieve, add items 5 and 6, and press with low-compression force.
3. Compress into 270-mg tablets, using 9-mm biconvex punches.

Irbesartan Tablets (75 mg/150 mg/300 mg), Avapro

Avapro is available for oral administration in unscored tablets containing 75, 150, or 300 mg of irbesartan. Inactive ingredients include lactose, microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, poloxamer 188, silicon dioxide, and magnesium stearate.

Irbesartan Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Irbesartan[a]	75.00
15.38	2	Lactose monohydrate	15.38
22.50	3	Microcrystalline cellulose (Avicel PH 101)	22.50
22.50	4	Pregelatinized starch	22.50
7.50	5	Croscarmellose sodium	7.50
4.50	6	Poloxamer 188 (Pluronic F 68)	4.50
1.12	7	Silicon dioxide colloidal	1.12
1.50	8	Magnesium stearate	1.50
–	9	Water, purified[b]	QS

[a]Use different fill weights for 150-mg and 300-mg strength tablets.
[b]The tablets are prepared by a wet granulation process wherein the total amount of water employed (by weight) is up to 50% of the total solids weight.

Manufacturing Directions

1. Charge irbesartan, lactose, pregelatinized starch, and a portion (one-half) of croscarmellose sodium in a mixer. Mix the materials for 20 minutes.
2. Pass the powder blend in step 1 through sizing equipment (cone mill or oscillator), and mix in a mixer.
3. Dissolve poloxamer 188 in purified water (25% of the weight of total solids), and use it to wet granulate (with the further addition of water in an amount up to 25% of the weight of total solids, as needed) the mixed powder in step 2.
4. Dry the granules (tray or fluid-bed dryer) until the LOD is 2% or less.
5. Pass the dried granules through a screen, or mill them to obtain the proper size (1–3 mm).
6. Mix the sized granules with silicon dioxide, microcrystalline cellulose, and the remaining croscarmellose sodium in a mixer.
7. Add and mix for 1 minute magnesium stearate.
8. Compress 150 mg for 75-mg strength, 300 mg for 150-mg strength, and 600 mg for 300-mg strength.

Iron (Polymer-Coated Particle) Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Elemental iron; use ferrous sulfate polymer-coated particles (233 mg iron per g ferrous sulfate)	450.60
200.00	2	Cellulose microcrystalline	200.00
254.40	3	Lactose monohydrate	254.40
36.00	4	Sodium starch glycolate	36.00
9.00	5	Magnesium stearate	9.00

Note: Factor in potency of ferrous sulfate polymer-coated particles.
Adjust with item 3. Item 1 is prepared by first granulating ferrous sulfate using alcohol and water, drying, and sieving particles over 1200 μm in size. Regranulate smaller particles. Apply enteric (HPMC) coating to the granules in a fluid-bed dryer.

Manufacturing Directions

1. Charge a suitable mixer/blender with microcrystalline cellulose and disperse the ferrous sulfate polymer-coated powder.
2. To this mix, add about half the lactose (item 3) and blend for 5 minutes.
3. Pass the sodium starch glycolate through a 500-μm sieve, followed by about half of the remaining lactose.
4. Add to the mix.
5. Blend for a further 5 minutes.
6. Pass the magnesium stearate (item 5) through a 500-μm sieve, followed by the remaining lactose.
7. Add to the previous mix.
8. Blend for a further 5 minutes.
9. Compress into 950-mg tablets at 8 to 14 kpi, using 8 × 16 mm punches; 16 mm punches; do not rework tablets.
10. Coat the tablets using a HPMC coating solution. (See Appendix.)

Isoniazid Tablets (100 mg)

Bill of Materials			
Scale (mg/Tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Isoniazid	105.00
2.00	2	Starch maize	2.00
1.25	3	Gelatin	1.25
1.25	4	Magnesium stearate	1.25
1.25	5	Talc	1.25
–	6	Water, purified	QS

Manufacturing Directions

1. Sift item 1 through a 250-μm sieve into a blending vessel.
2. In a separate vessel, charge item 3 and a suitable quantity of item 6, heat to 50°C, and dissolve item 3. Then add item 2 into step 1, and form a smooth slurry.
3. Add step 2 and form a suitable wet mass.
4. Pass the wet mass through a 2.38-mm sieve onto paper-lined trays, and dry at 60°C for 8 hours to an LOD of not more than 2.5%. Transfer the wet mass to a suitable blending vessel.
5. Sift items 4 and 5 through a 500-μm sieve, and add to step 4. Blend these materials for 1 minute.
6. Compress into 125-mg tablets, using 7.3-mm punches.

Isosorbide Dinitrate Tablets (5 mg) Indur

Each Ismo tablet contains 20 mg of isosorbide mononitrate. The inactive ingredients in each tablet are D&C Yellow No. 10 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 20, povidone, silicon dioxide, sodium starch glycolate, titanium dioxide, and hydroxypropyl cellulose.

Imdur tablets contain 30, 60, or 120 mg of isosorbide mononitrate in an extended-release formulation. The inactive ingredients are aluminum silicate, colloidal silicon dioxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxide, magnesium stearate, paraffin wax, polyethylene glycol, titanium dioxide, and trace amounts of ethanol.

Isosorbide Dinitrate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Isosorbide dinitrate (40% in Lactose)	13.15
25.00	2	Microcrystalline cellulose (Avicel PH 102)	25.00
58.60	3	Lactose (spray dried)	58.60
0.75	4	Magnesium stearate	0.75
2.50	5	Starch (maize, dried)	2.50

Manufacturing Directions

Note: Protect the product from heat and moisture. Heat and moisture affect the potency of isosorbide.

1. Dry mixing and sieving
   a. Mix items 1 to 3 in a suitable stainless steel drum. Pass these materials through a 630-μm sieve using a sifter. Collect in a stainless steel drum.
   b. Load the powders into the drum blender.
2. Mixing
   a. Mix items 4 and 5 in a bag. Pass the material through 250-μm sieve. Collect in a bag.
   b. Take about 1.25 g powder from step 1b and add to step 2a. Mix manually, and transfer to step 1b.
3. Mix for 5 minutes using a drum blender.
4. Check and record the weight of the granules. The theoretical weight of the granules is 100.0 g.
5. Compression: Compress into 100 mg of the granules using a rotary tabletting machine with 6-mm punches.

Isosorbide Dinitrate Tablets (5 mg)

Formulation: Isosorbide dinitrate + lactose (4 + 6), 12.5 g; lactose monohydrate, 152.1 g; Kollidon 30, 5.4 g; Kollidon CL, 9.0 g; magnesium stearate, 1.0 g.

Manufacturing Directions

1. Mix all components, and pass through a 0.8-mm sieve.
2. Press with low-compression force at 184 mg.

Isosorbide Dinitrate Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Isosorbide dinitrate (40% in lactose)	26.30
50.00	2	Microcrystalline Cellulose (Avicel PH 102)	50.00
117.20	3	Lactose (spray dried)	117.20
1.50	4	Magnesium Stearate	1.50
5.00	5	Starch (maize, dried)	5.00

Manufacturing Directions

See the manufacturing directions for the 5-mg formulation.

Isovaleramide Sustained-Release Tablets

Manufacturing Directions

1. Preparation of the tablet core
   a. Active drug (e.g., Isovaleramide; NPS 1776; Oread, Lawrence, Kans.; cGMP grade) is dispersed by passage through a #30-mesh screen.
   b. Drug, xanthan gum (e.g., XANTURAL; Monsanto, St. Louis, MO; NF grade) and lactose (e.g. monohydrate form, spray dried,: Oread, Palo Alto,CA; NF grade) are mixed into a 1-L glass jar and blended in a mixer for 4 minutes at 96 rpm.
   c. Magnesium stearate (e.g. Oread, Palo Alto,CA; NF grade) is added and the mixture blended for 1 minute.
   d. The final blend is compressed into caplets by using 0.32 in. × 0.75-in. × 0.060-in. tooling to a target weight of 800 mg, target hardness of 8 kPa, and target thickness of 0.25 in.
2. Coating of the tablet cores
   a. Hydroxypropyl methylcellulose (HPMC; e.g., Dow Chemical Co., Midland, MI; NF grade) solution is prepared by adding HPMC slowly to purified water heated to approximately 80°C. The solution is allowed to cool to room temperature by placing vessel in a cold water bath. Additional water is added to prepare the final requisite amount of HPMC solution.
   b. AQUACOAT ECD/dibutyl sebecate mixture is prepared by adding dibutyl sebacate (DBS: e.g., Morflex Inc., Greenboro, NC; NF grade) to AQUACOAT ECD (e.g., FMC Pharmaceutical Division, Philadelphia, PA) while mixing. Mixing is continued for a minimum of 30 minutes.
   c. The HPMC solution is added slowly to the AQUACOAT ECD/DBS mixture.
   d. The core tablets are loaded into a coating apparatus (Vector LCDS 3 coater) fitted with a 1.3-L coating pan and warmed until an outlet temperature of 40°C is reached.
   e. The tablets are spray coated until the planned theoretical weight gain (based on core tablet weight) is achieved; however, after curing, the actual coating solids applied are less than the theoretical value (e.g., 8% or 15% theoretical can be 5% and 12% coat, respectively after curing). Thus, extra spray may need to be added to account for the loss upon curing. Conditions for coating are as follows: Inlet temperature, 70°C; outlet temperature, 40°C to 43°C; spray rate, 4 5 g/min; pan speed, 14 rpm; fluidizing air, 30 40 scfm; atomization air pressure 26 psi.
   f. Spraying is stopped when the requisite amount of coating suspension is applied. The tablets are dried for approximately 5 minutes in the coating pan. The inlet temperature is adjusted during drying to keep outlet temperature below 45°C.
   g. The tablets are cured in an oven at 60°C for 18 hours.

Kaolin–Pectin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
QS	1	Distilled purified water	300 mL
50.00	2	Cornstarch	50.00
50.00	3	Povidone (K-29–32)	50.00
QS	4	Distilled purified water	0.50 L
630.00	5	Hydrated aluminum–magnesium silicate	630.00
100.00	6	Kaolin (powder)	100.00
50.00	7	Pectin	50.00
80.00	8	Cornstarch	80.00
80.00	9	Sodium lauryl sulfate	7.00
10.00	10	Magnesium stearate	10.00

Manufacturing Directions

1. Heat purified water (item 1) to 75°C to 80°C, and add cornstarch (item 2) with continuous stirring until a translucent paste is formed; use this paste within 1 hour.
2. Dissolve Povidone in purified water (item 4) in a separate container. Ensure that dissolution is complete.
3. Charge the following into a suitable planetary mixer: hydrated aluminum–magnesium silicate, kaolin, and pectin.
4. Mix for 5 minutes.
5. Add freshly prepared starch paste from the first step and the Povidone solution to the powder blend from the third step; mix until a mass of suitable consistency is obtained.
6. Add extra purified water, if needed.
7. Spread the wet mass on paper-lined trays and dry in the oven at 50°C for 2 hours.
8. Pass the semidried mass through a 4.8-mm (4-mesh) screen by hand or by using a suitable granulator, and load the granule mass onto paper-lined trays.
9. Dry in the oven at 50°C until the moisture content is between 10.0% and 15.0%.
10. Pass the dried granules through a 1.0-mm (18-mesh) screen on a comminuting mill at medium speed, knives forward, into clean, tared, polyethylene-lined drums; seal and weigh.
11. Transfer the dried granules to a suitable blender.
12. Screen the following items through a 595-μm (30-mesh) screen, and add to the blender: cornstarch (item 8), sodium lauryl sulfate, and magnesium stearate.
13. Blend for 5 to 10 minutes.
14. Compress on a suitable compression machine using 1/2- in. round standard concave punches, upper punch with logo, and lower punch with a bisect line.
15. Compress into 977-mg tablets at 10 to 18 kpi.
16. Coat using an aqueous methocel coating and polish as desired.

Ketotifen Tablets (1 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Ketotifen, use ketotifen fumarate DC	1.38
1.90	2	Magnesium stearate	1.90
32.50	3	Maize starch	32.50
154.20	4	Calcium hydrogen phosphate anhydrous	154.20
QS	5	Water purified	QS

Manufacturing Directions

1. Granulation
   a. Make a 10% paste with maize starch using a sufficient quantity of purified water and one-half the quantity of maize starch.
   b. Add calcium hydrogen phosphate anhydrous with one-half the quantity of the starch paste.
   c. Add one-half the quantity of maize starch with ketotifen; mix in a planetary mixer.
   d. Add mixture from step 1b to 1c, and mix for 5 minutes. Add the balance of the maize starch powder, and mix for another 10 minutes.
   e. Pass the wet mass through a #20-mesh screen over lined trays and dry at 95°C until an LOD of not more than 3% is achieved.
2. Lubrication: Mix dry granules with magnesium stearate for 3 minutes.
3. Compression: Compress using round, flat, beveled edge, scored punch with the logo on one side; diameter is 7 mm, weight is 190 mg.

Khellin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Khellin	25
124.0	2	Ludipress®	124
1.00	3	Magnesium stearate	1

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix intensively, and press.
2. Compress into 150-mg tablets, using 8-mm biplanar punches.

Labetalol Tablets (50 mg)

Formulation: Labetalol, fine powder (Joy Sun), 50.0 g; Ludipress, 98.4 g; Aerosil 200, 0.8 g; Magnesium stearate, 0.8 g.

Manufacturing Directions

1. Mix all components, and sieve through a 0.8-mm screen.
2. Press with low-compression force at 150 mg.

Lamotrigine Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Lamotrigine, 3% excess	103.00
48.00	2	Avicel PH 102	48.00
111.00	3	Lactose monohydrate	111.00
7.00	4	Primojel	7.00
7.00	5	PVP K30	7.00
1.00	6	Iron oxide yellow	1.00
12.00	7	Avicel PH 102	12.00
8.00	8	Primojel	8.00
1.50	9	Magnesium stearate	1.50
1.50	10	Iron oxide yellow	1.50
–	11	Water purified, ca	75 mL

Manufacturing Directions

1. Charge items 1 to 4 after sifting through a 500-μm sieve into a suitable mixer.
2. In a separate vessel, charge items 5, 6 and 11; dissolve and homogenize for 5 minutes at medium speed.
3. Add step 2 to step 1, and knead for 1 to 2 minutes; mix until a suitable mass is obtained.
4. Dry granules on trays at 55°C for 12 hours to and LOD of 0.8%.
5. Grind the dried granules through 1.25-mm sieve.
6. Transfer step 5 to a blender, and add items 7 to 9 after passing them through a 500-μm sieve. Blend for 2 minutes.
7. Compress into 300-mg tablets, using 9.5-mm round punches.

Lansoprazole Tablets (10 mg or 20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lansoprazole	10.00
200.00	2	Calcium glycerophosphate	200.00
400.00	3	Sodium bicarbonate	400.00
12.00	4	Croscarmellose sodium	12.00
3.00	5	Pregelatinized starch	3.00

Lansaprazole Enteric-Coated Tablet

1. Core material non-pareil cores, 400 g; lansoprazole, 400 g; hydroxypropyl methylcellulose, 80 g; sodium lauryl sulfate, 3 g; water purified 1360 g.
2. Separating layer core material (step 1 above), 100 g; hydroxypropyl methylcellulose, 9 g; polyethyleneglycol 6000, 1 g; talc, 18 g; ethanol 95%, 250 g; water purified, 250 g.
3. Enteric coating layer sub-coated pellets (step 2 above), 100 g; hydroxypropyl methylcellulose phthalate, 40 g; acetyltributyl citrate, 8 g; cetanol, 2 g; ethanol 95%, 162 g; acetone, 378 g. Suspension layering is performed in a Wurster equipped fluid-bed apparatus.
4. Lansoprazole is sprayed onto inert non-pareil cores from a water suspension containing lansoprazole, the dissolved binder, and the wetting agent.
5. The prepared core material is coating layered with a separating layer in the same equipment by spraying a suspension of talc in a HPMC/PEG solution. PEG is added to act as a plasticizer for the HPMC.
6. Enteric coating layer is applied in the same equipment by spraying the enteric coating polymer solution (including additives according to above) onto the pellets (layered with a separating layer). The obtained enteric coating layered pellets are mixed with prepared granules and other component as described in example 1, and compressed into effervescent

Lansoprazole Tablets (10 mg or 20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lansoprazole	10.00
175.00	2	Calcium glycerophosphate	175.00
175.00	3	Calcium lactate	175.00
250.00	4	Sodium bicarbonate	250.00
20.00	5	Polyethylene glycol 6000	20.00
12.00	6	Croscarmellose sodium	12.00
3.00	7	Peppermint flavor	3.00
1.00	8	Magnesium silicate	1.00
1.00	9	Magnesium stearate	1.00

Lansoprazole Tablets Chewable (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lansoprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
250.00	4	Sodium bicarbonate	250.00
0.50	5	Aspartame calcium	0.50
12.00	6	Silicon dioxide colloidal	12.00
15.00	7	Starch (maize)	15.00
12.00	8	Croscarmellose sodium	12.00
10.00	9	Dextrose, anhydrous	10.00
3.00	10	Peppermint flavor	3.00
3.00	11	Maltodextrin	3.00
3.00	12	Mannitol	3.00
3.00	13	Pregelatinized starch	3.00

Manufacturing Directions

1. Pass all ingredients through a 250-μm mesh, and blend in a suitable blender.
2. Compress into 672-mg tablets, using 15-mm biplanar punches. For 20-mg tablets, increase the quantity of item 1, and compress an additional 10 mg.

Lansoprazole Tablets, Rapid Dissolution (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Lansoprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
500.00	4	Sodium bicarbonate	500.00
50.00	5	Calcium hydroxide	50.00
12.00	6	Croscarmellose sodium	12.00

Levamisole Hydrochloride Tablets (40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Levamisole hydrochloride, with excess	47.40
10.00	2	Starch (maize)	10.00
20.00	3	Lactose monohydrate	20.00
10.00	4	Sodium starch glycolate	10.00
30.60	5	Starch (maize)	30.60
1.00	6	Magnesium stearate	1.00
5.00	7	Talc	5.00
1.00	8	Aerosil 200	1.00
–	9	Water, purified, ca	50 mL

Manufacturing Directions

1. Sift items 1 to 4 through a 250-μm sieve, and charge in a suitable mixer. Mix the items for 15 minutes.
2. In a separate vessel, charge item 5, mix with hot item 9, and form a smooth slurry.
3. Add step 2 into step 1, and mix the items to achieve a lump-free mass.
4. Pass the wet mass through a #8 sieve onto paper-lined trays.
5. Dry the granules at 50°C overnight to reach an LOD of no more than 2%. Transfer to a blender.
6. Pass items 6 to 8 through a 250-μm sieve, add to step 5, and blend for 2 minutes.
7. Compress into 125-mg tablets, using 7-mm punches.
8. Coat tablets with an HPMC methylene chloride coating. (See Appendix.)

Levamisole Tablets (150 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Levamisole hydrochloride	150.00
300.00	2	Ludipress	300.00
4.00	3	Magnesium stearate	4.00

Manufacturing Directions

1. Mix all components, pass the mixture through a 0.8-mm sieve.
2. Press with low-compression force.
3. Compress into 458-mg tablets, using 12-mm biplanar punches.

Levofloxacin Tablets (250 mg) Levaquin

Levaquin tablets are available as film-coated tablets and contain the following active ingredients: *250 mg (as expressed in the anhydrous form):* hydroxypropyl methylcellulose, crospovidone, microcrystalline cellulose, magnesium stearate, polyethylene glycol, titanium dioxide, polysorbate 80, and synthetic red iron oxide; *500 mg (as expressed in the anhydrous form):* hydroxypropyl methylcellulose, crospovidone, microcrystalline cellulose, magnesium stearate, polyethylene glycol, titanium dioxide, polysorbate 80, and synthetic red and yellow iron oxides.

Levothyroxine Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.05	1	Levothyroxine sodium	0.05
10.00	2	Citric acid anhydrous	10.00
1.00	3	Magnesium citrate	1.00
89.00	4	Ludipress	89.00

Manufacturing Directions

1. Prepare a premix of items 1 and 2. Add items 3 and 4, and pass the mixture through a 0.8-mm sieve.
2. Mix and press with low-compression force.
3. Compress into 101-mg tablets, using 6-mm biplanar punches. Item 2 may be omitted and compensated with item 4. If the content uniformity of formulation No. 1 does not meet the requirements, add a small part of the Ludipress and item 3 mixture, and the mixture of items 1 and 2. The function of citric acid in formulation No. 2 is to stabilize the active ingredient.

Levothyroxine Tablets

The inactive ingredients in synthroid tablets are acacia, confectioner's sugar (contains cornstarch), lactose, magnesium stearate, povidone, and talc. The following are the color additives by tablet strength: *25 mcg:* FD&C Yellow No. 6; *50 mcg:* none; *75 mcg:* FD&C Red No. 40 and FD&C Blue No. 2; *88 mcg:* FD&C Blue No. 1, FD&C Yellow No. 6, and D&C Yellow No. 10; *100 mcg:* D&C Yellow No. 10, FD&C Yellow No. 6; *112 mcg:* D&C Red No. 27 and 30; *125 mcg:* FD&C Yellow No. 6, FD&C Red No. 40, FD&C Blue No. 1; *150 mcg:* FD&C Blue No. 2; *175 mcg:* FD&C Blue No. 1, D&C Red No. 27 and 30; *200 mcg:* FD&C Red No. 40, *300 mcg:* D&C Yellow No. 10, FD&C Yellow No. 6, and FD&C Blue No. 1.

Levothyroxine Tablets (50 mcg) Synthroid

The inactive ingredients in synthroid tablets are as follows: acacia, confectioner's sugar (contains cornstarch), lactose, magnesium stearate, povidone, and talc. The following are the color additives by tablet strength: *25 mcg:* FD&C Yellow No. 6; *50 mcg:* none; *75 mcg:* FD&C Red No. 40 and FD&C Blue No. 2; *88 mcg:* FD&C Blue No. 1, FD&C Yellow No. 6, and D&C Yellow No. 10; *100 mcg:* D&C Yellow No.10, FD&C Yellow No. 6; *112 mcg:* D&C Red No. 27 and 30; *125 mcg:* FD&C Yellow No. 6, FD&C Red No. 40, and FD&C Blue No. 1; *150 mcg:* FD&C Blue No. 2; *175 mcg:* FD&C Blue No. 1 and D&C Red No. 27 and 30; *200 mcg:* FD&C Red No. 40; and *300 mcg:* D&C Yellow No. 10, FD&C Yellow No. 6, and FD&C Blue No. 1.

Levothyroxine Tablets (0.025 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.025	1	Levothyroxine	0.025
11.42	2	Prosolv SMCC 50	11.42
104.29	3	Prosolv SMCC 90	104.29
6.14	4	Sodium starch glycolate	6.14
0.86	5	Magnesium stearate	0.86
0.28	6	FD&C Yellow No. 6	0.28

Manufacturing Directions

1. Add items 1 and 2 in a suitable blender. Blend the items for 10 minutes, and pass through #60 mesh.
2. In a separate container, take 50% of item 3 and item 6, and blend for 10 minutes.
3. Add the balance of item 3 to step 1, and blend for 1 minute.
4. Add step 3 into step 1, and mix.
5. Add items 4 and 5, one at a time, and blend.
6. Compress into 123-mg tablets.

Levothyroxine Sodium Fast-Melt Tablets

Manufacturing Directions

1. Mix levothyroxine sodium, 30%; sodium bicarbonate, 24%; citric acid, anhydrous, 24%; anhydrous lactose, 10%; xylitol, 10%; and sucrose stearate, 2%.
2. Dry the above ingredients at elevated temperatures to significantly reduce the moisture content of each material.
3. Blend for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix LS-EGF (20–80 mesh), 55%; microcrystalline cellulose, 26%; Mannitol, 10%; cross povidone, 5%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; and fumed silicon dioxide, 0.1%.
5. Blend for approximately 5 minutes prior to compression.
6. Levothyroxine sodium tablets are then compressed to a hardness of approximately 1 to 5 kPa (depending upon the dose of the drug) and tablets disintegrate in water in approximately 15 to 35 seconds.

Linezolid Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Linezolid	400.00
40.00	2	Starch (maize)	40.00
78.40	3	Microcrystalline cellulose PH 101	78.40
8.00	4	Hydroxypropyl cellulose	8.00
28.00	5	Sodium starch glycolate	28.00
5.60	6	Magnesium stearate	5.60

Manufacturing Directions

Mix all ingredients, and compress into 560-mg tablets, using 12-mm biplanar punches.

Lisinopril and Hydrochlorothiazide Tablets (10/12.50)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
10.00	1	Lisinopril	10.00
12.50	2	Hydrochlorothiazide	12.50
68.20	3	Dibasic calcium phosphate Anhydrous, DC Grade	68.20
30.00	4	Mannitol	30.00
6.50	5	Starch 1500	6.50
0.50	6	Yellow ferric oxide	0.50
1.00	7	Red ferric oxide	1.00
1.30	8	Magnesium stearate	1.30

Manufacturing Directions

1. Pass item 3 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 2, 5, 6, and 7 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (= 5.20 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 4 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 8 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 130-mg tablets, using a suitable punch (5.0 mm × 6.0 mm, oval).

Lisinopril and Hydrochlorothiazide Tablets (20/12.5)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Lisinopril	20.00
12.50	2	Hydrochlorothiazide	12.50
73.50	3	Dibasic calcium phosphate Anhydrous, DC Grade	73.50
35.00	4	Mannitol	35.00
7.50	5	Starch 1500	7.50
1.50	6	Magnesium stearate	1.50

Manufacturing Directions

1. Pass item 3 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 2, and 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (=5.5 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 4 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 150-mg tablets, using a suitable punch (6.5 mm, round).

Lisinopril and Hydrochlorothiazide Tablets (20/25)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Lisinopril	20.00
25.00	2	Hydrochlorothiazide	25.00
110.50	3	Dibasic calcium phosphate anhydrous, DC grade	110.50
30.00	4	Mannitol	30.00
10.00	5	Starch 1500	10.00
1.50	6	Yellow ferric oxide	1.50
1.00	7	Red ferric oxide	1.00
2.00	8	Magnesium stearate	2.00

Manufacturing Directions

1. Pass item 3 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 2, 5, 6, and 7 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 10% (=5.50 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 4 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 8 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 200-mg tablets, using a suitable punch (6.5 mm × 7.5 mm, oval).

Lisinopril Tablets (10 mg), Zestril

Zestril is supplied as 2.5-, 5-, 10-, 20-, and 40-mg tablets for oral administration. The inactive ingredients are as follows: *2.5-mg tablets:* calcium phosphate, magnesium stearate, mannitol, and starch; *5-, 10-, and 20-mg tablets:* calcium phosphate, magnesium stearate, mannitol, red ferric oxide, and starch; *40-mg tablets:* calcium phosphate, magnesium stearate, mannitol, starch, and yellow ferric oxide.

Lisinopril Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lisinopril	10.00
139.00	2	Ludipress	139.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve.
2. Mix intensively, and press with low-compaction force (10 kN).
3. Compress into 152-mg tablets, using 8-mm biplanar punches.

Lisinopril Tablets (2.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
2.50	1	Lisinopril	2.50
66.50	2	Dibasic calcium phosphate Anhydrous, DC Grade	66.50
25.00	3	Mannitol	25.00
5.00	4	Starch 1500	5.00
1.00	5	Magnesium stearate	1.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass item 1 and item 4 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (= 4.6 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 5 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 100-mg tablets, using a suitable punch (5.0 mm × 5.5 mm, oval).

Lisinopril Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
5.00	1	Lisinopril	5.00
61.50	2	Dibasic calcium phosphate anhydrous, DC grade	61.50
27.00	3	Mannitol	27.00
5.00	4	Starch 1500	5.00
0.50	5	Red ferric oxide	0.50
1.00	6	Magnesium stearate	1.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 20% (= 6.2 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 100-mg tablets, using a suitable punch (5.0 mm, round).

Lisinopril Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
10.00	1	Lisinopril	10.00
81.20	2	Dibasic calcium phosphate Anhydrous, DC Grade	81.20
30.00	3	Mannitol	30.00
6.50	4	Starch 1500	6.50
1.00	5	Red ferric oxide	1.00
1.30	6	Magnesium stearate	1.30

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass item 1, item 4 and item 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (= 6.0 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress to 130-mg tablets, using a suitable punch (5.0 mm × 6.0 mm, oval).

Lisinopril Tablets (15 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
15.00	1	Lisinopril	15.00
89.50	2	Dibasic calcium phosphate Anhydrous, DC Grade	89.50
35.00	3	Mannitol	35.00
7.50	4	Starch 1500	7.50
1.50	5	Red ferric oxide	1.50
1.50	6	Magnesium stearate	1.50

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (= 6.7 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 150-mg tablets, using a suitable punch (7 mm, round).

Lisinopril Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
20.00	1	Lisinopril	20.00
121.00	2	Dibasic calcium phosphate anhydrous, DC grade	121.00
45.00	3	Mannitol	45.00
10.00	4	Starch 1500	10.00
2.00	5	Red ferric oxide	2.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 10% (= 6.0 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 200-mg tablets, using a suitable punch (7.5 mm × 8.0 mm, oval).

Lisinopril Tablets (40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000Tablets (g)
20.00	1	Lisinopril	20.00
121.00	2	Dibasic calcium phosphate Anhydrous, DC Grade	121.00
45.00	3	Mannitol	45.00
10.00	4	Starch 1500	10.00
2.00	5	Red ferric oxide	2.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 10% (= 7.1 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass item 3 through 0.7-mm sieve and charge in step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 250-mg tablets, using a suitable punch (8.0 mm, round).

Lithium Carbonate Tablets

Manufacturing Directions

1. Sodium chloride (8000 g) is milled through a Whistler Mill using a small slotted screen and 60,000 g of lithium carbonate are charged into a 5 ft^3 ribbon blender and the blending is carried out for 5 minutes.
2. The blender is discharged and the powder mixture is passed through a FitzMill at a high speed (hammers). The powder is then returned to the blender and wet granulated (16,000 g of water) with povidone.
3. The binder solution in water is added while the mixer is running. The resultant wet mass is passed through the FitzMill (1/2 in., perforated band, hammers forward) at high speed. The resultant mass is trayed and dried overnight (16 hours at 55°C).
4. The dried mixture is sized through the FitzMill (2A with knives at medium speed). The resultant blend is returned to the ribbon blender.
5. Sorbitol powder is passed through a 40-mesh screen along with Stearowet C (a combination of calcium stearate and sodium lauryl sulfate). 2000 g of the Stearowet C and 8000 g of the sorbitol powder are added to the blender along with 200 g of the sodium starch glycolate and the blend is mixed for 5 minutes.
6. The resultant mixture is compressed into 200,000 tablets using a 3/8-in. standard concave tooling, uppers plain, lowers plain.
7. Each tablet weighs 406 mg and has the following composition: lithium carbonate, 300 mg; sodium chloride, 49 mg; polyvinyl pyrrolidone, 15 mg; Stearowet C, 10 mg; sorbitol, 40 mg; and sodium starch glycolate, 1 mg. The compressed tablets have a hardness of 8 to 10 kPa, a friability of NMT 0.4%, and a thickness of 0.175 in.
8. The tablets are optionally coated using conventional procedures. The tablets are placed in Accela-Cota and 10,000 mL of a conventional clear film seal solution are sprayed thereon. Subsequently, 30,000 mL of a colored film seal (e.g., 1300 g of Opaspray K-1-1243 in 30,000 mL of a clear film seal solution) are sprayed. This is followed by spraying of 10,000 mL of half-strength film and color solution (e.g., 215 g of the same ingredient in 10,000 mL of half-strength film seal solution). The spraying is finished with 5000 mL of half-strength film seal solution. The coated tablets are dried in a pan for 1 hour using 800 to 1000 cfm of air at 30°C to 35°C. They are trayed and dried at 20°C to 23°C overnight. After submission of, e.g., 150 tablets to quality control for approval, the tablets are polished in a pan with 2 g of carnauba wax.

Lomefloxacin Hydrochloride Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Lomefloxacin, use lomefloxacin hydrochloride	442.00
123.00	2	Microcrystalline cellulose	123.00
13.50	3	Croscarmellose sodium Type A	13.50
1.80	4	Hydroxy propyl cellulose	1.80
3.50	5	Silicon dioxide, colloidal	3.50
2.70	6	Polyoxyl 40 stearate	2.70
81.00	7	Starch (maize)	81.00
7.50	8	Magnesium stearate	7.50
—	9	Water, purified, ca	65 mL
QS	10	Ethanol, ca	90 mL

Manufacturing Directions

1. If necessary, mill all items to remove any lumps.
2. Mix in a suitable mixer (double-cone or Y). Before this, sieve items 1 to 3 and item 7 through a 60-mesh screen (0.25 mm). Then mix at medium speed for 15 minutes.
3. In a suitable container, mix disperse items 4 and 6 and add items 9 and 10. Mix until dissolved. Allow to stand overnight.
4. Add the binder solution from step 3 to the mix obtained in step 2, and pass the wet mass through a 20-mesh sieve to obtain granules.
5. Dry the granules at 55°C for 15 hours to get a moisture content of not more than 2.5% (determined at 80°C for 4 hours).
6. Blend the granules with item 5 for over 5 minutes, then add item 8, and mix again for 3 minutes.
7. Compress tablets with a target weight of 675 mg.
8. Coat, using an HPMC coating. (See Appendix.)

Loperamide Hydrochloride Fast-Melt Tablets

Manufacturing Directions

1. Prepare granules by using loperamide hydrochloride, 5%; sodium bicarbonate, 27%; citric acid anhydrous, 27%; tartaric acid, 3%; microcrystalline cellulose, 15%; anhydrous lactose, 8%; xylitol, 12%; and Crodesta F160, 3%.
2. The above ingredients are dried at elevated temperature in the presence of a desiccant to significantly reduce the moisture content of each material.
3. The ingredients are then blended for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) to form granules containing the effervescent ingredients.
4. Granules are passed through a screen and then blended with the following ingredients: LH-EFG (30–80 mesh) 50%, microcrystalline cellulose 31%, Mannitol 8%, AcDiSol 5%, L-HPC LH-11 2%, aspartame 3%, redberry flavor 0.4%, magnesium stearate 0.5%, and Cab-O-Sil M5P 0.1%, which are mixed for 5 minutes prior to compression.
5. Loperamide FICI tablets are then compressed to a hardness of approximately 1 to 3 kPa and tablets disintegrate in purified water in approximately 15 to 35 seconds.

Loperamide Hydrochloride Tablets (2 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Loperamide hydrochloride	2.00
68.00	2	Starch (maize)	68.00
46.00	3	Lactose monohydrate	46.00
3.00	4	Starch (maize)	3.00
56.00	5	Dicalcium phosphate	56.00
2.00	6	Talc	2.00
2.00	7	Magnesium stearate	2.00
—	8	Water, purified, ca	60 mL

Manufacturing Directions

1. Sift items 2, 3, and 5 through a 250-μm sieve, and sift item 1 through #40 mesh. Charge them in a suitable mixing vessel by a geometric dilution process for item 1, and then mix for 30 minutes (this step is critical to content uniformity).
2. Charge item 3 in a suitable vessel, and add item 8. Heat it and mix to prepare a smooth slurry.
3. Add step 2 to step 1 slowly, and mix to obtain a lump-free mass.
4. Pass the wet mass through #6 mesh onto paper-lined trays.
5. Dry the granules in a fluid-bed dryer at 50°C for 1 hour to LOD of not more than 2.5%. Transfer to a blender.
6. Pass item 6 through a 500-μm sieve and item 7 through a 250-μm sieve, and add to step 6; blend for 2 minutes.
7. Compress into 170-mg tablets, using 8-mm punches.

Loratadine and Pseudoephedrine Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Loratidine	25.00
180.00	2	Pseudoephedrine sulfate	180.00
5.00	3	Polyvinylpyrrolidone	5.00
75.00	4	Low-substitutued hyydroxypropyl cellulose	75.00
75.00	5	Crospovidone	75.00
1.50	6	Colloidal silicon dioxide	1.50
250.00	7	Crystalline sugar seeds	250.00
120.00	8	Purified water	120.00

Manufacturing Directions

1. A binder solution is prepared by dissolving 5.0 g of polyvinylpyrrolidone in 120 g of water.
2. 25 g of loratadine, 180 g of pseudoephedrine sulfate, 25 g of microcrystalline cellulose, 75 g of low-substituted hydroxypropyl cellulose, 75 g of crospovidone, and 1.5 g of colloidal silicon dioxide are mixed and screened through a 20-mesh sieve to give a mixed powder.
3. The binder solution of step 1 is sprayed onto 250 g of crystalline sugar seeds in a centrifugal granulator, the mixed powder is dusted onto the crystalline sugar seeds in the centrifugal granulator to afford pellets using the rotation panel rate of 140 to 200 rpm, the spraying rate of the binder solution of 2 to 20 mL/min, air spraying pressure of 1 to 2 kg/cm^2, air spraying volume of 5 to 300 L/min, and powder (step 2) spraying rate of 5 to 30 g/min).

Loratidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Loratidine	10.00
69.93	2	Pregelatinized starch	69.93
69.63	3	Microcrystalline cellulose	69.63
0.37	4	Colloidal silicon dioxide	0.37
0.25	5	Magnesium stearate	0.25

Manufacturing Directions

1. A multistep blending process is used in order to ensure proper distribution of the active. Initially, half of the Starch 1500® is combined with the drug and colloidal silicon dioxide.
2. This mixture is blended in a twin-shell V-blender for 5 minutes.
3. The mixture is then discharged and passed through a 40-mesh screen by hand.
4. This step not only breaks up the silicon dioxide but also helps to distribute the active.
5. The screened mixture is returned to the blender and the remainder of the Starch 1500® is added and blended for an additional 5 minutes.
6. Microcrystalline cellulose is then added and blended for 10 minutes.
7. Magnesium stearate is added last and blended for 5 minutes.
8. Magnesium stearate is passed through a 60-mesh screen prior to weighing.
9. Tablets are compressed at 100 mg or proportionally for different strengths.

Loratidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Loratidine	10.00
67.30	2	Lactose monohydrate	67.30
22.00	3	Maize starch	22.00
10.00	4	Maize starch	10.00
5.00	5	Maize starch, dried	5.00
0.70	6	Magnesium stearate	0.70
QS	7	Purified water	QS

Manufacturing Directions

1. Sift items 1 to 3 through a 630-μm stainless steel sieve, load in mixer, and mix for 5 minutes.
2. In a separate container, prepare binder solution by mixing item 4 using purified water at 30°C to 40°C; heat translucent slurry to 90°C to 95°C, and cool to 45°C to 50°C.
3. Mix the binder solution with the first step, and granulate; dry on trays at 55°C for 8 hours; dry to LOD of 2% to 3% (2 hours after beginning drying, crush mixture for uniform drying).
4. Heat for additional 1 hour at 55°C if LOD is not within limits.
5. Add magnesium stearate, tumble mix, and compress using 7.00-mm round punches to 10 tablet weight of 1.15 (within 3%) to achieve thickness of 2.3 ± 0.3 mm and hardness of 4 to 7 kPa.

Loratidine and Chlorpheniramine Sustained-Release Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Loratidine	5.00
141.50	2	Lactose monohydrate	141.50
55.00	3	Microcrystalline cellulose	55.00
22.00	4	Starch	22.00
1.50	5	Magnesium stearate	1.50
18.00	6	Eudragit S100	18.00
9.00	7	Triethyl citrate	9.00
4.50	8	Talc	4.50
0.315	9	Ammonium hydroxide 1N solution	0.315
qs	10	Water	qs
14.00	11	Eudragit EPO	14.00
8.00	12	Citric acid	8.00
Qs	13	Water	Qs
4.00	14	Chlorpheniramine maleate	4.00
45.00	15	Lactose fine powder	45.00
15.00	16	Sucrose fine powder	15.00
2.00	17	Flavor optional	2.00
0.10	18	Polyvinylpyrrolidone	0.10
Qs	19	Ethanol 95%	Qs
qs	20	Water	qs

Manufacturing Directions

1. Prepare a granulation containing loratadine, lactose, microcrystalline cellulose, and starch.
2. Blend with magnesium stearate for 5 minutes.
3. Compress about 225 mg.
4. Compress the above granulation into CAT unit using tooling and tabletting apparatuses.
5. Prepare the coating solution by mixing water, Eudragit S100, ammonium hydroxide solution, triethyl citrate, and talc to form a uniform dispersion.
6. Coat loratadine from step 3 with Eudragit S coating solution using a coating pan or a fluid-bed coater until a desired coat weight is achieved (256.80).
7. Prepare a coating solution containing Eudragit E and citric acid in water.
8. Coat tablets from step 6 to 278.80 mg.
9. Prepare the solvent mixture containing polyvinylpyrrolidone, ethyl alcohol, and water.
10. Blend chloropheniramine maleate, lactose, sucrose, and flavoring agent. Screen to break lumps.
11. Mix until a moistened powder blend is achieved.
12. Double compress loratidine tablet with chlorpheniramine triturate.
13. The product contains 4 mg of chloropheniramine maleate in the molded triturate tablet for intraoral release and 5 mg of loratadine in the delayed release form as incorporated in the matrix. Enteric-coated loratadine starts to release 4 to 8 hours after administration of the dosage form.

Loratadine and Pseudoephedrine Sulfate Tablets (10 mg/240 mg) Claritin-D

Claritin-D® 12-hour extended-release tablets—These tablets contain 5 mg of loratadine in the tablet coating for immediate release and 120 mg of pseudoephedrine sulfate, which is equally distributed between the tablet coating for immediate release and the barrier-coated extended-release core. The inactive ingredients are acacia, butylparaben, calcium sulfate, carnauba wax, cornstarch, lactose, magnesium stearate, microcrystalline cellulose, neutral soap, oleic acid, povidone, rosin, sugar, talc, titanium dioxide, white wax, and zein.

Claritin-D 24-hour extended-release tablets—These tablets contain 10 mg of loratadine in the tablet film coating for immediate release and 240 mg pseudoephedrine sulfate in the tablet core, which is released slowly, allowing for once-daily administration. The inactive ingredients for oval, biconvex Claritin-D 24-hour extended-release tablets are calcium phosphate, carnauba wax, ethylcellulose, hydroxypropyl methylcellulose, magnesium stearate, polyethylene glycol, povidone, silicon dioxide, sugar, titanium dioxide, and white wax.

Loratidine and Pseudoephedrine Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
240.00	1	Pseudoephedrine sulfate	240.00
15.00	2	Microcrystalline cellulose (Avicel PH 101)	15.00
200.00	3	Xanthan gum Keltrol TF	200.00
80.00	4	Sodium alginate keltone HVCR	80.00
53.00	5	Calcium carbonate	53.00
6.00	6	Magnesium stearate	6.00
6.00	7	Aerosil 200	6.00
10.00	8	Loratadine	10.00
95.00	9	Lactose monohydrate	95.00
66.50	10	Microcrystalline cellulose (Avicel PH 101)	66.50
1.00	11	FD&C Yellow No. 10	1.00
20.00	12	Starch (maize)	20.00
6.00	13	Starch (maize)	6.00
1.50	14	Magnesium stearate	1.50
–	15	Water, purified	60.00

Manufacturing Directions

1. Charge pseudoephedrine sulfate, microcrystalline cellulose, xanthan gum, sodium alginate, calcium carbonate, and one-half of the lubricants in a suitable mixer after sieving through a #44 sieve.
2. Pass the blend through a roll-compactor.
3. Sieve the compact through a #22 sieve to obtain granules.
4. Mix the granules with the remaining lubricants (items 6 and 7), and compress into tablets (600 mg) to form the first tablet layer.
5. Charge items 8 to 12 after passing through a #100 sieve in a suitable mixer. Blend these items for 10 minutes.
6. Charge item 13 in a separate vessel, and make a paste (10%) using item 14.
7. Add step 6 into step 5, and granulate.
8. Dry the granules and blend or sift item 14.
9. Compress into 200-mg tablets (the second layer).
10. Use appropriate tabletting equipment for bilayer tabletting or core tabletting.

Loratidine Fastab

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Loratadine (micronized)	10.00
180.60	2	Pharmaburst	180.60
2.70	3	Acesulfame K	2.70
2.00	4	Magnesium stearate	2.00
2.00	5	Talc (fine powder)	2.00
2.70	6	Dry anise flavor	2.70

Manufacturing Directions

1. Sift and mix items 1, 2, 3, and 6.
2. Lubricate with magnesium stearate and fine talc powder.
3. Compress into 200-mg tablets, using 6-mm punches.

Loratadine Tablets (10 mg), Claritin

Claritin® tablets contain 10 mg of micronized loratadine, an antihistamine, to be administered orally. They also contain the following inactive ingredients: cornstarch, lactose, and magnesium stearate.

Claritin Reditabs (rapidly disintegrating tablets) contain 10 mg of micronized loratadine, an antihistamine, to be administered orally. It disintegrates in the mouth within seconds after placement on the tongue, allowing its contents to be subsequently swallowed with or without water. Claritin Reditabs also contain the following inactive ingredients: citric acid, gelatin, mannitol, and mint flavor.

Loratidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Loratadine	10.00
67.30	2	Lactose monohydrate	67.30
22.00	3	Starch (maize)	22.00
10.00	4	Starch (maize)	10.00
5.00	5	Starch (maize, dried)	5.00
0.70	6	Magnesium stearate	0.70
–	7	Purified water	40.00

Manufacturing Directions

Note: Avoid overmixing the lubricants, otherwise hardness is reduced.

1. Sieving and dry mixing: Sift items 1 to 3 through a stainless steel 630-μm sieve in a sifter. Load into mixer. Mix for 5 minutes at low speed.
2. Preparing the binder: Prepare a slurry of item 4 in 10 g of item 7 (30–40°C). Then make a translucent paste in a Guisti steam jacked vessel, using 30 g of item 7 (90–95°C). Cool to 45°C to 50°C. Check the unity of the paste. The theoretical weight is 50 g.
3. Kneading
   a. Knead the powder with starch paste, while mixing at low speed over a period of 2 minutes.
   b. Scrape sides and backs. Mix and chop at speed 1 for 2 minutes. Check the end point of granulation. If required, add additional purified water to get the end point. (The end point of the granulation is the point when the wet mass consists of little or no lumps of the granules.)
   c. Unload the wet granules into a stainless steel tray for drying.
4. Drying and LOD
   a. Dry the wet granules in an oven at 55°C for 8 hours. After 2 hours of drying, scrape the semidried granules to break any lumps (for uniform drying).
   b. Check the LOD, with a limit of 2% to 3%.
   c. If required, dry further at 55°C for 1 hour. Check the LOD.
   d. Transfer the dried granules into stainless steel drums.
5. Grinding and lubricating
   a. Grind the dried granules through a 1.25-mm sieve using a granulator at medium speed. Collect in stainless steel drums. Load the granules into a drum blender.
   b. Sift items 5 and 6 through a 500-μm sieve using a sifter, and add it into a drum blender. Mix for 2 minutes.
   c. Unload into stainless steel drums.
6. Compressing: Compress the granules using a rotary tabletting machine with a 7-mm flat, bevel-edge punches to 115 mg per tablet.

Lorazepam Tablets (0.50 mg/1 mg/2 mg), Ativan

Ach Ativan tablet, to be taken orally, contains 0.5, 1, or 2 mg of lorazepam. The inactive ingredients present are lactose and other ingredients.

Lorazepam Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	Lorazepam	0.50
50.00	2	Lactose	50.00
20.00	3	Starch (maize)	20.00
2.00	4	Methyl cellulose	2.00
25.00	5	Microcrystalline cellulose (Avicel PH 101)	25.00
1.00	6	Magnesium stearate	1.00

Manufacturing Directions

1. Mix lorazepam, lactose, starch, and one-half of the microcrystalline cellulose in a suitable mixer.
2. Granulate with a solution of methyl cellulose in water.
3. Dry the granules. Mix the remaining microcrystalline cellulose and magnesium stearate. Compress. Adjust the 1- and 2-mg strengths with lactose.

Losartan and Hydrochlorothiazide Tablets (50 mg/12.5 mg)

Hyzaar is available for oral administration, containing 50 mg of losartan potassium, 12.5 mg of hydrochlorothiazide, and the following inactive ingredients: microcrystalline cellulose, lactose hydrous, pregelatinized starch, magnesium stearate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, titanium dioxide, and D&C Yellow No. 10 Aluminum Lake. Hyzaar contains 4.24 mg (0.108 mEq) of potassium.

Losartan Potassium Tablets (50 mg), Cozar

Cozaar is available for oral administration, containing either 25 or 50 mg of losartan potassium and the following inactive ingredients: microcrystalline cellulose, lactose hydrous, pregelatinized starch, magnesium stearate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, titanium dioxide, D&C Yellow No. 10 Aluminum Lake, and FD&C Blue No. 2 Aluminum Lake. Cozaar 25- and 50-mg tablets contain potassium in the following amounts: 2.12 mg (0.054 mEq) and 4.24 mg (0.108 mEq), respectively.

Losartan Potassium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Losartan potassium	50.00
46.00	2	Microcrystalline cellulose	46.00
75.50	3	Lactose, spray dried	75.50
7.50	4	Starch 1500	7.50
1.00	5	Magnesium stearate	1.00
3.00	6	Hypromellose	3.00
0.75	7	Talc, fine powder	0.75
0.75	8	Titanium dioxide	0.75
0.50	9	Polyethylene glycol	0.50
–	10	Ethanol	QS
–	11	Purified water	QS

Manufacturing Directions

1. Sift losartan potassium, lactose spray dried, and microcrystalline cellulose through a stainless steel 500-µm sieve.
2. Load sifted powder into a blender and blend well.
3. Sift magnesium stearate and Starch 1500 through a stainless steel 250-µm sieve.
4. Load step 3 into the blender (step 2), and blend well.
5. Compress into 185-mg tablets, using 12-mm punches.
6. Coat the tablet using Eudragit L-100 coating. (See Appendix.)

Lycopene Tablet Cores (6 mg)

Formulation: LycoVit 10% dry powder, 60 g; Ludipress, 330 g; Kollidon CL, 6 g; magnesium stearate, 4 g.

Manufacturing Directions

1. Mix LycoVit dry powder with the other components.
2. Sieve through a 0.8-mm screen and press with medium- to high-compression force at 400 mg.

Magaldrate Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Magaldrate, USP	500.00
400.00	2	Lactose monohydrate	400.00
50.00	3	Orange flavor (FDO)	50.00
20.00	4	Kollidon® 90F	20.00
6.00	5	Banana flavor (FDO)	6.00
6.00	6	Cocoa flavor (FDO)	6.00
1.00	7	Saccharin sodium	1.00
180.00	8	Water	180.00
5.00	9	Aerosil® 200	5.00
3.00	10	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with solution of items 4 to 8, pass through an 0.8-mm sieve, dry, mix with items 9 and 10, and press with low-compression force.
2. Compress into 1-g tablets, using 16-mm biplanar punches.

Magaldrate Chewable Tablets (500 mg)

Formulation: I—Magaldrate USP, 500 g; lactose monohydrate [8], 400 g; orange flavor (FDO), 50 g. II—Kollidon 90F [1], 20 g; banana flavor (FDO), 6 g; cocos flavor (FDO), 6 g; saccharin sodium, 1 g; water, 180 g. III—Aerosil 200, 5 g; magnesium stearate, 3 g.

Manufacturing Directions

Wet granulation: Granulate mixture I with solution II, pass through a 0.8-mm sieve, dry, mix with III, and press with low-compression force at 1000 mg.

Magaldrate Chewable Tablets (1000 mg)

Formulation: Magaldrate (Reheis), 1000 g; Ludipress LCE, 930 g; Lutrol E4000F [1], 60 g; aspartame, potassium (Searle), 10 g; peppermint flavor, q.s.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force at 2 g.

Magaldrate-Dispersible Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
700.00	1	Magaldrate	700.00
435.00	2	Lactose monohydrate	435.00
10.00	3	Kollidon® 90F	10.00
50.00	4	Kollidon® CL	50.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with low-compression force (4–6 kN).
2. Compress into 1.2-g tablets, using 16-mm biplanar punches.

Magaldrate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Magaldrate (powder, 100 mesh)	400.00
325.00	2	Sucrose	325.00
60.00	3	Cellulose (microcrystalline) (Avicel™ PH101)	60.00
30.00	4	Cornstarch	30.00
8.84	5	Guar gum	8.84
0.50	6	Saccharin sodium	0.50
–	7	Purified water	100.00 mL
–	8	Alcohol SD 3A (200 proof)	100.00 mL
QS	9	Flavor	0.60 mL
QS	10	Flavor	1.00 mL
0.06	11	Ethyl vanillin	0.06
8.00	12	Talc	8.00
16.00	13	Magnesium stearate	16.0

Manufacturing Directions

1. Pass granulated sugar (take about 10% excess) through 500-μm stainless steel screen on comminuting mill (impact forward, high speed).
2. Screen the milled sugar through 250-μm aperture on sieve shaker.
3. Weigh the required quantity and charge into a suitable mixer.
4. Discard remaining sugar.
5. Screen magaldrate powder (take about 5% excess) through 150-μm stainless steel screen on sieve shaker.
6. Weigh the required quantity and add to the blend above.
7. Mix well.
8. Screen, if necessary, microcrystalline cellulose, cornstarch, and guar gum through 500-μm aperture on sieve shaker.
9. Add to the first step and mix well.
10. Dissolve saccharin sodium in water.
11. To this add alcohol and mix well.
12. Add this hydroalcoholic solution to magaldrate blend and knead well.
13. Add more water, if necessary, and QS to mass.
14. Pass wet mass through 2.8-mm aperture on sieve shaker or oscillating granulator and spread uniformly on stainless steel trays.
15. Tray-dry granules at 70°C to 75°C.
16. After 3 to 4 hours of drying, screen semidried granules through 1.4-mm aperture on sieve shaker, and reload for further drying.
17. (This step helps in drying granules faster and more uniformly.) Dry to LOD of 1% to 1.5%.
18. Screen dried granules through 1.0-mm aperture on sieve shaker, and store in drums doubly lined with polyethylene bags.
19. Charge half of the granulation into a suitable blender.
20. From the balance of the granules, take out the fines (about 40 g of fines for a batch of 1000 tablets) through 250-μm aperture on sieve shaker.
21. Retain coarse particles for later use.
22. Mix together the flavors in a suitable vessel.
23. Add and dissolve the ethyl vanillin.
24. Check that the solution is clear before proceeding.
25. Charge a suitable mixer with the fines from above.
26. While mixing, disperse the flavor solution.
27. Add magnesium stearate and talc and mix thoroughly.
28. Pass the blend through a 250-μm aperture on sieve shaker.
29. Add the dispersed flavor blend to the granules.
30. Add remaining granules and blend for 8 to 10 minutes.
31. Discharge blended granules into suitable air-tight containers doubly lined with polyethylene bags.
32. Compress on a suitable machine fitted with 14.4-mm-diameter round punches with beveled edges.
33. Weight: 8.5 g/10 tablets; thickness: ~3.6 to 3.8 mm; hardness: 8 to 10 kPa.

Magaldrate with Simethicone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
525.00	1	Sucrose, NF	525.00
15.00	2	Lactose monohydrate, NF	15.00
60.00	3	Simethicone, USP	60.00
60.00	4	Cellulose microcrystalline (Avicel™ PH101), NF	60.00
12.00	5	Silione dioxide colloidal (International)	12.00
400.00	6	Magaldrate, USP	400.00
40.00	7	Acacia (special grade), NF	40.00
0.05	8	Dye	0.05
–	9	Distilled purified water, USP	100.00 mL
–	10	Alcohol SD 3A (200 proof)	100.00 mL
1.50	11	Flavor	1.50
0.15	12	Ethyl vanillin, NF	0.15
5.00	13	Silicon dioxide (colloidal)	5.00
30.00	14	Starch monohydrate	30.00
10.00	15	Lactose monohydrate	10.00
80.00	16	Talc powder, USP	80.00
5.30	17	Magnesium stearate	5.30

Manufacturing Directions

1. Pass the granulated sucrose (with about 10% excess) through a 500-μm-aperture stainless steel screen on comminuting mill (impact forward, high speed).
2. Screen the milled sugar through a 250-μm screen on sieve shaker.
3. Weigh the required quantity and charge into a suitable mixer (planetary mixer or dough mixer). Discard the remainder.
4. Screen lactose (item 2) through a 250-μm aperture screen on sieve shaker and add to powdered sugar from step above. Mix well.
5. While mixing vigorously, add and disperse simethicone (add slowly in a fine stream of flow to avoid lump formation). Mix well.
6. Rough blend colloidal silicon dioxide (item 5) and microcrystalline cellulose, and add to the simethicone dispersed mass from previous step.
7. Mix initially at low speed for 4 to 5 minutes and thereafter mix vigorously for 5 to 10 minutes.
8. Either screen simethicone dispersed mass through a 1.0-mm aperture on sieve shaker or pass through a comminuting mill using a 1.4-mm aperture screen (impact forward, medium speed).
9. Load into a mass mixer and continue mixing.
10. Screen magaldrate powder (with about 7% excess) through a 150-μm aperture screen on sieve shaker and weigh the required quantity.
11. To this quantity add acacia and rough blend.
12. Add this blend in the dough mixer, dispersing in small quantities, and mix well for 30 to 40 minutes until simethicone is well absorbed in the dry blend. Discard remaining magaldrate powder.
13. Dissolve dye in water, then add alcohol, and mix well.
14. Wet down mass with colored hydroalcoholic solution and knead well.
15. Add more hydroalcoholic solution, if necessary (1:1 water-to-alcohol ratio), to mass.
16. Screen wet mass through a 2.8-mm aperture screen on sieve shaker or oscillating granulator and spread uniformly on trays.
17. Tray-dry granules at 71°C to 74°C until LOD is within 1% to 1.5% (test at 105°C for 1 hour).
18. After about 3 to 4 hours of drying, screen semidried granules through a 1.4-mm aperture on sieve shaker and reload for further drying.
19. (*Note*: This step helps in drying granules faster and more uniformly and avoids color mottling on final product.) Screen dried granules through a 1.0-mm aperture screen on sieve shaker, and store in drums lined with double polyethylene bags. Alternative drying can be done in a fluid-bed dryer.
20. Pass dried granules through a 1.00-mm aperture screen on sieve shaker.
21. Pass coarse granules through a comminuting mill using a 1.4-mm aperture screen (knives forward, slow speed) and then through 1.0-mm aperture on sieve shaker.
22. Store granules in drums lined with double polyethylene bags.
23. Charge half of the base granulation into a suitable blender.
24. From the balance of the granules take out fines (about 50 g of fines for a batch of 1000 tablets) through a 250-μm aperture on sieve shaker, and hold in a suitable vessel.
25. Add and dissolve ethyl vanillin in liquid flavor.
26. Check for clarity and only then disperse over dried starch.

27. Rough blend colloidal silicon dioxide (item 13) with lactose monohydrate (item 15), talc, and magnesium stearate, and add to the flavored starch.
28. To this mixture, add fines from the second step above, and mix well by hand or in a suitable mixer.
29. Screen through a 250-µm aperture on sieve shaker.
30. Add this flavored, dispersed blend to the base granulation (first step) in a blender.
31. Add the remaining bulk granules from the second step to the base granulation and blend well for 8 to 10 minutes. (*Caution*: Do not mix for too long as the granules may crumble to a finer size, which may adversely affect hardness during compression.) Discharge blended granules into suitable airtight containers lined with double polyethylene bags until ready for compressing.
32. Compress on a suitable machine fitted with 14.4-mm-diameter round punches with beveled edges. Compress into 1244-mg tablets.

Magnesium Carbonate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
260.00	1	Magnesium carbonate, USP	262.00
238.00	2	Ludipress®	238.00
4.00	3	Magnesium stearate	4.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with medium-compression force.
2. Compress into 500-mg tablets, using 12-mm biplanar punches.

Mebendazole Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Mebendazole	100.00
196.00	2	Ludipress	196.00
4.00	3	Magnesium stearate	4.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 294-mg tablets, using 12-mm biplanar punches.

Meclizine Hydrochloride Tablets (25 mg)

Meclizine hydrochloride tablets are multiple-layered tablets (MLT) available in 12.5-, 25-, and 50-mg strengths for oral administration. Each tablet contains the following inactive ingredients: colloidal silicon dioxide, lactose, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, starch, stearic acid, and other ingredients. In addition, the 12.5-mg tablet contains FD&C Blue No. 1; the 25-mg tablet contains D&C Yellow No. 10 and FD&C Yellow No. 5; and the 50-mg tablet contains D&C Yellow No. 10, FD&C Blue No. 1, and FD&C Yellow No. 5.

Medroxyprogesterone Acetate Tablets (2.5 mg/5 mg/10 mg), Provera

Each Provera tablet for oral administration contains 2.5, 5, or 10 mg of medroxyprogesterone acetate. The inactive ingredients are calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sucrose, and talc. The 2.5-mg tablet contains FD&C Yellow No. 6.

Mefenamic Acid and Dicyclomine Hydrochloride Tablets (250 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Mefanamic acid	250.00
10.00	2	Dicyclomine hydrochloride	10.00
30.00	3	Lactose monohydrate	30.00
16.00	4	Starch (maize)	16.00
4.80	5	Gelatin	4.80
3.20	6	Polyvinylpyrrolidone potassium 30	3.20
6.00	7	Talc	6.00
6.00	8	Magnesium stearate	6.00
6.00	9	Sodium starch glycolate	6.00
4.00	10	Aerosil 200	4.00
0.80	11	Methyl paraben	0.80
0.08	12	Propyl paraben	0.08
–	13	Water, purified, ca	75 mL

Manufacturing Directions

1. Charge items 1 to 3 in a suitable mixer after passing them through a 250-μm sieve. Mix the items for 10 minutes.
2. In a separate vessel, bring to boil item 13 and add items 11 and 12 at 90°C to dissolve. Add items 4 to 6 to the hot solution, and stir to disperse into a smooth slurry. Cool to 50°C.
3. Add step 2 into step 1, and mix thoroughly to obtain a lump-free wet mass. Pass the wet mass through a 2.38-mm sieve onto paper-lined trays. Dry the granules at 50°C overnight until an LOD of not more than 2% is reached.
4. Pass the dried granules through a 1.19-mm mesh screen into a suitable tumbler.
5. Sift items 9 and 10 through a 500-μm sieve and item 8 through a 250-μm sieve into step 4, and blend for 3 minutes.
6. Compress into 335-mg tablets, using 9.5-mm punches.

Mefenamic Acid Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Mefenamic acid	250.00
40.00	2	Starch (maize)	40.00
5.00	3	Kollidon 90F	50.00
–	4	Isopropyl alcohol	QS
12.00	5	Kollidon CL	12.00
85.00	6	Microcrystalline cellulose (Avicel PH 101)	85.00
5.00	7	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate a mixture of items 1 and 2 with the solution of items 3 and 4, sieve, dry, and add a mixture of items 5 to 7.
2. Compress with medium-compression force. Compress into 404-mg tablets, using 12-mm punches.

Mefloquine Hydrochloride Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00 275.00	1	Mefloquine, use mefloquine hydrochloride	250.00 275.00
50.00	2	Lactose monohydrate	50.00
65.00	3	Maize (starch)	65.00
3.00	4	Polyoxyl 40 stearate	3.00
10.00	5	Polyvinyl pyrrolidone (PVP K-30)	10.00
65.00	6	Microcrystalline cellulose (Avicel PH 102)	65.00
25.00	7	Crospovidone (Kollidone CL)	25.00
2.00	8	Magnesium stearate	2.00
5.00	9	Talc, fine powder	5.00
QS	10	Purified water	QS

Manufacturing Directions

1. Sift mefloquine hydrochloride, lactose monohydrate, and maize starch through a 0.500-mm stainless steel sieve.
2. Dissolve polyoxyl 40 stearate and PVP K-30 in purified water (70–80°C) by slow stirring, until it becomes clear. Cool the solution to 25°C to 30°C. This is the granulating solution.
3. Knead the powder mix with granulating solution to get the desired wet mass.
4. Pass the wet mass through #8 mesh onto drying trays.
5. Dry the granules to a targeted LOD of 2%.
6. Pass the dried granules through #16 mesh.
7. Sift Avicel PH 102 and Kollidone CL through a 0.500-mm stainless steel sieve.
8. Load the ground granules from step 5 and the powder mix from step 6 into a suitable blender. Blend for 2 minutes to get a homogeneous mixture.
9. Sift magnesium stearate and talc fine powder through a stainless steel 500-μm sieve. Add the powder mix in step 7. Blend these items for 1 minute.
10. Compress into 500-mg tablets, using 15-mm suitable punches.
11. Coat using a hypermellose coating. (See Appendix.)

Meprobamate and Phenobarbital Tablets (400 mg/30 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Meprobamate	400.00
30.00	2	Phenobarbital	30.00
76.00	3	Microcrystalline cellulose (Avicel PH 101)	76.00
13.00	4	Kollidon VA 64	13.00
21.00	5	Kollidon CL	21.00
8.00	6	Talc	8.00
1.00	7	Aerosil 200	1.00
1.00	8	Calcium arachinate	1.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with low-compression force.
2. Compress into 551-mg tablets, using 12-mm biplanar punches.

Meprobamate and Phenobarbital Tablets (400 mg/30 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Meprobamate	400.00
30.00	2	Phenobarbital	30.00
13.00	3	Kollidon VA 64	13.00
—	4	Isopropyl alcohol	QS
21.00	5	Kollidon CL	21.00
50.00	6	Starch (maize)	50.00
8.00	7	Talc	8.00
1.00	8	Aerosil 200	1.00
1.00	9	Calcium arachinate	1.00

Manufacturing Directions

1. Granulate a mixture of items 1 and 2 with a solution of items 3 and 4. Dry, pass through a 0.8-mm sieve, mix with items 5 to 9, and press with low-compression force.
2. Compress into 559-mg tablets, using 12-mm biplanar punches.

Meprobamate Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Meprobamate	400.00
80.00	2	Microcrystalline cellulose (Avicel PH 101)	80.00
30.00	3	Starch (maize)	30.00
20.00	4	Kollidon VA 64	20.00
20.00	5	Kollidon CL	20.00
7.00	6	Talc	7.00
3.00	7	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force (20 kN).
2. Compress into 560-mg tablets, using 12-mm biplanar punches.

Meprobamate Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Meprobamate	400.00
100.00	2	Starch (maize)	100.00
15.00	3	Kollidon 25 or Kollidon VA 64	15.00
4.50	4	Lutrol E 400[a]	4.50
–	5	Isopropyl alcohol	QS
2.00	6	Talc	2.00
0.20	7	Aerosil 200	0.20
0.30	8	Calcium arachinate	0.30

[a]Use only if selecting Kollidon 25 as item 3.

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 to 5. Pass through a 0.8-mm sieve, add items 6 to 8, and press.
2. Compress into 520-mg tablets (515 mg if deleting item 4), using 12-mm biplanar punches.

Metamizol Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metamizol sodium (dipyrone)	500.00
100.00	2	Ludipress	100.00
10.00	3	Kollidon CL	10.00
10.00	4	Magnesium stearate	10.00

Manufacturing Directions

1. Mix all components, pass through a 0.5-mm sieve, and press with low-compression force.
2. Compress into 625-mg tablets, using 12-mm biplanar punches.

Metamizol Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metamizol sodium (dipyrone)	500.00
100.00	2	Microcrystalline cellulose (Avicel PH 101)	100.00
15.00	3	Kollidon 30	15.00
25.00	4	Kollidon CL	25.00
1.00	5	Aerosil 200	1.00
8.00	6	Talc	8.00
1.00	7	Calcium arachinate	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.5-mm sieve, and press with low-compression force.
2. Compress into 654-mg tablets, using 12-mm biplanar punches.

Metformin Hydrochloride Biphasic Tablet

Manufacturing Directions

1. 25 g of ethylcellulose N10 NF is dissolved/dispersed in 100 mL of 95% ethanol.
2. This dispersion is gradually added to 500 g of metformin hydrochloride in a planetary mixer to produce a uniform damp granulation.
3. The granulation is dried at 55°C for 1 hour and passed through a 0.8 mm aperture screen to break down agglomerates.
4. The metformin–ethylcellulose granules (541 g) are blended with 351.5 g of hydroxypropyl methylcellulose 2208 USP (100,000 cps grade), 10 g of hydroxypropyl methylcellulose 2910 USP (5 cps grade), and 100.5 g of microcrystalline cellulose in a planetary mixer for 10 minutes.
5. Finally this mix is lubricated with 1% w/w magnesium stearate and compressed into capsule shaped tablets, each containing 500 mg of metformin hydrochloride.

Metformin Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin hydrochloride	500.00
100.00	2	Dicalcium phosphate	100.00
15.00	3	Kollidon 90F	15.00
8.00	4	Kollidon 90F	8.00
—	5	Isopropyl alcohol	90.00
5.00	6	Kollidon CL	5.00
15.00	7	Polyethylene glycol 6000 powder	15.00

Manufacturing Directions

1. Granulate the mixture of items 1 to 3 with the solution of items 4 and 5. Mix these granules with items 6 and 7, pass through a 0.8-mm sieve, and press with medium-compression force.
2. Compress into 650-mg tablets, using 12-mm biplanar punches. If hardness is the problem, reduce the amount of Kollidon 90F.

Metformin Hydrochloride Tablets, Extended Release (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin hydrochloride	500.00
240.00	2	Lactose anhydrous	240.00
250.00	3	Hydroxypropyl cellulose	250.00
5.00	4	Colloidal silicon dioxide	5.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

1. Pass items 1 to 4 through a 250-μm mesh, and charge in a suitable blender. Mix these materials for 15 minutes.
2. Add item 5, and mix for 3 to 7 minutes.
3. Compress 1000 mg to a hardness of 16 to 20 kPa in a suitable 15-mm punch. Adjust the weight and punch size for lower or higher strength.

Metformin Tablets (500 mg)

Metformin HCl tablets contain 500 and 850 mg of metformin HCl. In addition, each tablet contains the following inactive ingredients: povidone, magnesium stearate, and hydroxypropyl methylcellulose (hypromellose) coating.

Metformin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin hydrochloride	500.00
190.00	2	Lactose anhydrous	190.00
300.00	3	Polyethylene oxide	300.00
5.00	4	Colloidal silicon dioxide	5.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

Compress 1000 mg; adjust the weight for higher or lower strength.

Metformin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin hydrochloride	500.00
160.00	2	Lactose anhydrous	160.00
330.00	3	Hydroxypropyl cellulose	330.00
5.00	4	Colloidal silicon dioxide	5.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

Compress 1000 mg; adjust the weight for lower or higher strength.

Metformin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin hydrochloride	500.00
45.90	2	Dibasic calcium phosphate	45.90
329.60	3	Hydroxypropyl cellulose	329.60
92.70	4	Ethyl cellulose	92.70
51.50	5	Povidone	51.50
5.15	6	Colloidal silicon dioxide	5.15
5.15	7	Magnesium stearate	5.15

Compress 1030 mg; adjust the weight for higher or lower strength.

Metformin Tablets, Extended Release (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metformin	500.00
240.00	2	Lactose monohydrate	240.00
250.00	3	Hydroxypropyl cellulose	250.00
5.00	4	Silicon dioxide colloidal	5.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

1. Charge items 1 to 3 in a suitable blending vessel, after passing through a 250-μm sieve.
2. Sift items 4 and 5 through a 250-μm sieve, and add to step 1.
3. Blend for 3 to 5 minutes.
4. Compress into 1000-mg tablets at 18 to 20 kp.

Methenamine Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Methenamine powder	500.00
0.50	2	Gelatin powder	0.50
4.50	3	Magnesium stearate	4.50

Manufacturing Directions

1. Accurately weigh methenamine, gelatin, and magnesium stearate.
2. Mix methenamine and gelatin in a suitable blender for 15 minutes. Add magnesium stearate, and mix for additional 5 minutes.
3. Compress into 505-mg tablets, using 3/8-in. round punch at 5 kg of pressure.

Methyclothiazide and Deserpidine Tablets (5 mg/0.25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Methyclothiazide	5.00
0.25	2	Deserpidine	0.25
7.80	3	Starch (corn)	7.80
166.80	4	Lactose monohydrate	166.80
6.80	5	Starch (corn)	6.80
QS	6	Water, purified, ca	30 mL
6.80	7	Talc	6.80
1.50	8	Magnesium stearate	1.50

Manufacturing Directions

Caution: This is an expensive preparation—keep losses to a minimum. Deserpidine is poisonous—handle carefully. Maintain a low relative humidity during processing and storing.

1. Granulation
   a. Load methyclothiazide, deserpidine, and starch (item 3) together with an equal quantity of lactose into a mixer, and blend for 30 minutes. Cover the mixing bowl during this operation.
   b. Pass blended materials from step 1 through a 250-μm sieve aperture screen at high speed (hammers forward using an Apex mill or similar mill).
   c. Load the milled ingredients from step 2 into the mixer, add the balance of the lactose, and dry blend for 30 minutes.
   d. Mix starch (item 5) with 30 mL of cold purified water, and heat to make a paste.
   e. Add the hot starch paste to the blended powders in the mixer, and mass for 1 to 3 minutes. *Note:* Overmixing and overwetting will prolong tablet disintegration time.
   f. Pass the wet mass through a 4.76-mm aperture screen, and spread onto trays.
   g. Load trays of wet granulation into the oven, and dry for 4 hours at 49°C. *Note:* It is essential to use a full oven load of trays.
   h. Remove the dried granulation from the oven, and pass through an 840-μm aperture screen, or pass mill-dried granulation through a 600-μm aperture screen using a FitzMill, impact forward, high speed into polyethylene-lined drums. Tie liners tightly. *Note:* The FitzMill method may improve dissolution.
2. Lubrication
   a. Load approximately 20% of granulation into blender.
   b. Mix talc and magnesium stearate, while milling through a 600-μm aperture screen, impact forward, high speed on a FitzMill or similar mill, and load into the blender.
   c. Charge the remaining granulation into blender, and *blend only for 14 minutes. Note:* If lumps are present after several minutes of blending, it may be necessary to put the entire granulation through a 1.19-mm aperture, and then continue blending to the required time. Also note that overblending results in increased tablet disintegration time.
   d. Discharge into polyethylene-lined drums. Seal containers well.
3. Compression: Compress using standard 7-mm concave square punches.

Methyclothiazide Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
5.20	1	Starch (corn)	5.20
QS	2	Dyes	QS
5.00	3	Methyclothiazide	5.00
9.40	4	Starch (corn)	9.40
166.40	6	Lactose monohydrate	166.40
QS	7	Water, purified, ca	25 mL
6.80	8	Talc	6.80
2.00	9	Magnesium stearate	2.00

Manufacturing Directions

1. Granulation and lubrication
   a. Make starch paste, using cornstarch (item 1) and purified water.
   b. Mix dyes with item 3, cornstarch (item 4), and an equal amount of lactose, and mill through a comminuting mill using a 177-μm aperture screen, impact forward, high speed. Charge into the mixer. Add the balance of lactose to the mixer (mill through a 420-μm aperture screen, impact forward, high speed, if lumpy), and dry mix for 10 minutes.
   c. Add hot starch paste from step 1 to the mixer. Mix until granular but not longer than 5 minutes. If necessary, 1.8 mL of purified water may be added to wet the mass during mixing. *Note:* Over mixing and over wetting will prolong the tablet disintegration time.
   d. Granulate the wet mass through a comminuting mill, using a 15.88-mm aperture band, and spread on trays.
   e. Dry at 60°C until the LOD is 1%, or less, when tested for 60 minutes in a Brabender (or equivalent) set at 105°C.
   f. Sift the dried granulation through a 1.19-mm aperture screen, and mill the coarse material through a comminuting mill fitted with a 1.59-mm aperture band, knives forward, at medium speed.
   g. Charge one-half of the granulation into the blender. Mix talc and magnesium stearate, while milling through a 600-μm aperture screen, impact forward, high speed, and charge into the blender. Charge the remaining half of the granulation into the blender, and *blend only for 4 minutes*.
   h. Discharge a portion of the granulation from the blender, and check for white lumps. If present, discharge the entire granulation from the blender through a 1.19-mm aperture screen to break lumps, and then return to the blender. Charge the remaining granulation into the blender, and *blend only for 10 minutes*. *Note:* Over blending results in increased tablet disintegration time.
   i. Discharge the blender into tared, polyethylene-lined drums. Seal, weigh, and deliver the drums to the storage area.
2. Compress using concave 7.1-mm punches; weight is 195 mg (to be determined based on amount of dyes used).

Methyl Cysteine Tablets (100 mg)

Formulation: Methyl cysteine hydrochloride, 100 g; Ludipress, 200 g; magnesium stearate, 3 mg; menthol, 4 mg

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with low-compression force at 307 mg.

Methylphenidate Hydrochloride Tablets Extended Release (18 mg/36 mg), Concerta

Concerta also contains the following inert ingredients: butylated hydroxytoluene, carnauba wax, cellulose acetate, hydroxypropyl methylcellulose, lactose, phosphoric acid, poloxamer, polyethylene glycol, polyethylene oxides, povidone, propylene glycol, sodium chloride, stearic acid, succinic acid, synthetic iron oxides, titanium dioxide, and triacetin. Concerta uses osmotic pressure to deliver methylphenidate HCl at a controlled rate. The system, which resembles a conventional tablet in appearance, comprises an osmotically active trilayer core surrounded by a semipermeable membrane with an immediate-release drug overcoat. The trilayer core is composed of two drug layers containing the drug and excipients and a push layer containing osmotically active components. There is a precision-laser-drilled orifice on the drug-layer end of the tablet. In an aqueous environment, such as the gastrointestinal tract, the drug overcoat dissolves within 1 hour, providing an initial dose of methylphenidate. Water permeates through the membrane into the tablet core. As the osmotically active polymer excipients expand, methylphenidate is released through the orifice. The membrane controls the rate at which water enters the tablet core, that, in turn, controls drug delivery. The biologically inert components of the tablet remain intact during gastrointestinal transit and are eliminated in the stool as a tablet shell, along with insoluble core components.

Methylergotamine Malate Tablets (0.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	Methylergotamine malate, 10% excess	0.55
0.15	2	Maleic acid	0.15
5.25	3	Starch (maize)	5.25
47.08	4	Lactose monohydrate	47.08
1.00	5	Starch (maize)	1.00
0.50	6	Stearic acid	0.50
2.30	7	Talc	2.30
2.30	8	Magnesium stearate	2.30
	9	Water, purified, ca	60 mL

Manufacturing Directions

1. Sift items 2, 4, and 5 through a 250-μm sieve in a suitable mixing vessel. Mix the items for 5 minutes.
2. In a separate vessel, charge item 5 and add a sufficient amount of hot item 9 to make a paste.
3. Add step 2 into step 1, and make a suitable wet mass. Pass the wet mass through a 2.38-mm sieve onto drying trays.
4. Dry the granules at 50°C overnight to an LOD of not more than 3%.
5. Pass the granules through a #20-mesh sieve into a blending vessel.
6. Pass item 1 through a 250-μm sieve, and, using a geometric dilution with granules in step 5, add and mix item 1 into step 5.
7. Pass items 6 and 7 through a 500-μm sieve and item 8 through a 250-μm sieve, and add all three items to step 6. Blend for 2 minutes. (Do not over blend.)
8. Compress into 58-mg tablets, using 3-mm punches.
9. Provide a sugar coating to a final weight of 100 mg per tablet and a diameter of 5 mm. (See Appendix for sugar coating formulations.)

Methylprednisolone Tablets (2 mg/4 mg/8 mg/16 mg/24 mg/32 mg), Medrol

Each Medrol tablet for oral administration contains 2, 4, 8, 16, 24, or 32 mg of methylprednisolone. The inactive ingredients found in Medrol are as follows. *2 mg:* calcium stearate, cornstarch, erythrosine sodium, lactose, mineral oil, sorbic acid, and sucrose; *4 and 16 mg:* calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, and sucrose; *8 and 32 mg:* calcium stearate, cornstarch, FD&C Yellow No. 6, lactose, mineral oil, sorbic acid, and sucrose; *24 mg:* calcium stearate, cornstarch, FD&C Yellow No. 5, lactose, mineral oil, sorbic acid, and sucrose.

Metoclopramide Tablets (10 mg), Reglan

Reglan tablets (metoclopramide tablets, USP), 10 mg, are white, scored, capsule-shaped tablets engraved with "Reglan" on one side and "AHR 10" on the opposite side. Each tablet contains 10 mg of metoclopramide base (as the monohydrochloride monohydrate). The inactive ingredients are magnesium stearate, mannitol, microcrystalline cellulose, and stearic acid.

Reglan tablets, 5 mg, are green, elliptical-shaped tablets engraved with "Reglan 5" on one side and "AHR" on the opposite side. Each tablet contains 5 mg of metoclopramide base (as the monohydrochloride monohydrate). The inactive ingredients are cornstarch, D&C Yellow No. 10 Lake, FD&C Blue No. 1 Aluminum Lake, lactose, mic rocrystalline cellulose, silicon dioxide, and stearic acid.

Metoclopramide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Anhydrous metoclopramide hydrochloride; use metoclopramide hydrochloride	10.54
7.00	2	Maize starch (dried)	7.00
1.00	3	Silicon dioxide (colloidal)	1.00
0.76	4	Magnesium stearate	0.76
5.00	5	Starch (pregelatinized)	5.00
101.24	6	Lactose	101.24
QS	7	Purified water	~15.00 mL

Manufacturing Directions

1. Dried maize starch must be used for lubrication.
2. Dry the starch at 80°C for 36 hours prior to its use in manufacturing.
3. Check LOD of starch; the LOD must be less than 2.0%.
4. Pass the lactose, pregelatinized starch, and metoclopramide hydrochloride through a 1.25-mm aperture screen, and transfer it to a suitable mass mixer; mix for 5 minutes.
5. Add the water slowly to the mixer, and mix for 30 minutes or until a suitable consistency is obtained. Add extra water, if required.
6. Pass the mass through a 4.80-mm aperture screen or an oscillating granulator (or by hand), and dry in a tray dryer or fluid-bed dryer at 50°C until the moisture content is below 5.5%.
7. Pass the granules through a 875-μm aperture screen on an oscillating granulator (or comminuting mill at medium speed, knives forward) into tared, polyethylene-lined drums; seal and weigh.
8. Carry out remaining steps at a relative humidity below 50% and temperature below 26°C.
9. Transfer the dried granulation to a suitable blender.
10. Screen the starch (item 2), magnesium stearate, and silicon dioxide through a 250-μm aperture screen on a sieve shaker, and add to the blender.
11. Blend for 10 minutes.
12. Discharge the granules into polyethylene-lined drums; seal and weigh for yield.
13. Compress into 1.255-g per 10 tablets, using 6.35- or 7.14-mm standard concave punches.

Metoclopramide Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Metoclopramide hydrochloride	10.00
89.50	2	Ludipress	89.50
0.50	3	Magnesium stearate	0.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force.
2. Compress into 100-mg tablets, using 6-mm biplanar punches.

Metoclopramide Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Metoclopramide hydrochloride anhydrous, use metoclopramide hydrochloride	10.54
7.00	2	Starch (maize), dried	7.00
1.00	3	Silicon dioxide colloidal	1.00
0.76	4	Magnesium stearate	0.76
5.00	5	Starch pregelatinized	5.00
101.24	6	Lactose	101.24
–	7	Water purified (deionized)	15.00 mL

Manufacturing Directions

1. Granulation
   Note: Dried cornstarch must be used for lubrication. Dry the starch at 80°C for 36 hours before its use in manufacturing. Check the LOD of the starch. The LOD must be less than 2% (1 hour on Brabender at 105°C or equivalent).
   a. Pass the lactose, starch pregelatinized, and metoclopramide hydrochloride through a 1.25-mm aperture screen, transfer to a suitable mass mixer, and mix for 5 minutes.
   b. Add the water slowly to the mixer, and mix for 30 minutes or until a suitable consistency is obtained. Add extra water if required.
   c. Pass the mass through a 4.8-mm aperture screen or an oscillating granulator (or by hand), and dry in a tray dryer or fluid-bed dryer at 50°C until the moisture content is below 5.5%.
   d. Arrange for samples.
   e. Pass the granule through an 875-μm aperture screen on an oscillating granulator (or comminuting mill at medium speed, knives forward) into tared polyethylene-lined drums. Then seal the drums and weigh.
2. Lubrication
   Note: Carry out at a relative humidity below 50% and temperature below 26°C.
   a. Transfer the dried granulation to a suitable blender.
   b. Screen the starch (item 2), magnesium stearate, and silicon dioxide through a 250-μm sieve aperture screen on a sieve shaker, and add to the blender. Blend for 10 minutes.
   c. Discharge the granules into polyethylenelined drums, seal, and weigh for yield.
3. Compressing
   Note: Carry out at a relative humidity below 50% and at temperature below 26°C.
   a. Compress using 7.14-mm round, standard concave punches or 6.35-mm round, standard concave punches.
   b. Compress to the following specifications: weight of 10 tablets = 1.255 g ± 3%.

Metoprolol Succinate Tablets (95 mg) Toprol

Toprol-XL is formulated to provide a controlled and predictable release of metoprolol for once-daily administration. The tablets comprise a multiple unit system containing metoprolol succinate in a multitude of controlled-release pellets. Each pellet acts as a separate drug delivery unit and is designed to deliver metoprolol continuously over the dosage interval. The tablets contain 47.5, 95, and 190 mg of metoprolol succinate equivalent to 50, 100, and 200 mg of metoprolol tartrate, USP, respectively. The inactive ingredients are silicon dioxide, cellulose compounds, sodium stearyl fumarate, polyethylene glycol, titanium dioxide, and paraffin.

Metoprolol Succinate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
95.00	1	Metoprolol succinate	95.00
25.00	2	Polyoxol 40 hydrogenated	25.00
230.00	3	Hydroxypropyl methyl cellulose	230.00
94.00	4	Aluminum silicate	94.00
–	5	Alcohol	QS

Manufacturing Directions

1. Mix metroprolol with polyoxyl 40 hydrogenated castor oil, and then carefully mix it with the carrier materials (HPMC and aluminium silicate).
2. Granulate the mixture with ethanol, and dry the granules.
3. Add lubricant, and compress.

Metoprolol Tartrate Tablets

Metoprolol tartrate is a selective β_1-adrenoreceptor blocking agent, available as 50- and 100-mg tablets for oral administration and in 5-mL ampules for intravenous administration. Each ampule contains a sterile solution of metoprolol tartrate (5 mg) and sodium chloride (45 mg). Metoprolol tartrate is (±)-1-(isopropylamino)-3-(*p*-(2-(methoxyethyl)phenoxy)-2-propanol (2:1) *dextro*-tartrate salt.

Metoprolol tartrate is a white, practically odorless, crystalline powder with a molecular weight of 684.82. It is very soluble in water; freely soluble in methylene chloride, in chloroform, and in alcohol; slightly soluble in acetone; and insoluble in ether.

The Lopressor tablets contain the following inactive ingredients: cellulose compounds, colloidal silicon dioxide, D&C Red No. 30 Aluminum Lake (50-mg tablets), FD&C Blue No. 2 Aluminum Lake (100-mg tablets), lactose, magnesium stearate, polyethylene glycol, propylene glycol, povidone, sodium starch glycolate, talc, and titanium dioxide.

Metronidazole Tablet Cores (400 mg)

Formulation: Metronidazole, 400 g; Avicel PH 102, 150 g; Kollidon VA 64, 25 g; Kollidon CL, 15 g; Aerosil 200, 5 g; polyethylene glycol 6000, powder, 50 g;

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with high-compression force (25–30 kN) at 645 mg.

Metronidazole Tablets (200 mg)

Formulation: Metronidazole, 200 g; Avicel PH 101, 200 g; Kollidon, 6 g; Kollidon CL, 10 g; Aerosil 200, 5 g; magnesium stearate, 5 g;

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with high-compression force (25–30 kN) at 426 mg.

Metronidazole Effervescent Vaginal Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Materials Name	Quantity/1000 Tablets (g)
500.00	1	Metronidazole	500.00
600.00	2	Sodium bicarbonate	600.00
30.00	3	Kollidon 30	30.00
10.00	4	Kollidon 30	10.00
–	5	Isopropyl alcohol	150 mL
500.00	6	Tartaric acid	500.00
50.00	7	Polyethylene glycol 6000 powder	50.00

Manufacturing Directions

1. Granulate items 1 and 2 with the solution of items 3 and 4. Pass through a 0.8-mm sieve, mix with items 6 and 7, and press.
2. Compress into 1700-mg tablets, using 16-mm biplanar punches.

Metronidazole, Furazolidone, and Loperamide Tablets (200 mg/25 mg/2 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Metronidazole	200.00
25.00	2	Furazolidone	25.00
2.00	3	Loperamide	2.00
200.00	4	Starch (maize)	200.00
175.00	5	Dicalcium phosphate	175.00
5.00	6	Gelatin	5.00
110.00	7	Starch (maize)	110.00
1.16	8	Yellow dye	1.16
4.00	9	Magnesium stearate	4.00
2.00	10	Talc	2.00
–	11	Water, purified, ca	500 mL

Manufacturing Directions

1. Sift items 1, 2, 4, and 5 through a #40-mesh sieve into a mixing vessel.
2. Mix for 10 minutes, and use this mix to dilute item 1 into the same vessel.
3. In a separate vessel, heat item 11°C to 90°C, and add items 6 to 8. Stir to make a smooth slurry containing 30% starch.
4. Add the slurry in step 3 into step 2, and mix until a suitable mass for granulation is obtained.
5. Pass the wet mass through a 2.38-mm sieve onto paper-lined trays.
6. Dry the granules at 50°C overnight to meet an LOD of not more than 2.5%.
7. Pass the dried granules through a 1.19-mm mesh into a blending vessel.
8. Pass item 9 though a 250-µm sieve and item 10 through a 500-µm sieve into step 6. Blend for 2 minutes.
9. Compress into 680-mg tablets, using 13-mm punches.

Metronidazole Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Metronidazole	200.00
200.00	2	Avicel PH 101	200.00
6.00	3	Kollidon 30	6.00
10.00	4	Kollidon CL	10.00
5.00	5	Aerosil 200	5.00
5.00	6	Magnesium stearate	5.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force (25–30 kN).
2. Compress into 426-mg tablets, using 12-mm biplanar punches.

Metronidazole Tablets (200 mg/400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Metronidazole	400.00
150.00	2	Lactose monohydrate	150.00
37.50	3	Starch (corn)	37.50
30.00	4	Povidone K 29–32	30.00
37.50	5	Starch (corn)	37.50
QS	6	Water, purified	121.00 mL
13.00	7	Starch (corn)	13.00
1.25	8	Magnesium stearate	1.25

Note: For 200-mg strength, scale down the BOM proportionally, as given above, and compress using a 9.5-mm round, standard concave punch. The thickness should be 4.3 to 4.9 mm (range: *not more than* ± 5%); hardness: NTL 7 to 17 kPa; disintegration time: *not more than* 15 minutes in water.

Manufacturing Directions

1. Granulation
   a. Make a starch paste using starch (corn) (item 3) and purified water (distilled) (item 6) in a stainless steel container.
   b. Pass the following items through a 595-μm aperture screen, and transfer to a suitable mixer: metronidazole, lactose, and starch (corn) (item 5).
   c. Add the povidone to the mixer, and mix for 5 minutes.
   d. Add the starch paste from step 1 to the mixer, and mix until a suitable consistency mass is obtained. Add extra water if required.
   e. Pass the wet mass through a 2.36-mm screen on a suitable granulator.
   f. Spread the granules on paper-lined trays, and dry in an oven at 50°C until the moisture content is not more than 5.5%.
   g. Request samples for moisture content.
   h. Pass the dried granules through a 1.59-mm aperture screen on a suitable comminuting mill, at medium speed, with knives forward, into tared, polyethylene-lined drums. Then seal the drums and weigh.
2. Lubrication
   a. Transfer the dried granulation to a suitable blender.
   b. Screen the following items through a 595- μm aperture screen, and add the following to the blender: starch (corn) (item 7) and magnesium stearate. Blend for 5 minutes.
   c. Discharge the granule into polyethylenelined drums, seal, and weigh for yield.
3. Compression: Compress using 12.7-mm round, standard concave punches.
4. Coating: Coat using a methocel coating. (See Appendix.)

Metronidazole Tablets (400 mg)

Metronidazole is an oral synthetic antiprotozoal and antibacterial agent, 1-(β-hydroxyethyl)-2-methyl-5-nitroimidazole. Metronidazole tablets contain 250 mg or 500 mg of metronidazole. Inactive ingredients include cellulose, FD&C Blue No. 2 Lake, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol, stearic acid, and titanium dioxide.

Bill of Materials			
Scale (mg/tablet)	Item	Materials Name	Quantity/1000 Tablets (g)
400.00	1	Metronidazole	400.00
150.00	2	Avicel PH 102	150.00
25.00	3	Kollidon VA 64	25.00
15.00	4	Kollidon CL	15.00
5.00	5	Aerosil 200	5.00
50.00	6	Polyethylene glycol 6000, powder	50.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force (25–30 kN).
2. Compress into 645-mg tablets, using 12-mm biconvex punches.

Metronidazole Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Metronidazole	500.00
220.00	2	Sorbitol, crystalline	220.00
10.00	3	Kollidon 90F	10.00
–	4	Ethanol 96%, ca	75.00
20.00	5	Kollidon CL	20.00
4.00	6	Talc	4.00
0.50	7	Aerosil 200	0.50
0.50	8	Calcium arachinate	0.50

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with the solution of items 3 and 4. Pass the mixture through a 0.8-mm sieve, dry it, mix it with items 5 to 7, and press it with medium-compression force.
2. Compress into 755-mg tablets, using 16-mm biplanar punches.

Midodrine Hydrochloride Controlled-Release Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Midodrine hydrochloride	15.00
18.80	2	Microcrystalline cellulose PH101	18.80
65.20	3	Lactose monohydrate	65.20
1.00	4	Sodium carboxymethyl cellulose	1.00
28.00	5	Water	28.00

Manufacturing Directions

1. The following preparation provides a zero-order release profile.
2. Items 1 to 4 are mixed in mixer intensely.
3. Apply item 5 to step 2 and continue mixing until wet properly.
4. Extrude the mass in step 3 through a screen with apertures between 0.4 and 1.0 mm to give spheronized pellets with smooth surface.
5. Apply inner coat using a fluid-bed to increase the weight of pellets by 8.5% w/w using hydroxypropylmethylcellulose (13.5 g), magnesium stearate (2.9 g), talc (25.2 g), Eudragit NE 30 D (895.1 g), and purified water (1135.4 g).
6. Apply outer coat in a fluid-bed to increase the weight by another 1% w/w using hydroxypropylmethylcellulose (20.0 g), talc (20.0 g), and purified water (460.0) g.
7. The release profile can be changed by mixing fractions of pellets with different amounts of inner coating applied or the release profile can be changed by coating with other acrylic resins such as Eudragit RL 30 D, Eudragit RS 30 D or combinations thereof, or using other types of film forming agents such as ethylcellulose or silicone polymers. Furthermore, the release profile can be changed by applying a fraction of non-coated pellets or by applying an enteric coating to a fraction of pellets.

Midodrine Hydrochloride Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Midodrine hydrochloride	50.00
2.00	2	Klucel MF	2.00
93.00	3	Methocel E50	93.00
1.50	4	Midodrine hydrochloride	1.50
6.6	5	Klucel MF	6.6
156.90	6	Methocel E50	156.90
2.80	7	Midodrine hydrochloride	2.80
247.20	8	Methocel E50	247.20
1.20	9	Midodrine hydrochloride	1.20
9.70	10	Methocel E50	9.70
8.50	11	Talc	8.50

Manufacturing Directions

1. Ingredients 1 to 3, 4 to 6, and 7 to 8 are compressed as the core, the first, and the second layer, respectively. Using the core composition, a core weighing 100 mg is compressed using a punch 6 mm in diameter. The core is compression coated using 165 mg of the 1st compression layer composition and a punch of 9 mm in diameter. The thus compression-coated core is compression coated again using 250 mg of the 2nd compression layer composition and a punch of 11 mm in diameter.
2. Ingredient 9 to 11 are applied as spray coating.

Midodrine Hydrochloride Triple Layer Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Midodrine hydrochloride	5.00
2.00	2	Klucel MF	2.00
93.00	3	Methocel E50	93.00
1.50	4	Midodrine hydrochloride	1.50
6.60	5	Klucel MF	6.60
156.90	6	Methocel E50	156.90
2.80	7	Midodrine hydrochloride	2.80
247.20	8	Methocel E50	247.20
1.20	9	Midodrine hydrochloride	1.20
9.70	10	Methocel E5	9.70
8.50	11	Talc	8.50

Manufacturing Directions

1. Items 1 to 3 are compressed to form a core using 6-mm diameter punch.
2. Coat the core using items 4 to 6 using 9-mm diameter punch.
3. Coat the tablet above (step 2) with items 7 to 8 using 11-mm diameter punch.
4. Spray coat step 3 with items 9 to 11.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.66	1	Midodrine hydrochloride	1.66
48.34	2	Hydroxypropylmethyl cellulose E50	48.34
10.00	3	Croscarmellose sodium	10.00
0.62	4	Midodrine hydrochloride	0.62
126.38	5	Hydroxypropylmethyl cellulose E15	126.38
135.00	6	Hydroxypropylmethyl cellulose K100 LV8	135.00
1.99	7	Midodrine hydrochloride	1.99
143.01	8	Hydroxypropyl methyl cellulose E50	143.01
1.79	9	Hydroxypropylmethyl cellulose E5	1.79
1.25	10	Talc	1.25
0.36	11	Propylene glycol	0.36
0.73	12	Midodrine hydrochloride	0.73
3.58	13	Hydroxypropylmethyl cellulose E5	3.58
2.51	14	Talc	2.51
0.71	15	Propylene glycol	0.71

Manufacturing Directions

1. Compress core using 6-mm punch using items 1 to 3.
2. Compress core in step 1 with items 4 to 6 in 9-mm diameter punch.
3. Compress tablet in step 2 using items 7 and 8 using 11-mm diameter punch.
4. Apply coating by spray method using items 9 to 12.
5. Apply coating by spray method using items 12 to 15.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Midodrine hydrochloride	10.00
340.00	2	Klucel LF	340.00
0.20	3	Methocel E5	0.20
0.10	4	Magnesium stearate	0.10
0.40	5	Talc Ponderax	0.40
0.0048	6	Antifoam agent	0.0048
4.50	7	Eudragit NE 30D	4.50
1.80	8	Methocel E5	1.80
1.80	9	Talc Ponderax	1.80

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Midodrine hydrochloride	10.00
340.00	2	Klucel MF	340.00
0.20	3	Methocel E5	0.20
0.10	4	Magnesium stearate	0.10
0.40	5	Talc Ponderax	0.40
0.0048	6	Antifoam	0.0048
4.50	7	Eudragit NE30D	4.50
1.80	8	Methocel E5	1.80
1.80	9	Talc Ponderax	1.80

Manufacturing Directions

1. Core: items 1 and 2.
2. Insoluble inner coat: items 3 to 7.
3. Soluble outer coat: items 8 and 9.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Core (non pareil)	200.00
4.00	2	Midodrine hydrochloride	4.00
0.30	3	Methocel E5M	0.30
0.06	4	Magnesium stearate	0.06
0.50	5	Talc Ponderax	0.50
0.004	6	Antifoam agent	0.004
5.20	7	Eudragit NE 30D	5.20
3.00	8	Midodrine hydrochloride	3.00
0.30	9	Methocel E5M	0.30
0.06	10	Magnesium stearate	0.06
0.50	11	Talc ponderax	0.50
0.004	12	Antifoam	0.004
6.10	13	Eudragit NE 30D	6.10
2.00	14	Midodrine hydrochloride	2.00
0.30	15	Methocel E5 M	0.30
0.08	16	Magnesium stearate	0.08
0.70	17	Talc ponderax	0.70
0.006	18	Antifoam	0.006
1.00	19	Midodrine hydrochloride	1.00
0.40	20	Methocel E5M	0.40
0.08	21	Magnesium stearate	0.08
1.00	22	Talc ponderax	1.00
0.006	23	Antifoam	0.006
78.00	24	Eudragit NE 30D	78.00
1.00	25	Methocel E5	1.00
1.00	26	Talc ponderax	1.00

Manufacturing Directions

1. Coat item with items 2 to 7.
2. Coat step 1 with items 8 to 13.
3. Coat step 2 with items 14 to 18.
4. Coat step 3 with items 19 to 24.
5. Coat step with final outer coat with items 25 and 26
6. Cure tablets at 70°C

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Non-pareil seeds	200.00
4.00	2	Midodrine hydrochloride	4.00
0.30	3	Paraffin solid	0.30
0.10	4	Acetyltributyl citrate	0.10
1.90	5	Ethylcellulose	1.90
0.028	6	Aerosil 200	0.028
3.00	7	Midodrine hydrochloride	3.00
0.30	8	Paraffin solid	0.30
0.10	9	Acetyltributylcitrate	0.10
2.20	10	Ethylcellulose	2.20
0.032	11	Aerosil 200	0.032
2.00	12	Midodrine hydrochloride	2.00
0.40	13	Paraffin solid	0.40
0.20	14	Acetyltributyl citrate	0.20
2.80	15	Ethyl cellulose	2.80
0.04	16	Aerosil 200	0.04
0.50	17	Paraffin solid	0.50
0.20	18	Acetyltributyl citrate	0.20
3.30	19	Ethylcellulose	3.30
0.05	20	Aerosil 200	0.05

Manufacturing Directions

1. Coat item 1 with items 2 to 6.
2. Coat step 1 with items 7 to 11.
3. Coat step 2 with items 12 to 16.
4. Final outer coat use items 17 to 20.

Montelukast Sodium Tablets Mirtazapaine, Rameron, Singulair

Each 10-mg film-coated Singulair tablet contains 10.4 mg of montelukast sodium. Remeron is supplied for oral administration as scored film-coated tablets containing 15 or 30 mg of mirtazapine and unscored film-coated tablets containing 45 mg of mirtazapine. Each tablet also contains cornstarch, hydroxypropyl cellulose, magnesium stearate, colloidal silicon dioxide, lactose, and other inactive ingredients. Singular tablet is equivalent to 10 mg of free acid, and the following inactive ingredients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, hydroxypropyl cellulose, and magnesium stearate. The film coating consists of hydroxypropyl methylcellulose, hydroxypropyl cellulose, titanium dioxide, red iron oxide, yellow iron oxide, and carnauba wax.

Each 5-mg chewable Singulair tablet contains 5.2 mg of montelukast sodium, which is the molar equivalent to 5 mg of free acid, and the following inactive ingredients: mannitol, microcrystalline cellulose, hydroxypropyl cellulose, red ferric oxide, croscarmellose sodium, cherry flavor, aspartame, and magnesium stearate.

Morphine Sulfate and Granisetron Hydrochloride Sustained-Release Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Morphine sulfate	30.00
130.00	2	Hydroxypropyl methyl cellulose	130.00
70.00	3	Lactose monohydrate	70.00
10.00	4	Polyvinylpyrrolidone	10.00
2.00	5	Silicon dioxide	2.00
1.12	6	Granisetron hydrochloride	1.12
60.00	7	Lactose fine powder	60.00
5.00	8	Sucrose fine powder	5.00
1.00	9	Flavor	1.00
0.06	10	Polyvinylpyrrolidone	0.06
qs	12	Ethyl alcohol 95%	qs
qs	13	Water	qs

Manufacturing Directions

1. Prepare a granulation blend containing morphine sulfate, hyproxypropyl methylcellulose, lactose, and polyvinylpyrrolidone. Add silicon dioxide and stearic acid to the granulation and blend for additional 5 to 10 minutes.
2. Compress the above morphine sulfate sustained-release granulation using appropriate tooling and tabletting machine to fill weight of 244 mg.
3. Prepare the solvent mixture containing polyvinylpyrrolidone in water or a mixture of water and ethanol.
4. Blend Granisetron hydrochloride, lactose, sucrose, and the flavoring agent. Screen to break lumps.
5. Add the mixture of step 3 to that of step 4, while mixing until a moistened powder blend is achieved.
6. Compress about 67.80 mg of moistened blend with morphine sulfate tablet.

Morphine Sulfate Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
24.00	1	Morphine sulfate	24.00
27.00	2	Sodium bicarbonate	27.00
27.00	3	Citric acid anhydrous	27.00
10.00	4	Microcrystalline cellulose	10.00
10.00	5	Xylitol	10.00
2.00	6	Sucrose stearate	2.00

Manufacturing Directions

1. Morphine sulfate is dried at 100°C for 2 to 4 hours to reduce the moisture content of the material. Other ingredients are dried at 40°C to 60°C to significantly reduce the moisture content of the material.
2. Items 1 to 6 are blended for 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent couple.
3. Granules are then screened and blended with the ingredients: MS-EGF (30–60 mesh), 50%; microcrystalline cellulose, 31%; Mannitol, 10%; AcDiSol, 5%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; Cab-O-Sil M5P, 0.1%, for 5 minutes prior to compression.
4. Morphine sulfate tablets are then compressed to a hardness of approximately 1 to 5 kPa and tablets disintegrate in water in approximately 15 to 35 seconds.

Multivitamin and Beta-Carotene Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
7.00	2	Beta-carotene; use beta-carotene dry powder (10%, Pharma)	70.00
2.20	3	Thiamine mononitrate	2.20
2.20	4	Riboflavin	2.20
6.50	5	Nicotinamide	6.50
11.50	6	Calcium D-pantothenate	11.50
2.20	7	Pyridoxine hydrochloride	2.20
0.06	8	Cyanocobalmine; use cyanocobalamin dry powder (0.1%)	6.00
85.00	9	Ascorbic acid (powder)	85.00
32.00	10	Vitamin E acetate (dry powder; SD 50)	32.00
210.00	11	Ludipress®	210.00
7.00	12	Kollidon® VA 6 4	7.00
3.00	13	Magnesium stearate	3.00
7.00	14	Orange flavor	7.00
2.50	15	Saccharin sodium	2.50

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 448-mg tablets, using 12-mm planar punches.

Multivitamin and Carbonyl Iron Tablets

Bill of Materials			
Scale (per tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5000 IU	1	Vitamin A acetate (dry powder; 500000 IU/g)	10.00
2.20 mg	2	Thiamine mononitrate, BASF	2.20
2.20 mg	3	Riboflavin	2.20
16.50 mg	4	Nicotinamide	16.50
11.50 mg	5	Calcium D-pantothenate	11.50
2.20 mg	6	Pyridoxine hydrochloride	2.20
6.00 mg	7	Cyanocobalamin (dry powder; 0.1%)	6.00
85.00 mg	8	Ascorbic acid (powder)	85.00
31.00 mg	9	Vitamin E acetate (dry powder; SD 50)	31.00
311.00 mg	10	Ludipress®	311.00
10.00 mg	11	Carbonyl iron (powder OF)	10.00
3.00 mg	12	Magnesium stearate	3.00
7.20 mg	13	Orange flavor	7.20
2.50 mg	14	Saccharin sodium	2.50

Manufacturing Directions

1. Mix all ingredients, pass through an 0.8-mm sieve, mix, and press with high-compression force (20 kN).
2. Compress into 500-mg tablets, using 12-mm biplanar punches.

Multivitamin and Fluoride Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.20	1	Riboflavin; use coated riboflavin (25% excess)	5.28
0.30	2	Folic acid (powder)	0.31
1.00	3	Fluoride; use sodium fluoride (powder)	2.21
19.50	4	Starch (Bright Yellow 2 LA)	19.50
1.05	5	Pyridoxine; use pyridoxine hydrochloride (6% excess)	4.02
1.05	6	Thiamine HCl; use coated thiamine mononitrate (5% excess)	3.21
13.50	7	Niacin; use nicotinamide	40.20
4.50 μg	8	Vitamine B12; use cyanocobalamin oral powder in starch (10% excess)	5.17
20.00	9	Ascorbic acid; use surface-coated ascorbic acid and sodium	21.00
40.00	10	Sodium ascorbate; use surface-coated sodium ascorbate (5% excess)	47.25
7.49	11	Anhydrous citric acid	7.49
15 IU	12	Vitamin E; use vitamin E (*d,l*-α-tocopheryl) (5% excess)	31.50
400 IU (10 μg)	13	Vitamin D; use vitamin D3 beadlets (25% excess)	0.65
9.36	14	Flavor	9.36
2500 IU or 0.75 mg	15	Vitamin A; use vitamin A palmitate beadlets (500 mU/g), USP (60% excess)	8.25
500.60	16	Sugar (compressible)	500.60

Manufacturing Directions

Manufacture this product at less than 40% relative humidity and a temperature below 26.7°C.

1. If lumpy, hand screen riboflavin through an 8-mesh screen, and then mix with folic acid, sodium fluoride powder, and approximately 3.5 g of Bright Yellow starch in a suitable blender until the yellow color of premix is uniform.
2. Cross-feed the premixed items, pyridoxine hydrochloride, thiamine mononitrate, nicotinamide, cyanocobalamin oral powder in starch, ascorbic acid, citric acid, and vitamin E through an 846-μm screen on a comminuting mill (knives forward, medium speed).
3. Transfer the powders to a suitable blender.
4. Clear mill with a part of the compressible sugar, and transfer to the blender.
5. Charge vitamin D3 beadlets, sodium ascorbate, flavor, and vitamin A palmitate into the blender.
6. Blend for 10 minutes.
7. Discharge the contents of the blender into polyethylene-lined drums.
8. Pass the remaining compressible sugar through an 846-μm screen on a comminuting mill (knives forward, medium speed).
9. Transfer to the blender.
10. Screen the material from previous step, magnesium stearate, and the remaining Bright Yellow starch through an 846-μm screen, and transfer to the blender. (*Note*: Mill material not passing through the screen through an 846-μm screen on a comminuting mill at medium speed with knives forward.) Blend for 20 minutes.
11. Discharge blender into polyethylene-lined drums, and weigh for yield.
12. Use precompression, if available, to obtain a tablet with adequate friability.
13. Coat as needed. (See Appendix.)

Multivitamin and Mineral Tablets

Bill of Materials			
Scale (per tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4000 IU/400 IU	1	Vitamin A/vitamin D crystalets (500000 A/50000 D per g) (25% excess)	10.00
40.00 mg	2	Vitamin A acetate (powder; 500 MA) (20% excess)	50.00
10.00 mg	3	Thiamine hydrochloride (10% excess)	11.00
5.00 mg	4	Riboflavin	5.00
100.00 mg	5	Nicotinamide niacinamide (white powder)	100.00
200.00 mg	6	Ascorbic acid (white powder) (10% excess)	220.00
20.00 mg	7	Calcium pantothenate (dextro) (30% excess)	26.00
5.00 mg	8	Pyridoxine hydrochloride	5.00
7.33 mg	9	Povidone (K-29–32)[a]	7.33
29.16 mg	10	Anydrous refined alcohol isopropyl	29.16
24.20 mg	11	Talc powder	24.20
6.07 mg	12	Magnesium stearate (impalpable powder)	6.07
4.75 mg	13	Stearic acid (fine powder)	4.75
10.0 mg	14	Iron, use; iron sulfate (dried)	31.26
1.00 mg	15	Copper[a]	1.00
0.15 mg	16	Iodine[a]	0.15
1.00 mg	17	Manganese[a]	1.00
5.00 mg	18	Magnesium[a]	5.00
1.50 mg	19	Zinc[a]	1.50
0.10 mg	20	Cobalt; use cobalt sulfate	0.47
5.00 mg	21	Potassium; use potassium sulfate	11.14
0.20 mg	22	Molybdenum; use sodium molybdate (dihydrate)	0.50
6.00 μg	23	Vitamin B12; use cyanocobalamin (1000 μg/g oral powder in gelatin; 5% excess)	6.30

[a]Provided as mineral mix (includes 3% excess).

Bill of Materials: Mineral Mix			
Scale (mg/Tablet)	Item	Material Name	Quantity/1000 Tablets (g)
13.85	1	Copper sulfate	14.28
0.01175	2	Calcium iodate monohydrate	0.01212
0.1228	3	Manganese sulfate monohydrate	0.1267
0.1480	4	Zinc sulfate (pure dry powder)	0.1526

Manufacturing Directions

1. Mineral mix processing: Grind copper sulfate, calcium iodate, manganese sulfate, and zinc sulfate through FitzMill screen 0 band (high speed, impact forward).
   Note: Vitamin A is susceptible to destruction by oxidation and also excessive exposure to actinic light and moisture. Compression of this tablet should be done with relative humidity less than 40%. Protect granulation with CO_2 if material is not to be compressed soon after granulation.
2. Hand screen vitamin A and D crystallets and vitamin A acetate through 1.2-mm aperture screen.
3. Load into mass mixer (screen using 1.2-mm aperture screen, if necessary) thiamine HCl, riboflavin, nicotinamide, ascorbic acid, calcium pantothenate, pyridoxine HCl, and the vitamin A and D mix from above.
4. Blend for 10 minutes.
5. Dissolve Povidone in alcohol (~26 mL).
6. Add Povidone solution to blended materials, and mix for 5 minutes.
7. Scrape mixer, and then add alcohol to mass (~11 mL).
8. Pass wet mass through a 15.88-mm aperture (or similar), band-fitted to rotary granulator. (*Note*: Wet mass can set hard; therefore, granules should be spread quickly onto trays.) Dry the granulation at 49°C until LOD is less than 1.0%.

9. Pass the dried granulation through a 1.2-mm aperture screen fitted to an oscillating granulator.
10. Mill the talc (item 11), magnesium stearate, stearic acid, iron sulfate, mineral mix, cobalt sulfate, potassium sulfate, and sodium molybdate through a 595-μm-aperture screen at high speed, impact forward.
11. Load half of the granulation into a suitable blender; add mineral mix and cyanocobalamin oral powder.
12. Add balance of granulation and blend for 30 minutes.
13. Compress and coat using a sealing subcoating of polyvinylpyrrolidone (PVP) (see Appendix), followed by HPMC coating solution and clear methocel gloss.

Multivitamin and Mineral Tablets with Beta Carotene

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Beta carotene (dry powder; 10%)	150.00
2.50	2	Thiamine mononitrate	2.50
2.90	3	Riboflavin	2.90
2.00	4	Pyridoxine hydrochloride	2.00
22.00	5	Nicotinamide	22.00
12.00	6	Calcium D-pantothenate	12.00
110.00	7	Ascorbic acid for direct compression	110.00
550.00	8	Calcium phosphate (dibasic)	550.00
82.00	9	Ferrous fumarate	82.00
166.00	10	Magnesium oxide	166.00
2.50	11	Cupric sulfate	2.50
13.80	12	Manganese sulfate	13.80
57.20	13	Potassium chloride	57.20
37.00	14	Zinc sulfate	37.00
57.00	15	Avicel™ PH102	57.00
50.00	16	Kollidon® CL	50.00
5.70	17	Stearic acid	5.70
5.00	18	Magnesium stearate	5.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with high-compression force.
2. Compress into 1300-mg tablets, using 16-mm biplanar punches.

Multivitamin + Calcium + Iron Tablets (1 RDA of Vitamins)

Formulation: Vitamin A acetate dry powder, 5.0 g, 500,000 IU/g (BASF); Vitamin D dry powder,2.0 g, 100000 IU/g; thiamine mononitrate, 1.2 g; riboflavin,1.8 g; nicotinamide, 12.0 g; vitamin E acetate dry powder SD, 50.4.0 g; ascorbic acid, powder, 50.0 g; ferrous fumarate, 60.0 g; dibasic calcium phosphate [9], 200.0 g; granulated with 5% Kollidon 30; calcium carbonate,125.0 g; Avicel PH 101, 45.0 g; Aerosil 200, 1.5 g.

Manufacturing Directions

Mix all components, pass through a sieve, and press to tablets at 500 mg.

Multivitamin, Calcium, and Iron Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Vitamin A acetate (dry powder)	5.00
2.00	2	Vitamin D (dry powder; 500000 IU/g)	2.00
1.20	3	Thiamine mononitrate (100000 IU/g)	1.20
1.80	4	Riboflavin, BASF	1.80
12.00	5	Nicotinamide	12.00
4.00	6	Vitamin E acetate (dry powder; SD 50)	4.00
50.00	7	Ascorbic acid (powder), BASF	50.00
60.00	8	Ferrous fumarate	60.00
200.00	9	Dibasic calcium phosphate granulated with 5% Kollidon® 30	200.00
125.00	10	Calcium carbonate	125.00
45.00	11	Avicel™ PH101	45.00
1.50	12	Aerosil® 200	1.50

Manufacturing Directions

1. Mix all components, pass through a sieve, and press to tablets.
2. Compress into 500-mg tablets, using 11-mm biplanar punches.

Multivitamin + Carbonyl Iron Tablets (1–2 RDA of Vitamins)

Formulation: Vitamin A acetate dry powder 500,000 IU/g, 10.0 g; thiamine mononitrate, 2.2 g; riboflavin, 2.2 g; nicotinamide, 16.5 g; calcium D-pantothenate, 11.5 g; pyridoxine hydrochloride, 2.2 g; cyanocobalamin, dry powder 0.1%, 6.0 g; ascorbic acid, powder, 85.0 g; vitamin E acetate dry powder SD 50, 31.0 g; Ludipress, 311.0 g; carbonyl iron powder, 10.0 g; magnesium stearate, 3.0 g; orange flavor, 7.2 g; saccharin sodium, 2.5 g.

Manufacturing Directions

Mix all ingredients, pass through a 0.8-mm sieve, mix, and press with high-compression force (20 kN) at 500 mg.

Multivitamin Chewable Tablets for Children

Formulation: Vitamin A acetate dry powder, 7.0 g, 500000 IU/g; thiamine mononitrate, 1.2 g; riboflavin, 1.2 g; nicotinamide, 20.0 g; pyridoxine hydrochloride, 1.8 g; cyanocobalamin 0.1%, dry powder, 6.5 g; ascorbic acid, powder, 60.0 g; vitamin D3 acetate dry powder, 100,000 IU/g, 5.0 g; vitamin E acetate, 31.0 g; dry powder SD 50; sorbitol, crystalline [10], 200.0 g; sucrose, crystalline, 200.0 g; Kollidon VA 64, 20.0 g; Aerosil 200, 1.0 g; orange flavor, dry powder, 30.0 g; raspberry flavor, dry powder, 6.0 g; passion fruit flavor, dry powder, 3.0 g; cyclamate sodium, 2.0 g.

Manufacturing Directions

Mix all ingredients, pass through a 0.8-mm sieve, and press with medium- to high-compression force (20 kN) at 575 mg.

Multivitamin Chewable Tablets for Children

Bill of Materials			
Scale (per tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3500 IU	1	Vitamin A acetate (dry powder; 500,000 IU/g)	7.00
1.20 mg	2	Thiamine mononitrate	1.20
1.20 mg	3	Riboflavin	1.20
20.00 mg	4	Nicotinamide	20.00
1.80 mg	5	Pyridoxine hydrochloride	1.80
6.50 mg	6	Cyanocobalamin (dry powder; 0.1%), BASF	6.50
60.00 mg	7	Ascorbic acid (powder)	60.00
5.00 mg	8	Vitamin D3 acetate (dry powder; 100000 IU/g)	5.00
31.00 mg	9	Vitamin E acetate (dry powder, SD 50)	31.00
200.00 mg	10	Sorbitol (crystalline)	200.00
200.00 mg	11	Sucrose (crystalline)	200.00
20.00 mg	12	Kollidon® VA 64	20.00
1.00 mg	13	Aerosil® 200	1.00
30.00 mg	14	Orange flavor (dry powder)	30.00
6.00 g	15	Raspberry flavor (dry powder)	6.00
3.00 mg	16	Passion fruit flavor (dry powder)	3.00
2.00 mg	17	Cyclamate sodium	2.00

Manufacturing Directions

1. Mix all ingredients, pass through an 0.8-mm sieve, and press with medium- to high-compression force (20 kN).
2. Compress into 575-mg tablets, using 12-mm biplanar punches.

Multivitamin Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
13.00	1	Thiamine mononitrate	13.00
4.00	2	Riboflavin	4.00
11.00	3	Pyridoxine hydrochloride	11.00
66.00	4	Nicotinamide	66.00
17.00	5	Calcium D–pantothenate	17.00
360.00	6	Tartaric acid (powder)	360.00
550.00	7	Sodium bicarbonate	550.00
300.00	8	Sucrose (crystalline)	300.00
300.00	9	Sucrose (powder)	300.00
35.00	10	Kollidon® 30	35.00
5.00	11	Kollidon® 30	5.00
QS	12	Isopropanol	~80.00
6.00	13	Riboflavin	6.00
550.00	14	Ascorbic acid (powder)	550.00
20.00	15	Cyanocobalamin (dry powder, 0.1%)	20.00
12.00	16	Vitamin A palmitate (250000 IU/g dry powder CWD)	12.00
60.00	17	Vitamin E acetate (dry powder; 50%)	60.00
80.00	18	PEG-6000 (powder)	80.00
100.00	19	Kollidon® CL	100.00

Manufacturing Directions

1. Granulate the mixture of items 1 to 10 with solution of items 11 and 12; dry at 60°C with vacuum.
2. Mix with items 13 to 19, and press with high-compression force at maximum 30% of relative atmospheric humidity.
3. Compress into 2.5-g tablets, using 20-mm biplanar punches.

Multivitamin Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.50	1	Thiamine mononitrate	5.50
5.50	2	Riboflavin	5.50
6.50	3	Pyridoxine hydrochloride	6.50
60.00	4	Nicotinamide	60.00
30.00	5	Calcium D–pantothenate	30.00
200.00	6	Ascorbic acid (powder)	200.00
0.20	7	Cyanocobalamin (dry powder, 0.1%)	20.00
30.00	8	Vitamin A acetate (dry powder; 325000 IU/g CWD)	30.00
55.00	9	Vitamin E acetate (dry powder; 50%)	110.00
500.00	10	Citric acid (powder)	500.00
400.00	11	Tartaric acid (powder)	400.00
500.00	12	Sodium bicarbonate	500.00
600.00	13	Ludipress®	600.00
70.00	14	PEG-6000 (powder)	70.00
0.50	15	Saccharin sodium	0.50
40.00	16	Cyclamate sodium	40.00
200.00	17	Sucrose, crystalline	200.00
200.00	18	Fructose	200.00
100.00	19	Flavors (Firmenich)	100.00

Manufacturing Directions

1. Mix all components, and sieve through an 0.8-mm screen.
2. Press with high-compression force at maximum 30% relative atmospheric humidity.
3. Compress into 3-g tablets, using 20-mm biplanar punches.

Multivitamin Effervescent Tablets I, DC (1–2 RDA of Vitamins)

Formulation: Lucarotene dry powder 10%, 23.0 g, CWD G/Y; dry vitamin E acetate 50% DC, 40.0 g; thiamine mononitrate, 2.0 g; riboflavin C, 2.0 g; nicotinamide, 22.0 g; calcium D-pantothenate, 11.0 g; pyridoxine hydrochloride, 2.0 g; cyanocobalamin 0.1% dry powder, 6.0 g; ascorbic acid, powder, 85.0 g; Ludipress LCE, 477.0 g; sodium bicarbonate, 600.0 g; tartaric acid, 400.0 g; polyethylene glycol 6000, powder, 90.0 g; orange flavor (Dragoco), 60.0 g; apartame (Searle), 30.0 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, mix and press with high-compression force at a maximum of 30% of relative atmospheric humidity at 1850 mg.

Multivitamin Effervescent Tablets with Beta Carotene

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Thiamine mononitrate	2.00
2.00	2	Riboflavin	2.00
2.00	3	Pyridoxine hydrochloride	2.00
22.00	4	Nicotinamide	22.00
11.00	5	Calcium D-pantothenate	11.00
400.00	6	Tartaric acid (powder)	400.00
300.00	7	Lactose monohydrate	300.00
100.00	8	Cornstarch	100.00
3.00	9	Cornstarch	3.00
50.00	10	Water	50.00
23.00	11	Beta carotene (dry powder; 10% CWD; food grade)	23.00
6.00	12	Cyanocobalamin (powder; 0.1%)	6.00
85.00	13	Ascorbic acid (powder)	85.00
40.00	14	Vitamin E acetate (dry powder; 50%)	40.00
600.00	15	Sodium bicarbonate	600.00
80.00	16	Flavors	80.00
QS	17	Saccharin sodium	QS

Manufacturing Directions

1. Granulate mixture of items 1 to 6 with solution of items 9 and 10 prepared at 70°C.
2. Dry and sieve; add items 11 to 17, pass through a 0.4-mm sieve, and press with high-compression force at maximum 30% of relative atomspheric humidity.
3. Compress into 1.63-g tablets, using 16-mm biplanar punches.

Multivitamin Effervescent Tablets, DC (3–4 RDA of Vitamins)

Formulations: Thiamine mononitrate, 5.5 g; riboflavin, 5.5 g; pyridoxine hydrochloride, 6.5 g; nicotinamide, 60.0 g; calcium D-pantothenate, 30.0 g; ascorbic acid, powder, 200.0 g; cyanocobalamin 0.1% dry powder, 20.0 g; vitamin A palmitate dry powder 325000 IU/g CWD, 30.0 g; vitamin E acetate dry powder 50%, 110.0 g; tartaric acid, powder, 400.0 g; sodium bicarbonate, 500.0 g; Ludipress, 600.0 g; polyethylene glycol 6000, powder, 70.0 g; saccharin sodium, 0.5 g; cyclamate sodium, 40.0 g; sucrose, crystalline, 200.0 g; fructose, 200.0 g; flavors (Firmenich), 100.0 g;

Manufacturing Directions

Mix all components, sieve through a 0.8-mm screen, and press with high-compression force at maximum 30% relative atmospheric humidity.

Multivitamin + Minerals Tablets with Beta Carotene (1 RDA of Vitamins)

Formulation: Beta carotene dry powder, Betavit 20%, 16.5 g; thiamine mononitrate, 1.7 g; riboflavin, 1.9 g; nicotinamide (Degussa), 22.0 g; calcium D-pantothenate, 12.0 g; pyridoxine hydrochloride, 2.2 g; ascorbic acid, cryst., 72.0 g; vitamin E acetate dry powder 50%, 66.0 g; ferrous fumarate, 54.7 g; magnesium oxide, high density type, 165.8 g; copper II oxide, powder, 2.5 g; manganese sulfate, 6.9 g; zink oxide, 18.7 g; potassium chloride (Baker), 76.3 g; dicalcium phosphate, DI-TAB [9], 550.0 g; Avicel PH 102, 60.0 g; croscarmellose, 32.0 g; Syloid® 244 FP (Grace), 6.0 g; stearic acid, 6.0 g; magnesium stearate, 6.0 g.

Manufacturing Directions

All ingredients are passed through a 0.8-mm sieve, blended in a mixer, and then compressed with medium- to high-compression force at 1193 mg.

Multivitamin Tablet Cores with Beta-Carotene (1–2 RDA of Vitamins)

Formulation: Vitamin A acetate dry powder, 1.27%, 500,000 IU/g; beta carotene dry powder BetaVit 10%, 11.50%; thiamine mononitrate, 1.24%; Riboflavin, 0.96%; nicotinamide, 11.50%; calcium D-pantothenate, 1.91%; pyridoxine hydrochloride, 1.15%; cyanocobalamin gelatin coated 1%, 2.86%; D-biotin, 1% trituration, 1.91%; folic acid, 0.09%; ascorbic acid 38, 20%; vitamin D3 dry powder 100,000 IU/g, 0.76%; vitamin E acetate dry powder 50 DC, 28.40%; phytomenadione dry powder 5% (GFP 0.19%), 270.2 g; Ludipress, 69.1 g; magnesium stearate, 3.3 g;

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with high-compression force at 459 mg.

Multivitamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Thiamine mononitrate (powder), USP (5% excess; 5–10%)	10.50
5.00	2	Riboflavin, USP	5.00
100.00	3	Nicotinamide niacinamide (white powder), USP	100.00
200.00	4	Ascorbic acid, use sodium ascorbat (microcrystalline) (2% excess)	229.47
20.00	5	Calcium pantothenate; use calcium pantothenate racemic (20% excess)	48.00
5.00	6	Pyridoxine hydrochloride, USP	5.00
6.10	7	Povidone (PVP K-25), USP	6.10
—	8	Alcohol dehydrated (200 proof), USP	25.00 mL
21.90	9	PEG-8000, NF	21.90
25000 IU	10	Vitamin A (275000 IU[a]) (20% excess)	7.50 mg
400 IU	11	Vitamin D as D2 powder (850 mD[a])	1.77
6.00	12	Vitamin B12 oral powder in gelatin (5% excess)	6.30
16.00	13	PEG-8000 (milled), NF	16.00
5.30	14	Magnesium stearate	5.30
23.20	15	Talc	23.20

[a]Adjust quantities according to regulatory allowance for OTC label.

Manufacturing Directions

Vitamin A is susceptible to destruction by oxidation and also excessive exposure to actinic light and moisture. Oxidation and destruction are catalyzed by traces of copper and other heavy metals. Dry granulation and compression of this tablet should be done where relative humidity is less than 40%. Protect with CO_2 at blending and storage stages.

1. Charge the following into a suitable mixer (screen if necessary): thiamine mononitrate, riboflavin, nicotinamide, sodium ascorbate, calcium pantothenate, and pyridoxine HCl.
2. Dissolve PVP (item 7) in approximately 16 mL alcohol.
3. Add PVP solution to the powders from first step, and QS with alcohol to mass.
4. Granulate the mass through a 4-mesh (4.76-mm aperture, or similar) screen.
5. Dry at 50°C until the LOD is below 1.0%.
6. Grind to 16 mesh (1.2 mm, or similar).
7. Melt the PEG-8000 (item 10), and incorporate vitamins A and D with thorough agitation.
8. Mix until mass cools and becomes granular.
9. Screen through a 16-mesh (1.2-mm aperture, or similar) screen, and grind coarse material through a FitzMill, or similar, No. 2 band (1.59-mm aperture, or similar) at slow speed or a 16-mesh (1.2-mm aperture, or similar).
10. Reserve for lubrication.
11. Mix milled PEG-8000 (item 13) with talc and magnesium stearate, and pass through a FitzMill, using a 60-mesh (250-μm aperture, or similar) screen (impact forward, high speed).
12. If a FitzMill is unavailable, pass the mixture through a 30-mesh (595-μm aperture, or similar) screen.
13. Load base granulation into a mixer along with vitamin B12, the mixture from above, and the PEG-coated vitamin A and D mixture from the first step. Blend thoroughly.
14. Store dry mixed granulation with CO_2 protection.
15. Compress.
16. Apply a PVP subcoat, a CAP-carbowax or other aqueous coating and finish with a polish coat. (See Appendix.)

Multivitamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Riboflavin	10.00
100.00	2	Niacinamide (white powder)	100.00
5.00	3	Pyridoxine hydrochloride (15% excess)	5.75
15.00	4	Thiamine mononitrate (powder) (5% excess)	15.75
500.00	5	Ascorbic acid, EP	500.00
100.00	6	Lactose	100.00
40.00	7	Povidone (K-29–32)	40.00
100.00	8	Cellulose microcrystalline (Avicel™ PH101)	100.00
–	9	Alcohol SD 3A (200 proof)	QS
20.00	10	Calcium pantothenate; use racemic calcium pantothenate, USP (80 mesh; 15% excess)	46.00
11.50	12	Magnesium oxide (light powder calcined)	11.50
500.00	13	Ascorbic acid	500.00
3.83	14	Povidone (K-29–32)	3.83
–	15	Alcohol SD 3A (200 proof)	QS
4.00 μg	16	Vitamin B12; use vitamin B12 oral powder in gelatin (15% excess)	4.60
28.00	17	Acid stearic	28.00
9.60	18	Magnesium stearate	9.60

Manufacturing Directions

1. Dry-blend riboflavin, niacinamide, pyridoxine hydrochloride, thiamine mononitrate, ascorbic acid (item 5), and lactose for 10 minutes.
2. Dissolve Povidone (item 7) in 75 mL of alcohol (item 9).
3. While mixing in mass mixer, add Povidone solution to mass, and continue mixing for 10 minutes, or until a satisfactory granule mass is obtained.
4. Additional alcohol may be added, if required.
5. Granulate the mass through a 15.9-mm screen using a comminuting mill (knives forward, slow speed) or a 4-mm screen on an oscillating granulator.
6. Dry the granules between 41°C and 49°C in a hot air oven (for approximately 8 hours) or fluid-bed dryer until moisture content is below 1.5%.
7. Dry-screen the granule through a 1-mm screen on an oscillating granulator.
8. Dry-blend the calcium pantothenate and magnesium oxide in a suitable mixer for 10 minutes.
9. Dissolve Povidone (item 14) in 20 mL alcohol (item 15).
10. While mixing, add Povidone solution, and mix to produce a suitable mass.
11. Additional alcohol may be added, if required.
12. Granulate the mass through a 15.9-mm aperture screen using a comminuting mill (knives forward, slow speed) or a 4-mm screen on a oscillating granulator.
13. Dry the granule at 45°C in a hot air oven until moisture content is below 1.5%.
14. Dry-screen granule through a 1.0-mm screen on an oscillating granulator.
15. Mix the two granules made separately in a suitable mixer.
16. Add vitamin B12 powder, and blend for 10 minutes. If necessary, screen the stearic acid and magnesium stearate through a 250-μm screen.
17. Add the remainder of the granule together with magnesium stearate and stearic acid to the mixer and blend for 10 minutes.
18. Compress and coat. (See Appendix.)

Multivitamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Riboflavin	10.00
100.00	2	Niacinamide (white powder)	100.00
5.00	3	Pyridoxine hydrochloride (15% excess)	5.75
15.00	4	Thiamine mononitrate (powder) (5% excess)	15.75
40.00	7	Povidone (K-29–32)	40.00
25.00	8	Povidone (K-29–32)	25.00
–	9	Alcohol SD 3 A (200 proof)	QS
13.50	10	Stearic acid (fine powder)	13.50
2.70	11	Magnesium stearate	2.70

Manufacturing Directions

1. Mill niacinamide, riboflavin, pyridoxine hydrochloride, and thiamine mononitrate through a 500-μm screen on a comminuting mill (impact forward, slow speed).
2. Load screened material from previous step into a mass mixer, add Povidone (item 7) and cellulose microcrystalline, and dry blend for 5 to 15 minutes.
3. While mixing in the mass mixer, add alcohol (item 9) to mass, and continue mixing for 10 minutes or until a satisfactory granule mass is obtained.
4. If necessary, granulate the mass through a 15.9-mm screen using a comminuting mill (knives forward, slow speed) or a 4-mm screen on an oscillating granulator.
5. Dry the granule between 41°C and 49°C in a hot air oven (for approximately 8 hours) or fluid-bed dryer until moisture content is below 1.5%.
6. Dry-screen the granules through a 1.0-mm screen on an oscillating granulator.
7. Load ascorbic acid and Povidone (item 8) into the mixer and dry-blend for 10 minutes.
8. While mixing, add 15 mL of alcohol (item 9), and mix until a satisfactory mass is formed, adding more alcohol if necessary. If necessary, screen through a 4.00-mm screen and load onto trays.
9. Dry at 49°C for 8 hours.
10. Dry screen the granules through a 1.0-mm aperture screen on an oscillating granulator.
11. Screen magnesium stearate and stearic acid through a 500-μm aperture screen.
12. Mix the two granules, add the screened lubricants, and blend for 20 minutes.
13. Coat with a protective subcoat, a color coat, and a polish coat (see Appendix).

Multivitamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Vitamin A acetate (dry powder; 500,000 IU/g)	10.00
2.20	2	Thiamine mononitrate	2.20
2.20	3	Riboflavin	2.20
16.50	4	Nicotinamide	16.50
11.50	5	Calcium D-pantothenate	11.50
2.20	6	Pyridoxine hydrochloride	2.20
6.00	7	Cyanocobalamin (dry powder, 0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
321.00	10	Ludipress®[a]	321.00
21.00	11	Kollidon® VA 64	21.00
3.00	12	Magnesium stearate	3.00
7.20	13	Orange flavor	7.20
2.50	14	Saccharin sodium	2.50

[a]Can be replaced with 300 g of microcrystalline cellulose (Vitacel®).

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, mix, and press with medium-compression force (15 kN).
2. Compress into 500 mg tablets, using 12-mm biplanar punches.

Multivitamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Thiamine hydrochloride	2.20
2.20	2	Riboflavin	2.20
11.00	3	Calcium D-pantothenate	11.00
2.20	4	Pyridoxine hydrochloride	2.20
300.00	5	Mannitol	300.00
20.00	6	Kollidon® 30 or Kollidon® VA 64	20.00
–	7	Isopropanol	~80
5000 IU vitamin A, 500 IU vitamin D	8	Vitamin A and vitamin D; use crystallets of vitamin A acetate + vitamin D3 dry powder (500,000 + 50,000 IU/g) (10% excess)	11.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
0.06	10	Cyanocobalamin; use gelatin-coated cyanocobalamin (0.1%)	6.00
80.00	11	Ascorbic acid (crystalline)	80.00
20.00	12	Nicotinamide	20.00
65.00	13	Avicel™ PH101	65.00
7.00	14	Orange flavor	7.00
2.00	15	Saccharin sodium	2.00
3.00	16	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate mixture of items 1 to 5 with solution of items 6 and 9.
2. Pass through an 0.8-mm sieve, mix with items 8 to 16, and press with medium-compression force.
3. Compress into 560-mg tablets, using 12-mm biplanar punches.

Multivitamin Tablets for Dogs

Formulation: Vitamin A + D3 dry powder, 4.0 g, 500000 + 50000 IU/g; thiamine mononitrate, 0.5 g; riboflavin, 0.7 g; nicotinamide, 5.0 g; calcium D-pantothenate, 1.0 g; pyridoxine hydrochloride, 0.5 g; cyanocobalamin gelatin-coated 1%, 0.5 g; folic acid, 0.05 g; choline bitartrate, 20.0 g; vitamin E acetate dry powder SD 50, 20.0 g; Ludipress, 196.0 g; magnesium stearate, 2.0 g.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix and press with low-compression force at 250 mg.

Multivitamin Tablets for Dogs

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2000 IU Vitamin A 200 IU Vitamin D	1	Vitamin A + vitamin D3 (dry powder; 500,000 + 50,000 IU/g)	4.00
0.50	2	Thiamine mononitrate	0.50
0.70	3	Riboflavin	0.70
5.00	4	Nicotinamide	5.00
1.00	5	Calcium D-pantothenate	1.00
0.50	6	Pyridoxine hydrochloride	0.50
0.50	7	Cyanocobalamin (gelatin-coated, 1%)	0.50
0.05	8	Folic acid	0.05
20.00	9	Choline bitartrate	20.00
20.00	10	Vitamin E acetate (dry powder, SD 50)	20.00
196.00	11	Ludipress®	196.00
2.00	12	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with low-compression force.
2. Compress into 250-mg tablets, using 8-mm biplanar punches.

Multivitamin Tablets with Beta-Carotene

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Beta-carotene; use beta-carotene dry powder (Betavit®, 10%)	10.00
2.00	2	Thiamine mononitrate	2.00
2.00	3	Riboflavin	2.00
16.00	4	Nicotinamide	16.00
11.00	5	Calcium D-pantothenate	11.00
2.00	6	Pyridoxine hydrochloride	2.00
0.06	7	Cyanocobalmine; use cyanocobalamin dry powder (0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
321.00	10	Ludipress®	321.00
7.00	11	Kollidon® VA 64	7.00
3.00	12	Magnesium stearate	3.00
7.00	13	Orange flavor	7.00
2.00	14	Saccharin sodium	2.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 508-mg tablets, using 12-mm planar punches.

Multivitamin Tablets with Copper and Zinc

Formulation: Vitamin mixture (thiamine mononitrate), 3.9%; riboflavin, 100.0.4%; nicotinamide, 10.1%; calcium D-pantothenate, 2.9%; pyridoxine hydrochloride, 1.2%; cyanocobalamin gelatin coated 0.1%, 2.6%; folic acid, 0.1%; ascorbic acid fine powder, 63.4%; vitamin E acetate dry powder 500 SD, 9.1%; copper oxide, 0.3%; zinc sulfate 6.0%, 1000 g; Aerosil, 200.5 g; Ludipress, 150 g; Avicel PH102 [5], 120 g; Kollidon VA64 [1], 25 g; magnesium stearate,10 g; talc, 10 g.

Manufacturing Directions

Pass all components through a 0.8-mm sieve, mix, and press with high-compression force at 1350 mg.

Multivitamin Tablets, DC (1–2 RDA of Vitamins)

Formulation: Vitamin A acetate dry powder, 10.0 g, 500,000 IU/g; thiamine mononitrate, 2.2 g; Riboflavin, 2.2 g; nicotinamide, 16.5 g; calcium D-pantothenate, 11.5 g; pyridoxine hydrochloride, 2.2 g; cyanocobalamin 0.1% dry powder, 6.0 g; ascorbic acid, powder, 85.0 g; vitamin E acetate dry powder SD 50, 31.0 g; Ludipress, 321.0 g; magnesium stearate, 3.0 g; orange flavor, 7.2 g; saccharin sodium, 2.5 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, mix, and press with medium-compression force (15 kN).

Multivitamin with Beta-Carotene Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.85 IU	1	Vitamin A acetate (dry powder; 500,000 IU/g)	5.47
5.00	2	Beta-carotene; use beta-carotene dry powder (Betavit®, 10%)	50.00
15.34	3	Thiamine mononitrate	15.34
4.13	4	Riboflavin	4.13
50.00	5	Nicotinamide	50.00
8.23	6	Calcium D-pantothenate	8.23
5.00	7	Pyridoxine hydrochloride	5.00
0.04	8	Cyanocobalamin; use gelatin-coated cyanocobalamin (1%)	4.00
0.04	9	D-biotin; use 1% trituration	4.00
0.38	10	Folic acid	0.38
165	11	Ascorbic acid	165
327	12	Vitamin D3 (dry powder; 100000 IU/g)	3.27
122.00	13	Vitamin E acetate (dry powder; SD 50)	122.00
0.41	14	Phytomenadione; use phytomenadione dry powder (5% GFP)	0.82

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 432-mg tablets, using 12-mm biplanar punches.

Multivitamin with Zinc Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Niacin; use niacinamide (white powder)	99.20
750.00	2	Ascorbic acid; use microcrystalline sodium ascorbate[a]	843.68
20.00	3	Vitamin B6; use pyridoxine hydrochloride	34.03
QS	4	Povidone	40.00
15.00	5	Thiamine hydrochloride; use thiamine mononitrate (powder)	17.47
15.00	6	Riboflavin	16.50
20.00	7	Pantothenic acid; use calcium pantothenate	32.60
0.49	8	Folic acid (powder)	0.52
12.00 μg	9	Vitamin B12; use cyanocobalamin oral powder in gelatin 1:1000	15.00
60.00	10	Vitamin E (*d,l*-α-tocopherol acetate)	60.00
–	11	Alcohol SD 3A (200 proof)	138 mL 23 mL
22.50	12	Elemental zinc (pure zinc sulfate powder)	55.61
4.00	13	Povidone	4.00
–	14	Alcohol SD 3A (200 proof)	4 mL
–	15	Alcohol SD 3A (200 proof)	9 mL
10.80	16	Magnesium stearate	10.80
40.00	17	Cellulose microcrystalline	40.00
3.20	18	Silicon dioxide colloidal	3.20
6.00	19	Colloidal silicon dioxide	6.00

[a]May use ascorbic acid (750.00 g) instead.
The quantity of Povidone is reduced to 6.34 g, and the amount of alcohol SD used is adjusted.

Manufacturing Directions

1. Mill niacinamide, sodium ascorbate, pyridoxine, Povidone (item 4), and thiamine through a comminuting mill with hammers (impact forward) at high speed and fitted with a 0 band (686-μm aperture, or similar) screen.
2. Charge millings into mass mixer.
3. Screen riboflavin, calcium pantothenate, folic acid, vitamin B12, and vitamin E through 840-μm screen.
4. Charge into mass mixer, and dry mix for 5 to 10 minutes.
5. Add 89 mL alcohol to powder while mixing.
6. Add additional alcohol, if required (approximately 49 mL), to achieve satisfactory granulation.
7. Pass wet mass through 5/8- in. band (15.88-mm aperture, or similar) screen and spread out on paper-lined trays.
8. Dry granulation at 49°C, and dry until LOD is not more than 1.5%.
9. Sift dry granule through 1.19-mm screen, and coarse grind granule through a No. 2 band (1.59-mm aperture, or similar) screen fitted on a comminuting mill (knives forward, medium speed) to polyethylene-lined drums.
10. Mill zinc sulfate and Povidone through a comminuting mill fitted with a 0 band (686-μm aperture, or similar) screen at high speed with impact (hammers) forward.
11. Charge millings into mass mixer for 5 to 10 minutes.
12. Add 3.3 mL alcohol (item 14) to powders from first step while mixing.
13. If necessary, use additional alcohol (up to 0.83 mL) to achieve satisfactory granulation.
14. Granulate wet mass through 5/8- in. band (15.88-mm aperture, or similar) screen, and spread out on paper-lined trays.
15. Dry granule at 49°C, and dry until LOD is not more than 1.5%.
16. Sift dry granule through 1.19-mm screen, and coarse grind granule through a No. 2 band (1.59-mm aperture, or similar) screen fitted on a comminuting mill (knives forward, medium speed) and transfer to polyethylene-lined drums.
17. Charge approximately 1/10th of vitamin granulation into blender.
18. Premix magnesium stearate, microcrystalline cellulose, and silicon dioxide in a bowl, and sift through 840-μm screen into blender.
19. Charge another 1/10th more of vitamin granulation into blender, and blend for 5 minutes.
20. Discharge a portion of granulation from the blender, and check for white lumps.
21. If lumps are present, discharge entire granulation through a 1.68-mm aperture screen to break lumps, then return it to blender.
22. Charge zinc granulation into the blender.
23. Charge remaining vitamin granulation into blender, and blend for 15 minutes.
24. Discharge blender into polyethylene-lined drums, tie liners, close and seal drums, and deliver to storage area.
25. Compress and coat (see Appendix).

Nalidixic Acid Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Nalidixic acid	500.00
20.00	2	Lactose monohydrate	20.00
25.00	3	Starch (maize)	25.00
30.00	4	Starch (maize)	30.00
0.10	5	Propyl paraben	0.10
0.40	6	Methyl paraben	0.40
0.80	7	Sodium starch glycolate	0.80
2.50	8	Magnesium stearate	2.50
1.00	9	Talc	1.00
0.20	10	Aerosil 200	0.20
2.00	11	Starch (maize), dried	3.00
–	12	Water, purified, ca	400 mL

Manufacturing Directions

1. Sift items 1 and 2 through a #40-mesh sieve into a suitable blending vessel.
2. Sift item 3 through #80-mesh sieve, add to step 1, and mix for 10 minutes.
3. In a separate vessel, sift item 4 through #80 mesh, add items 5 and 6, and mix for 5 minutes. Add item 12 at 80°C to prepare a 30% starch paste that is smooth and lump-free.
4. Add step 3 into step 2, and make a wet mass suitable for granulation.
5. Pass the wet mass through a 10-mm sieve in a mill, and dry in a fluid-bed dryer at 50°C for 1 hour to an LOD of not more than 3%. Transfer to a blending vessel.
6. Sift items 7 to 11 through a 250-μm sieve screen, and add to step 5. Blend for 1 minute only.
7. Compress into 575-mg tablets, using 13-mm punches.

Nalidixic Acid Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Nalidixic acid	500.00
15.00	2	Kollidon 30	15.00
–	3	Water, purified	125.00
25.00	4	Kollidon CL	25.00
5.00	5	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate item 1 with the solution of item 2 in item 3. Dry, and pass through a 0.8-mm sieve. Add the mixture of items 4 and 5, mix during 10 minutes, pass again through a 0.8-mm sieve, and press with low-compression force (10 kN).
2. Compress into 545-mg tablets, using 12-mm biplanar punches.

Naproxen Tablets (250 mg)

Naproxen tablets for oral administration each contain 250, 375, or 500 mg of naproxen. Naproxen is a member of the arylacetic acid group of nonsteroidal anti-inflammatory drugs.

Naproxen Tablets

Bill of Materials			
Scale (mg/tablet)	item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Naproxen	250.00
6.00	2	Kollidon 90F	6.00
4.00	3	Kollidon 90F	4.00
4.00	4	Cremophor RH40	4.00
–	5	Water	41.00
150.00	6	Tablettose	150.00
1.00	7	Stearic acid	1.00
10.00	8	Ac-Di-Sol	10.00
1.00	9	Magnesium stearate	1.00
10.00	10	Polyethylene glycol 6000 powder	10.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 to 5, dry, pass through a 0.8-mm sieve, add items 6 to 9, and press with low-compression force.
2. Compress into 441-mg tablets, using 12-mm biplanar punches.

Naproxen Tablets (250 mg/500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Naproxen	250.00
78.40	2	Lactose monohydrate	78.40
7.00	3	Starch (corn)	7.00
4.00	4	Sodium starch glycolate	4.00
0.60	5	Yellow dye	0.60
5.00	6	Povidone K 29–32	5.00
5.00	7	Polysorbate 80	5.00
QS	8	Isopropyl alcohol, ca	200.00 mL
3.70	9	Talc	3.70
3.30	10	Magnesium stearate	3.30

Note: For 500-mg strength, use the same formula with higher fill weight.

Manufacturing Directions

1. Granulation
   a. Pass naproxen and lactose through a 16-mesh (1.2-mm aperture) screen into a planetary mixer (or something similar). Mix these items for 10 minutes.
   b. To a suitable blender, add starch (corn), sodium starch glycolate, and yellow dye. Blend these items for 10 minutes.
   c. Incorporate the blended powders from step 1b into the blend in step 1a. Mix for 10 minutes.
   d. Dissolve povidone and polysorbate 80 in alcohol isopropyl. The solution must be complete.
   e. While mixing the blended powders from step 1c, add the solution from step 1d. When all the solution is added, continue mixing for 2 minutes, until a characteristic mass is obtained. Add more alcohol isopropyl, if required. Record the additional amount of alcohol isopropyl.
   f. Pass the wet mass through an 8-mesh (2.38-mm aperture) screen by hand. Load the granular mass onto paper-lined trays, and oven dry at 49°C until the LOD is between 1.5% and 2.5%.
   g. Pass the dried granules through a FitzMill fitted with a 2A band (knives forward, medium speed) into tared, polyethylenelined drums.
2. Lubrication
   a. Transfer the dried granules from step 1 g to a suitable blender.
   b. Screen talc and magnesium stearate through a 30-mesh (595-μm aperture) screen, and add this to the blender. Blend this mixture for 10 minutes.
   c. Discharge the granules into clean, tared, polyethylenelined drums. Then seal the drums, and weigh for yield.
3. Compression: Compress on a suitable compression machine using 9.5-mm round, standard concave punches—tablet weight: 352 mg.

Naproxen Tablets (450 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
450.00	1	Naproxen	457.50
10.00	2	Kollidon CL	10.00
25.00	3	Kollidon 30	25.00
–	4	Water, purified	90.00
2.50	5	Magnesium stearate	2.50

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4, pass through a 0.8-mm sieve, add item 5, and press to tablets with low-compression force.
2. Compress into 496-mg tablets, using 12-mm biplanar punches.

Nelfinavir Mesylate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
730.62	1	Nelfinavir mesylate	730.62
240.00	2	Crospovidone	240.00
217.37	3	Calcium silicate	217.37
Qs	4	Purified water	Qs
12.00	5	Magnesium stearate	12.00

Manufacturing Directions

Wet granulation is used to prepare the compression mix, dried (to remove water), mixed with item 5, and then compressed.

Neomycin Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Neomycin sulfate	250.00
334.00	2	Ludipress	334.00
6.00	3	Magnesium stearate	6.00
10.00	4	Aerosil 200	10.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press to tablets with low-compression force.
2. Compress into 600-mg tablets, using 12-mm biplanar punches.

Niacin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Niacin	1000.00
40.00	2	Polyvinylpyrrolidone	40.00
10.00	3	Silicon dioxide	10.00
15.00	4	Sodium stearyl fumarate	15.00
400.00	5	Water	400.00

Manufacturing Directions

1. Niacin and lactose are placed in a fluidized bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1-mm mesh) and sodium stearyl fumarate is weighed, added and blended in a drum mixer.
4. The resulting mixture is pressed into tablets 1065.00 mg.
5. These tablet cores are then coated with the following formulation: ethylcellulose (Ethocel), 10.10; polyvinylpyrrolidone (Povidone), 5.50 mg; stearic acid, 2.40 mg.
6. Ethocel, povidone, and stearic acid are first dissolved in denatured alcohol (180 g).
7. The coating solution is then sprayed onto the tablet cores in a coating pan.

Nicardipine Hydrochloride Sustained-Release Tablets

Manufacturing Directions

1. First, 1200 g nicardipine hydrochloride and 1200 g hydroxypropylmethyl cellulose are dissolved in a mixture of 4800 g methanol and 4800 g dichloromethane.
2. 300 g of silicon dioxide (mean particle diameter of approximately 48 μm, particle diameter of 75 μm or smaller) is introduced to a fluidized bed granulator and coated with this solution by the side spraying method (spraying liquid volume 18 g/min, spraying air pressure 3 kg/cm^2, product temperature 30°C, inlet temperature 70°C) to obtain nicardipine hydrochloride particles.
3. Separately, 54 g of ethyl cellulose and 6 g of hydroxypropylmethyl cellulose are dissolved in a mixture of 57 g of purified water and 1083 g of methanol.
4. Nicardipine hydrochloride particles (300 g) are introduced to a fluidized bed granulator and coated with this solution by side spraying (spraying liquid volume of 8 g/min, spraying air pressure of 2.5 kg/cm^2, product temperature of 39°C, inlet temperature of 70°C) to obtain sustained-release fine particles.
5. 60 g of these sustained-release fine particles, 254.4 g mannitol, 63.6 g lactose that had been pulverized with a pin mill pulverizing device, and 12 g erythritol are granulated (spraying liquid volume 15 g/min, spraying air pressure of 0.5 kg/cm^2, product temperature of 39°C, inlet temperature of 50°C, spraying cycle of 5 seconds spraying-15 seconds drying) with an aqueous 5% w/w solution containing 8 g copolyvidone (Kollidon VA64) in a fluidized bed granulator to obtain the composition of the present invention. The ratio of ungranulated fine particles is 7.9%.
6. After further mixing 2 g of magnesium stearate with the composition that is obtained, 400-mg tablets containing 20 mg of nicardipine hydrochloride per tablet are made under an initial hardness of 0.6 kPa using a rotary tabletting machine.
7. Next, these tablets are heated for 10 minutes at 130°C using a program oven.
8. Then they are cooled at room temperature for 30 minutes. The tablets that are obtained showed a hardness of 3.7 kPa ($n = 5$), friability of 0.1% or less (100 rounds), and disintegration time in the buccal cavity of 20 seconds.

Nicotinamide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Nicotinamide (Degussa)	320.00
160.00	2	Avicel™ PH101	160.00
16.00	3	Kollidon® VA 64	16.00
3.00	4	Magnesium stearate	3.00
3.00	5	Aerosil® 200	3.00

Manufacturing Directions

With medium-compression force, compress into 506-mg tablets, using 12-mm biplanar punches.

Nicotinic Acid (Niacin) Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Nicotinic acid	200.00
200.00	2	Ludipress®	200.00
5.00	3	Kollidon® CL	5.00
1.50	4	Magnesium stearate	1.50
3.00	5	Aerosil® 200	3.00
10.00	6	PEG-6000	10.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve.
2. Mix and press with very low-compression force.
3. Compress into 410-mg tablets, using 12-mm biplanar punches.

Nicotinic Acid (=Niacin) Tablets (200 mg)

Formulation: Nicotinic acid (Lonza), 200.0 g; Ludipress, 200.0 g; Kollidon CL, 5.0 g; magnesium stearate, 1.5 g; Aerosil 200, 3.0 g; polyethylene glycol 6000, powder, 10.0 g.

Manufacturing Directions

Pass all components through a 0.5-mm sieve, mix, and press with very low-compression force at 419 mg.

Nicotinic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
375.00	1	Nicotinic acid	375.00
188.70	2	Hydroxypropyl methyl cellulose E10 M premium	188.70
12.90	3	Povidone K90	12.90
5.80	4	Stearic acid (Hystrene 5016)	5.80

Manufacturing Directions

1. Charge one half of the quantity of item 1 and items 2 and 3 and the powder bed is dry mixed in a Littleford granulator, with choppers on, for approximately 1 minute.
2. At the completion of the 1-minute premix cycle, an appropriate quantity about three times the quantity of item 3 and sprayed slowly for a period of 5 minutes.
3. The granulated unit is discharged into double polyethylene-lined containers and then manually loaded into a Glatt bowl while being passed through a #4-mesh screen, the Glatt bowl is loaded into a Glatt fluid-bed dryer with an inlet air temperature setting of about 70 ± 5°C.
4. The unit is dried until a moisture level of approximately 1.0% is obtained as determined using a Computrac® Moisture Analyzer.
5. The dried granulation is discharged into appropriately labeled, double polyethylene-lined drums and reconciled.
6. The dried and reconciled granulation is passed through a Kemutec BetaGrind mill equipped with an l.5-mm screen and running at approximately 1500 RPM.
7. The milled granulation is collected into appropriately labeled, double polyethylene-lined drums and reconciled.
8. The milled granulation is sampled and tested by quality control and released prior to further processing.
9. The released granulation units are charged to a Patterson-Kelley 20 ft^3 V-blender after which they are blended together for about 10 ± 1 minutes and then discharged to appropriately labeled, double polyethylene-lined containers.
10. Add item 4 blend and compress at 582.40 mg in caplet-shaped punches; compress 727.50 for 500-mg strength and 990.50 mg for 750-mg strength.

Nifedipine Coprecipitate Tablet

1. kg of nifedipine and 1.0 kg of polyvinylpyrrolidone are dissolved in 18 L of methylene chloride at room temperature.
2. The obtained solution is treated in a spray-dryer plant at a temperature equal to 90°C with double fluid nozzle with external mixing.
3. A solid coprecipitate having a ratio by weight between nifedipine and polyvinylpyrrolidone equal to 1:1 and a granulometry lower than 100 μm is obtained.
4. A tablet composition is prepared using the coprecipitate of nifedipine and polyvinylpyrrolidone 1:1, having a granulometry lower than 100 μm.
5. A granulate is first prepared introducing in a fluid-bed dryer hydroxypropylmethylcellulose, carboxypolymethylene, and talc, in addition to the coprecipitate of nifedipine and polyvinylpyrrolidone. Purified water is used in order to obtain the granules which, mixed with magnesium stearate and colloidal silica, allow to obtain some tablets, which are subsequently coated with an opaque, protective film.
6. In the final composition the proportion of all ingredients is as follows (by weight%): nifedipine 15.96%; polyvinylpyrrolidone 15.96%; talc 30.31%; hydroxypropylmethylcellulose 31.91%; carboxypolymethylene 1.60%; magnesium stearate 1.06%; colloidal silica 1.60%.
7. Substances of the coating: (by weight%): talc 0.49%; magnesium stearate 0.24%; titanium dioxide 0.37%; iron oxide 0.04%; acrylic acid copolymer 0.37%; polyethylene glycol 4000 0.08%.
8. The tablets had an average weight equal to 188 mg.

Nifedipine Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Nifedipine	5.00
60.00	2	Starch (maize)	60.00
40.00	3	Lactose monohydrate	40.00
40.00	4	Dicalcium phosphate	40.00
4.00	5	Polyvinylpyrrolidone K30	4.00
0.04	6	Isopropyl alcohol	40 mL
2.00	7	Magnesium stearate	2.00
1.00	8	Talc	1.00

Manufacturing Directions

1. Sift item 1 through #40 mesh into a suitable mixing vessel. Sift items 2 to 4 through a 250-μm sieve into the same vessel, portion by portion, mixing with item 1 to achieve geometric dilution. Dry the mix for 15 minutes.
2. In a separate vessel, prepare the binding solution by dissolving item 5 and item 6.
3. Add the binding solution from step 2 into step 1 slowly, and mix until a suitable mass is obtained.
4. Pass the wet mass through a #6 sieve onto trays, and dry it overnight in a dehumidified room.
5. Pass dried granules through a #18-mesh sieve. Load into a blending vessel.
6. Sift items 7 and 8 through a 250-μm sieve, and add to step 5. Blend for 1 minute.
7. Compress into 150-mg tablets, using 7-mm punches.
8. Coat with an HPMC organic coating. (See Appendix.)

Nifedipine Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Nifedipine	10.00
40.00	2	Kollidon 25	40.00
—	3	Methylene chloride	180.00
105.00	4	Microcrystalline cellulose (Avicel PH 102)	105.00
20.00	5	Starch (maize)	20.00
25.00	6	Kollidon CL	25.00
0.40	7	Magnesium stearate	0.40

Manufacturing Directions

1. Dissolve a mixture of items 1 and 2 in item 3. Granulate the mixture of items 4 to 6 with the solution prepared previously, then sieve, dry the obtained coprecipitate, add item 7, and press with low- to medium-compression force.
2. Compress into 223-mg tablets, using 8-mm punches.

Nimesulide-Dispersible Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Nimesulide	100.00
120.00	2	Lactose monohydrate	120.00
100.00	3	Starch (maize)	100.00
0.40	4	Sodium metabisulfite	0.40
0.40	5	Propyl paraben	0.40
30.00	6	Starch (maize)	30.00
5.00	7	Talc	5.00
1.50	8	Magnesium stearate	1.50
2.50	9	Flavor	2.50
11.20	10	Sodium starch glycolate	11.20
–	11	Water, purified	QS

Manufacturing Directions

1. Sift items 1 to 3 through a #40-mesh sieve into a suitable mixer, and mix for 15 minutes.
2. In a separate vessel, prepare the binding paste by taking an appropriate quantity of item 11, heating it to 90°C, adding item 5, and dissolving. Add item 4 and dissolve. Finally, add item 6, and make a smooth slurry (30% starch).
3. Add step 2 into step 1, and form a lump-free mass.
4. Pass the wet mass through an 8-mm sieve, and load onto trays. Dry the mass at 50°C, overnight, to less than 2% moisture.
5. Pass the dried granules through a #18-mesh sieve into a blending vessel.
6. Sift items 7 to 10 through a 250-μm sieve into step 4, and blend for 1 minute.
7. Compress into 358-mm tablets, using 40-mm punches.

Nitrendipine Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Nitrendipine	26.00
53.00	2	Ludipress	53.00
1.50	3	Kollidon CL	1.50
0.50	4	Magnesium stearate	0.50

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with low-compression force.
2. Compress into 82-mg tablets, using 6-mm biplanar punches.

Nitrofurantoin Tablets

Formulations: Nitrofurantoin sodium hydrate, 238 mg (equivalent to 200 mg nitrofurantoin); microcrystalline cellulose, 175 mg; sodium starch glycollate, 25 mg; cornstarch, 25 mg; talc, 20 mg; magnesium stearate, 1 mg.

Manufacturing Directions

1. The ingredients are mixed and screened and 488-mg convex core tablets compressed by direct compression using a suitable tablet press yielding tablets approximately 11 mm in diameter and 5.4 mm in height.
2. Coating solution: Eudragit-S 12.5% Isopropanol Suspension 45.7 Polyethylene glycol 6000 33% Aqueous Solution 3.5 Talc 2.5 Isopropanol/Acetone 1:1 48.3.
3. Use solution from step 2 to enteric coat by spraying the Eudragit-S suspension onto their surfaces as tablets rotate in a conventional coating pan. Coating thickness required to produce an even, uninterrupted surface distribution varies between 4.0 and 7.2 mg/cm^2 a lacquer dry substance. Coat thickness may vary beyond this range depending upon production scale and process equipment. Air suspension coating techniques are also applicable.

Nitrofurantoin Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Nitrofurantoin	100.00
20.00	2	Starch (maize)	20.00
38.00	3	Lactose monohydrate	38.00
10.00	4	Kollidon 30	10.00
–	5	Water, purified	QS
5.00	6	Kollidon CL	5.00
8.00	7	Starch (maize)	8.00
4.00	8	Talc	4.00
1.00	9	Magnesium stearate	1.00

Manufacturing Directions

1. Granulate a mixture of items 1 to 3 with a solution of items 4 and 5, dry, sieve, mix with items 6 to 9, and press.
2. Compress into 180-mg tablets, using 8-mm punches.

Nitrofurantoin Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Nitrofurantoin	100.00
200.00	2	Ludipress	200.00
2.00	3	Magnesium stearate	2.00
3.00	4	Aerosil 200	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 307-mg tablets, using 12-mm punches.

Nitroglycerin and Isosorbide Mononitrate Sustained-Release Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Isosorbide mononitrate	30.00
100.00	2	Hydroxypropyl methylcellulose	100.00
40.00	3	Lactose monohydrate	40.00
40.00	4	Ethylcellulose	40.00
18.00	5	Polyvinylpyrrolidone	18.00
2.00	6	Silicon dioxide	2.00
1.00	7	Magnesium stearate	1.00
8.00	8	Eudragit L100–55	8.00
1.80	9	Triethyl citrate	1.80
4.50	10	Talc	4.50
1.47	11	Polyethylene glycol 6000	1.47
0.29	12	Sodium hydroxide	0.29
Qs	13	Water	Qs
14.00	14	Eudragit EPO	14.00
8.00	15	Citric acid	8.00
Qs	16	Water	Qs
0.30	17	Nitroglycerin	0.30
65.00	18	Lactose fine powder	65.00
5.00	19	Sucrose fine powder	5.00
2.00	20	Flavor optional	2.00
0.10	21	Polyvinylpyrrolidone	0.10
qs	22	Ethyl alcohol 95%	qs

Manufacturing Directions

1. Blend isosorbide mononitrate, hyproxypropyl methylcellulose, ethylcellulose, and lactose to form a uniform blend.
2. Prepare polyvinylpyrrolidone in water or a mixture of water and ethanol solution.
3. Granulate step 1 with solution from step 2.
4. Dry the granulation and screen or mill to desired particle size.
5. Add silicon dioxide, stearic acid, and magnesium stearate and blend for additional 5 to 10 minutes.
6. Compress tablets at 233 mg.
7. Prepare the coating solution by mixing water, Eudragit L100-55, sodium hydroxide, PEG 6000, triethyl citrate, and talc to form a uniform dispersion.
8. Coat isosorbide mononitrate tablets with Eudragit L coating solution using a coating pan or a fluid-bed coater until a desired coat weight is achieved (259.50 g).
9. Prepare a coating solution containing Eudragit E and citric acid in water.
10. Coat isosorbide mononitrate enteric-coated tablets with the above coating solution in a coating pan or a fluid-bed coater until a desired coating weight is obtained (291 mg).
11. Prepare the solvent mixture containing polyvinylpyrrolidone, ethyl alcohol, and water.
12. Blend nitroglycerin, lactose, sucrose, and the flavoring agent. Screen to break lumps.
13. Add the mixture of step 11 to step 12 until a moistened powder blend is achieved.
14. Compress isosorbide mononitrate tablet (281.06 mg) with moistened nitroglycerin triturate (72.4 mg) in a tabletting machine for the total weight of 353.46 mg. The product contains 0.3 mg of nitroglycerin in the molded triturate tablet for intraoral release and 30 mg of isosorbide mononitrate as a sustained-release form, which releases isosorbide for a duration of 8 to 12 hours.

Nitroglycerin Retard Tablets

Manufacturing Directions

Formulation: Cetyl alcohol, 15.0% w/w; hydroxy ethyl cellulose, 5.0% w/w; lactose, 45.5% w/w; talc, 15.0% w/w; nitroglycerin 1:10, 16.0% w/w; talc and magnesium stearate q.s., 100.0% w/w.

1. Melt cetyl alcohol in a water jacketed tank fitted with a stirrer; add the lactose and blend. Granulate the free flowing mass through a No. 16 stainless steel screen.
2. Hydrate hydroxy ethyl cellulose with three volumes of water for each part by weight of hydroxy ethyl cellulose, and stir until a granular paste is obtained.
3. Add the granules from step 1 to the paste obtained from step 2. Continue the blend and add the talc and nitroglycerin powder. Blend until a uniform granular mass is obtained.
4. The granules are then dried at 45°C for 30 minutes and after drying, granulated through a No. 16 standard mesh screen.
5. The tablet lubricants (magnesium stearate and talc) are then added in suitable quantity and the mixture compressed into tablets.

Compression Data: tablet weight is 400 mg; punch size: 3/8 in.; flat bevelled edge.

Nitroglycerine Tablets (0.3 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.30	1	Nitroglycerin, use 1.95% mixture (diluted nitroglycerin)[a]	15.38
0.61	2	Glyceryl monostearate	0.61
16.37	3	Lactose monohydrate	16.37
0.065	4	Silicon dioxide colloidal	0.065
2.10	5	Pregelatinized starch	2.10
0.10	6	Calcium stearate	0.105

Adjust quantity based on assay with item 3. Do not add any excess.

Manufacturing Directions

1. Mill glyceryl monostearate (Myvaplex 600P) and lactose monohydrate in a suitable mixing vessel equipped with an intensifier bar.
2. Separately mill silicon dioxide and lactose monohydrate together.
3. Add diluted nitroglycerin USP to step 1. Blend for 10 minutes, with the intensifier bar set to "on."
4. Add step 2 into step 3, and mix for 3 minutes.
5. Add item 5 after passing through a 250-μm sieve to step 4, and mix for another 5 minutes, with the intensifier bar set to "on."
6. Add calcium stearate to the blend in step 5, and blend for 5 minutes.
7. Compress a suitable quantity into tablets.

Noramidopyrine Methansulfonate and Dicyclomine Hydrochloride Tablets (500 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Noramidopyrine methansulfonate	500.00
10.00	2	Dicyclomine hydrochloride	10.00
4.00	3	Lactose monohydrate	4.00
12.50	4	Starch (maize)	12.50
1.50	5	Gelatin	1.50
1.50	6	Magnesium stearate	1.50
1.50	7	Talc	1.50
1.50	8	Methyl carboxycellulose	1.50
1.50	9	Aerosil 200	1.50
1.50	10	Sodium metabisulfite	1.50
0.22	11	Methyl paraben	0.22
0.02	12	Propyl paraben	0.02
–	13	Isopropyl alcohol	QS
–	14	Water, purified	QS

Manufacturing Directions

1. Charge items 1 and 3 in a suitable mixing vessel, and 7 g of item 4, and mix for 5 minutes.
2. In a separate vessel, take a sufficient quantity of item 14, bring it to a boil, and dissolve in it items 11 and 12. Allow the mixture to cool to 50°C, add items 5 and 10, and dissolve. Add the balance of item 4, and mix well to prepare a smooth paste.
3. Add step 2 into step 1, and form a smooth wet mass. Pass the mass through a 2.38-mm sieve screen over paper-lined trays, and dry at 60°C, overnight, to an LOD of not more than 3%.
4. Pass the dried granules through a #16 mesh into a blending vessel.
5. Granulate item 2 with a sufficient quantity of item 13 (optionally containing a dye).
6. Dry the granules in step 4 in a dehumidified room.
7. Add step 6 into step 5, and mix for 5 minutes.
8. Sift items 6 to 9 through a 500-mm screen, and blend for 2 minutes.
9. Compress 625 mg in a suitable punch.

Norephedrine and Terfenidine Tablet

Formulation: 1(-)-norephedrine hydrochloride, 37.5 mg; terfenadine, 30.0 mg; lactose, 65.0 mg; hydroxypropylmethylcellulose, 15.0 mg; croscarmellose sodium, 5.0 mg; talc, 10.0 mg; hydrogenated castor oil, 8.0 mg. Total 70.5 mg.

Manufacturing Directions

The tablet is made by wet granulating l(-)-norephedrine hydrochloride, terfenadine, and lactose with a solution of hydroxypropylmethylcellulose. The granulation is dried, sized, and the remaining ingredients are sequentially dry blended and then compressed into tablets.

Norethindrone and Ethinyl Estradiol Tablets (0.75 mg/0.035 mg; 0.50 mg/0.035 mg; 1.0 mg/0.035 mg)

Each of the following products is a combination oral contraceptive containing the progestational compound norethindrone and the estrogenic compound ethinyl estradiol:

- Ortho-Novum 7/7/7—Each white tablet contains 0.5 mg of norethindrone and 0.035 mg of ethinyl estradiol. The inactive ingredients are lactose, magnesium stearate, and pregelatinized starch. Each light peach tablet contains 0.75 mg of norethindrone and 0.035 mg of ethinyl estradiol. The inactive ingredients are FD&C Yellow No. 6, lactose, magnesium stearate, and pregelatinized starch. Each peach tablet contains 1 mg of norethindrone and 0.035 of ethinyl estradiol. The inactive ingredients are FD&C Yellow No. 6, lactose, magnesium stearate, and pregelatinized starch. Each green tablet in the Ortho-Novum 7/7/7 28 package contains only inert ingredients, as follows: D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, microcrystalline cellulose, and pregelatinized starch.
- Ortho-Novum 10/11—Each white tablet contains 0.5 mg of norethindrone and 0.035 mg of ethinyl estradiol. The inactive ingredients are lactose, magnesium stearate, and pregelatinized starch. Each peach tablet contains 1 mg of norethindrone and 0.035 of ethinyl estradiol. The inactive ingredients are FD&C Yellow No. 6, lactose, magnesium stearate, and pregelatinized starch. Each green tablet in the Ortho-Novum 10/11 28 package contains only inert ingredients, as listed under the green tablets in the Ortho-Novum 7/7/7 28 package.
- Ortho-Novum 1/35—Each peach tablet contains 1 mg of norethindrone and 0.035 mg of ethinyl estradiol. The inactive ingredients are FD&C Yellow No. 6, lactose, magnesium stearate, and pregelatinized starch. Each green tablet

in the Ortho-Novum 1/35 28 package contains only inert ingredients, as listed under green tablets in the Ortho-Novum 7/7/7 28 package.

- Modicon—Each white tablet contains 0.5 mg of norethindrone and 0.035 mg of ethinyl estradiol. The inactive ingredients are lactose, magnesium stearate, and pregelatinized starch. Each green tablet in the Modicon 28 package contains only inert ingredients, as listed under the green tablets in the Ortho-Novum 7/7/7 28 package.

Norfloxacin Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Norfloxacin	400.00
90.00	2	Microcrystalline cellulose (Avicel PH 112)	90.00
26.00	3	Croscarmellose sodium (Ac-Di-Sol)	26.00
4.00	4	Magnesium stearate	4.00
–	5	Absolute alcohol (ethanol, dehydrated alcohol)	60.00

Manufacturing Directions

Note: Avoid overmixing lubricants, or hardness may be reduced.

1. Sieving and kneading
   a. Sift item 1 through a 900-μm sieve. Load it into the mixer.
   b. Add item 5 to step 1a, while mixing at low speed. Scrape sides and blades. Mix and chop at low speed for 2 minutes. Check the end point of granulation. If required, add additional absolute alcohol to get the end point. (The end point of the granulation is the point where there are little or no lumps in the granulation.)
2. Drying: Dry the wet granules in an oven at 55°C for 6 hours. After 2 hours of drying, scrape the semidried granules to break the lumps for uniform drying.
3. Check the LOD. The limit is 0.7% to 1%. If required, dry further at 55°C for 1 hour. Check the LOD.
4. Transfer the dried granules to stainless steel drums.
5. Grinding: Grind the dried granules through a 1.25-mm sieve, using a granulator at medium speed. Collect the granules in stainless steel drums. Load the granules into the blender.
6. Lubrication
   a. Sift items 2 and 3 through a 500-μm sieve, and add it to the blender. Mix the blend for 2 minutes.
   b. Sift item 4 through a 250-μm sieve. Add 5- to 100-g granules from bulk (see the previous step). Mix in a polythene bag for 1 minute. Then, add to the blender. Blend for 1 minute.
   c. Unload in stainless steel drums.
7. Compression
   a. Check the temperature and humidity before starting compression. The limits are that the temperature cannot exceed 25°C, and the relative humidity should be between 45% and 50%.
   b. Compress the granules using a rotary tabletting machine (diameter: 16.2 × 8.3 mm, compression weight: 520 mg).
8. Tablet coating: Coat with an HPMC solution. (See Appendix.)

Norfloxacin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Norfloxacin	400.00
48.56	2	Microcrystalline cellulose	48.56
47.12	3	Starch 1500	47.12
5.15	4	Stearic acid	5.15
2.58	5	Fumed silica	2.58
10.30	6	Croscarmellose sodium	10.30
1.29	7	Magnesium stearate	1.29

Manufacturing Directions

1. Pass Starch 1500 and fumed silica together through a 40-mesh screen.
2. Add norfloxacin, microcrystalline cellulose, stearic acid, and croscarmellose sodium to the material from step 1 and blend for 15 minutes in a twin-shell blender.
3. Add the magnesium stearate to the material from step 2 and blend for an additional 5 minutes.
4. Compress into 515-mg tablets.

Norgestimate and Ethinyl Estradiol Tablets (0.18 mg/0.035 mg; 0.215 mg/0.035; 0.25 mg/0.035 mg)

Each of the following products is a combination oral contraceptive containing the progestational compound norgestimate and the estrogenic compound ethinyl estradiol.

1. Ortho Tri-Cyclen® 21 Tablets and Ortho Tri-Cyclen® 28 Tablets
   a. Each white tablet contains 0.180 mg of the progestational compound, norgestimate (18,19-dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-,oxime,(17α)-(+)-) and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17α-pregna,1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include lactose, magnesium stearate, and pregelatinized starch.
   b. Each light blue tablet contains 0.215 mg of the progestational compound, norgestimate (18,19-dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-,oxime,(17α)-(+)-) and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17α-pregna,1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, and pregelatinized starch.
   c. Each blue tablet contains 0.250 mg of the progestational compound, norgestimate (18,19-dinor-17-pregn-4- en-20-yn-3-one,17-(acetyloxy)-13-ethyl-,oxime,(17α)-(+)-) and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17a-pregna,1,3,5 (10)-trien-20-yne-3,17-diol). Inactive ingredients include FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, and pregelatinized starch.
   d. Each green tablet in the Ortho Tri-Cyclen 28 package contains only inert ingredients, as follows: D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, microcrystalline cellulose, and pregelatinized starch.
2. Ortho-Cyclen 21 Tablets and Ortho-Cyclen 28 Tablets
   a. Each blue tablet contains 0.25 mg of the progestational compound, norgestimate (18,19-dinor-17-pregn-4- en-20-yn-3-one,17-(acetyloxy)-13-ethyl-,oxime,(17a)-(+)-) and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17a-pregna,1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, and pregelatinized starch.
   b. Each green tablet in the Ortho-Cyclen 28 package contains only inert ingredients, as follows: D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, microcrystalline cellulose, and pregelatinized starch.

Nystatin Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Nystatin	55.00
110.00	2	Ludipress	110.00
1.00	3	Aerosil 200	1.00
1.30	4	Magnesium stearate	1.30

Manufacturing Directions

1. Mix the components, and pass through a 0.8-mm sieve.
2. Press with very low-compression force.
3. Compress into 175-mg tablets, using 8-mm punches. For 100-mg strength, compress into 350-mg tablets using 10-mm punches.

Nystatin Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Nystatin	200.00
51.00	2	Lactose monohydrate	51.00
–	3	Isopropyl alcohol	40 mL
10.00	4	Kollidon CL	10.00
3.00	5	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate a mixture of items 1 and 2 with a solution of items 3 and 4. Dry, pass through a 0.8-mm sieve, add item 5, and press with medium-compression force.
2. Compress into 270-mg tablets, using 9-mm punches.

Olanzapine Orally Disintegrating Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Olanzapine	5.00
92.97	2	Mannitol DC Grade	92.97
0.50	3	Gelatin	0.50
0.50	4	Aspartame	0.50
0.02	5	Sodium methylparaben	0.02
0.01	6	sodium propylparaben	0.01
1.00	7	Colloidal silicon Dioxide (Aerosil-200)	1.00

For all other strengths adjust the total weight with item 2.

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1 and items 3 to 6 through 0.5-mm sieve and collect in a container.
4. Add 15% (=6.9 g) Mannitol from step 1 to step 3 and mix well.
5. Transfer step 4 into step 2.
6. Transfer balance quantity of step 1 into step 2.
7. Mix step 2 for 20 minutes using tumbler.
8. Pass item 7 through 0.500-mm sieve and add to step 7.
9. Mix step 8 for 2 minutes.
10. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).

Olanzapine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Olanzapine	10.00
200.00	2	Pregelatinized starch	200.00
25.00	3	Microcrystalline cellulose (Avicel PH 101)	25.00
15.00	4	Povidone	15.00
10.00	5	Croscamellose	10.00
3.75	6	Magnesium stearate	3.75
2.50	7	FD&C Yellow No. 2 Lake	2.50
–	8	Water, purified, ca	5 mL

Manufacturing Directions

1. Charge items 1 to 3, 5, and 7 in a suitable blender, and mix them.
2. In a separate vessel, prepare a binding solution using items 4 and 8.
3. Add to step 1 and granulate. Dry granules in trays at 40°C under vacuum.
4. Pass the dried granules through 60 mesh.
5. Add and blend item 6, and compress.

Olanzapine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Olanzapine	2.50
49.20	2	Lactose Spray Dried	49.20
35.00	3	Microcrystalline cellulose (Avicel PH102)	35.00
2.0	4	Crospovidone	2.00
0.50	5	Hydroxypropyl cellulose	0.50
0.80	6	Magnesium stearate	0.80
2.00	7	Hypromellose	2.00
0.45	8	Polyethylene Glycol 4000	0.45
0.60	9	Titanium dioxide	0.60
0.20	10	FD&C Blue No. 2 Aluminum Lake	0.20
–	11	Water, purified	30.00

Note: For all other strengths, adjust the total quantity with item 2.

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container.
3. Add 5.0% (=2.5 g) lactose from step 1 to step 2 and mix well.
4. Add 10.0% (=4.9 g) lactose from step 1 to step 3 and mix well.
5. Transfer step 4 into step 1.
6. Pass item 3 through 0.7-mm sieve and charge to step 1.
7. Mix step 1 for 20 minutes using tumbler.
8. Pass item 6 through 0.250-mm sieve and add to step 7.
9. Mix step 8 for 2 minutes.
10. Compress into 90-mg tablets, using a suitable punch (5.5 mm, round, imprinted 2.5).
11. Charge item 11 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
12. Add items 8 to 10 one by one to step 11 with stirring. Stir for 5 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
13. Load core tablets from step 10 in coating pan and apply coating dispersion from step 12 to get 2.5% to 3.0% weight gain.

Olanzapine Tablets Zyprexa

Each Zyprexa® tablet contains olanzapine equivalent to 2.5 mg (8 μmol), 5 mg (16 μmol), 7.5 mg (24 μmol), or 10 mg (32 μmol). The inactive ingredients are carnauba wax, color mixture white, crospovidone, FD&C Blue No. 2 Aluminum Lake, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, and other inactive ingredients.

Omeprazole and Ibuprofen Tablets (10 mg/400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Omeprazole, use magnesium omeprazole	12.00
12.00	2	Nonpareil cores	12.00
1.80	3	Hydroxypropyl methylcellulose	1.80
–	4	Water, purified	35.40
23.50	5	Hydroxypropyl cellulose	2.35
4.03	6	Talc	4.03
–	7	Water, purified	48.00
38.70	8	Methacrylic acid copolymer (30% suspension)	38.70
3.48	9	Triethyl citrate	3.48
0.58	10	Mono- and diglycerides	0.58
0.06	11	Polysorbate 80	0.06
–	12	Purified water	22.68
400.00	13	Ibuprofen	400.00
273.60	14	Microcrystalline cellulose	273.60
100.40	15	Polyvinylpyrrolidone cross-linked	100.40
33.30	16	Polyvinylpyrrolidone K-25	33.30
26.70	17	Sodium lauryl sulfate	26.70
–	18	Water, purified	297.00
4.0	19	Sodium stearyl fumarate	4.00

Manufacturing Directions

Note: The formulation and manufacturing directions given here can be used to formulate combinations of omeprazole with other NSAIDs, such as naproxen (250 mg) or piroxicam (20 mg). Omeprazole can be replaced with pantoprazole or lansoprazole.

1. Prepare a solution of items 1 and 3 in item 4, and spray onto item 2 to prepare nonpareil cores in a fluid-bed dryer.
2. Prepare a solution of items 5 to 7 and 8 to 12 separately. Alternate application of these solutions on step 1 to provide enteric properties to the cores.
3. Pass the enteric-coated cores through a sieve.
4. Prepare a granulating solution using items 16 to 18.
5. Dry blend items 13, 15 (one-tenth), and 16, and add step 4 to this step to granulate. Add more of item 18 to the mass. Pass granules through #8 mesh, and dry at 60°C for 6 hours. Pass dried granules through a 0.8-mm sieve.
6. Add step 3 and the balance of item 15, and blend for 10 minutes.
7. Compress into 886-mg tablets, using 15-mm punches. There is a disintegration time of less than 1 minute in simulated gastric juice (USP without enzymes).

Omeprazole Effervescent Tablets

Manufacturing Directions

1. Core material : magnesium omeprazole, 12.00 kg; non-pareil cores, 12.00 kg; hydroxypropyl methylcellulose, 1.8 kg; water purified, 35.4 kg. Suspension layering is performed in a fluid-bed apparatus. Magnesium omeprazole is sprayed onto inert suger seeds (non-pareil cores) from a water suspension containing the dissolved binder.
2. Separating layer core material (step 1), 23.50 kg; hydroxypropyl cellulose, 2.35 kg; talc, 4.03 kg; magnesium stearate, 0.34 kg; water purified, 48.00 kg. The prepared core material is coating layered with a separating layer in a fluid-bed apparatus with a hydroxypropyl cellulose solution containing talc and magnesium stearate.
3. Enteric coating layer pellets with the layer (step 2), 29.00 kg; methacrylic acid copolymer (30% suspension), 38.70 kg; triethyl citrate, 3.48 kg; mono- and diglycerides (NF), 0.58 kg; polysorbate 80, 0.06 kg; water purified, 22.68 kg. The enteric coating layer consisting of methacrylic acid copolymer, mono- and diglycerides, triethylcitrate, and polysorbate is sprayed onto the pellets (layered with a separating layer) in a fluid-bed apparatus. In the same type of apparatus the enteric coating layered pellets are coated with hydroxypropyl methylcellulose/Mg-stearate suspension.
4. Over-coating layer enteric-coated pellets (step 3), 44.7 kg; hydroxypropyl methylcellulose, 0.58 kg; mg-stearate, 0.02 kg; water purified, 11.6 kg. The pellets covered by an over-coating layer are classified by sieving.
5. The obtained enteric coating layered pellets are mixed with prepared granules and other components as described below and thereafter compressed to effevescent tablets.
6. Granulation (1000 tablets): citric acid anhydrous, 605 g; Mannitol dried, 200 g; riboflavin, 0.1 g; polyvinylpyrrolidone K-25 (PVP K-25), 6.0 g; EtOH 99% (w/v), 90 g.
7. PVP K-25 is dissolved in ethanol to give the granulating solution. In this solution riboflavin is dispersed. Citric acid and mannitol are mixed and the liquid is added and the mass further mixed. Then the mass is put on a tray and dried in a drying oven for approximately 2 hours at 55°C. The granulate is milled to pass sieve 1.0 mm.
8. A premix consisting of the following is prepared by dry mixing in a mixer: Sodium carbonate anhydrous, 36 g; sodium dodecyl sulfate, 1 g; sodium stearylfumarate, 14 g; essence orange, 2.0 g; saccharine sodium, 2.0 g; polyvinyl pyrrolidone cross-linked, 70 g; enteric-coated pellets from above, 95.7 g.
9. Final mixing: Granulate from above, 811.1 g, premix from above, 220.7 g, sodium bicarbonate, 453 g. The final mixing time is 4 minutes.
10. Compression to tablets is done on a tabletting machine equipped with punches giving 20-mm diameter flat tablets with bevelled edges. Tablet weight is 1485 mg.

Omeprazole Fast-Disintegrating Tablets

Manufacturing Directions

1. Croscarmellose sodium 300 g is added to the vortex of a rapidly stirred beaker containing 3.0 kg of deionized water.
2. This slurry of step 1 is mixed for 10 minutes.
3. Omeprazole 90 g (powdered) is placed in the bowl of a Hobart mixer. After mixing, the slurry of croscarmellose sodium is added slowly to the omeprazole in the mixer bowl, forming a granulation, which is then placed in trays and dried at 70°C for 3 hours.
4. The dry granulation is then placed in a blender, and 1500 g of Avicel AC-815 (85% microcrystalline cellulose coprocessed with 15% of a calcium, sodium alginate complex) and 1500 g of Avicel PH-302 (microcrystalline cellulose) are added.
5. After the mixture of step 4 is thoroughly blended, 35 g of magnesium stearate is added and mixed for 5 minutes.
6. The resulting mixture of step 5 is compressed into tablets on a standard tablet press with an average weight of about 0.75 g, and contain about 20 mg omeprazole.

Omeprazole Fast-Dissolving Tablets

Manufacturing Directions

1. Croscarmellose sodium (300 g) is added to the vortex of a rapidly stirred beaker containing 3.0 kg of deionized water.
2. The slurry in step 1 is mixed for 10 minutes.
3. 90 g of Omeprazole (powdered) is placed in the bowl of a Hobart mixer. After mixing, the slurry of croscarmellose sodium is added slowly to the omeprazole in the mixer bowl, forming a granulation which is then placed in trays and dried at 70°C for 3 hours.
4. The dry granulation is then placed in a blender, and to it is added 1500 g of Avicel AC-815 (85% microcrystalline cellulose coprocessed with 15% of a calcium, sodium alginate complex) and 1500 g of Avicel PH-302 (microcrystalline cellulose).
5. After the above mixture is thoroughly blended, 35 g of magnesium stearate is added and mixed for 5 minutes.
6. The resulting mixture is compressed into tablets on a standard tablet press with average weight of about 1.5 g that contains about 20 mg omeprazole. These tablets have low friability and rapid disintegration time. This formulation may be dissolved in an aqueous solution containing a buffering agent for immediate oral administration. Alternatively, the suspension tablet may be swallowed whole with a solution of buffering agent. In both cases, the preferred solution is sodium bicarbonate 8.4%. As a further alternative, sodium bicarbonate powder (about 975 mg per 20 mg dose of omeprazole (or an equipotent amount of other PPI)) is compounded directly into the tablet. Such tablets are then dissolved in water or sodium bicarbonate 8.4%, or swallowed whole with an aqueous diluent.

Omeprazole Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Omeprazole	20.00
200.00	2	Poloxamer (Pluronic PE 6800)	200.00
7.00	3	Colloidal silicon dioxide	7.00
10.00	4	Magnesium carbonate	10.00
12.00	5	Sodium starch glycollate	12.00
100.00	6	Titanium dioxide	100.00
226.00	7	Ludipress	226.00
25.00	8	Sodium stearyl fumarate	25.00
Enteric coating layer			
75.00	9	Polyvinyl acetate phthalate	75.00
0.25 mg	10	Antifoam emulsion	0.25 mg
12.00	11	Sodium hydroxide	12.00

Manufacturing Directions

1. The poloxamer is melted at a temperature of 80°C.
2. Omeprazole, together with 2 mg of colloidal silicon dioxide, 8 mg of magnesium carbonate, titanium dioxide, and 6 mg of sodium starch glycolate are added and mixed thoroughly. Mixing is continued until the melt solidified.
3. The melt is granulated and the rest of the ingredients added to the granulate. The granulate is then compressed into tablets containing 20-mg Omeprazole.
4. These tablets, which formed the substrate of the composition, are then transferred into a conventional coating pan and coated with the enteric coating layer, prepared in the following manner.
   a. First, the antifoam emulsion is dissolved in water to form an aqueous solution. Polyvinyl acetate phthalate is then stirred into this solution for a final concentration of about 10% weight per volume before sodium hydroxide is added.
   b. Sodium hydroxide (1 M solution) is then added to adjust the pH value of the solution to about 8, thereby obtaining a basic solution of the enteric coating material.
   c. This solution is then sprayed onto the tablets with an incoming air temperature of 40°C. The omeprazole cores can be alternately coated using hydroxypropyl methyl cellulose acetate succinate (HPMCAS) as the enteric coating layer.

Omeprazole Tablets (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Omeprazole	10.00
200.00	2	Calcium glycerophosphate	200.00
400.00	3	Sodium bicarbonate	400.00
12.00	4	Croscarmellose sodium	12.00
3.00	5	Pregelatinized starch	3.00

Omeprazole Tablets (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Omeprazole	10.00
175.00	2	Calcium glycerophosphate	175.00
175.00	3	Calcium lactate	175.00
250.00	4	Sodium bicarbonate	250.00
20.00	5	Polyethylene glycol 6000	20.00
12.00	6	Croscarmellose sodium	12.00
3.00	7	Peppermint flavor	3.00
1.00	8	Magnesium silicate	1.00
1.00	9	Magnesium stearate	1.00

Omeprazole Tablets, Chewable (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Omeprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
250.00	4	Sodium bicarbonate	250.00
0.50	5	Aspartame calcium	0.50
12.00	6	Silicon dioxide colloidal	12.00
15.00	7	Starch (maize)	15.00
12.00	8	Croscarmellose sodium	12.00
10.00	9	Dextrose anhydrous	10.00
3.00	10	Peppermint flavor	3.00
3.00	11	Maltodextrin	3.00
3.00	12	Mannitol	3.00
3.00	13	Pregelatinized starch	3.00

Manufacturing Directions

1. Pass all ingredients through a 250-μm mesh, and blend in a suitable blender.
2. Compress into 672-mg tablets, using 15-mm biplanar punches. For 20-mg tablets, increase the quantity of item 1 and compress an additional 10 mg.

Omeprazole Tablets, Rapid Dissolution (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Omeprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
500.00	4	Sodium bicarbonate	500.00
50.00	5	Calcium hydroxide	50.00
12.00	6	Croscarmellose sodium	12.00

Omega Fatty Acids Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
140.00 g	1	Omega fatty acids dry N-3	140.00
140.00 g	2	Avicel™ PH101	140.00
8.40 g	3	Kollidon® VA 64	8.40
2.00 g	4	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 289-mg tablets, using 9-mm biconvex punches.
3. The dry powder omega fatty acids dry N-3 contains 25% fish oil; this fish oil consists of about 30% EPA+DHA.
4. These tablet cores could be coated with an enteric coating of Kollicoat MAE 30 D. (See Appendix for more choices.)

Orlistat Chewable Tablets

Manufacturing Directions

1. Orlistat (60 g) and myristic acid (30 g) are melted together at 50°C.
2. Mannitol (400 g) and lactose (400 g) are added and the mixture is cooled to room temperature under continuously stirring.
3. Talcum (10 g) is added and homogeneously distributed.
4. The powder is pressed into tablets of 960 mg weight (=orlistat content of 120 mg).

Orlistat Chewable Tablets

Manufacturing Directions

1. Orlistat (120 g) and myristic acid (30 g) are melted together at 50°C.
2. Sucrose palmitate (PEG40 stearate, 12 g) and lactose (15 g) are added and the mixture is cooled to room temperature under continuously stirring.
3. The powder is pressed into tablets of 960 mg weight (=orlistat content of 120 mg).

Orlistat Chewable Tablets

Manufacturing Directions

1. Mix together orlistat (120 g), sodium laurate (30 g), mannitol (80 g), and HPMC 3cp (60 g) with stepwise addition of a (50:50% m/m) ethanol/water mixture (0.2 mL/g).
2. The formed granules are dried in vacuum at 30°C to constant weight and pressed into tablets (each containing 120 mg orlistat).

Oxprenolol Retard Tablets

Manufacturing Directions

1. 15.6 kg of 3-(4-chloro-3-sulfamoylphenyl)-3-hydroxy-isoindolin-1-one (chlortalidone), 3.0 kg of microcrystalline cellulose, 6.456 kg of dicalcium phosphate, 0.9 kg of cornstarch, 0.024 kg of iron yellow, and 0.120 kg of magnesium stearate are homogeneously mixed.
2. The pressing of the two active substance mixtures to form capsule-shaped tablets is carried out as described in Example 2. The tablets have a length of 18.0 mm, a width of 5.5 mm, a depth of approximately 5.6 mm, and a radius of curvature of 3.5 mm; the depth of the dividing notches provided on both sides is 1.47 mm in each case.

Oxprenolol Retard Tablets

Manufacturing Directions

1. A mixture of 9.6 kg of the ground hydrochloride of 1-(2-allyloxyphenoxy)-3-isopropylaminopropan-2-ol (oxprenolol) and 6.98 kg of ground lactose is granulated together with 16.0 kg of a 30% aqueous dispersion of the 70:30 copolymer of ethyl acrylate and methyl methacrylate in the fluidized bed; the spraying-in speed is 0.7 L/min and the temperature of the supply air is 38°C. The mixture is then dried in the same apparatus for 25 minutes at a supply air temperature of 40°C. With the simultaneous addition of 0.12 kg of colloidal silicon dioxide, 0.3 kg of calcium stearate, and 4.0 kg of stearic acid, the granulate is forced through a sieve of 1-mm mesh width and then mixed in a planetary mixer for 15 minutes.

2. The pressing of the granulate to form capsule-shaped biconvex tablets each weighing 410 mg is carried out on a tablet press having guided dies (the two opposing dies being provided with wedges for forming the dividing notches) having the following dimensions: length = 16.5 mm, width = 6.0 mm, and radius of curvature = 3.6 mm. The tapering dividing notches provided on both sides are each 1.47 mm in depth; the depth of the compact is approximately 5.4 mm.
3. Coating is carried out in a coating vessel of 55 cm diameter, which is equipped with baffle plates. With the aid of a binary nozzle 5 kg of compacts are sprayed continuously with a coating solution or suspension of the following composition. 0.1 kg of hydroxypropyl methylcellulose (viscosity 5 cps) are dissolved in 1.2 kg of demineralized water.
4. To this there are added while stirring, 0.005 kg of polysorbate 80, 0.05 kg of talc, and 0.1 kg of a 20% homogeneous suspension of titanium dioxide in a solution of 0.007 kg of hydroxypropyl methylcellulose (5 cps) in 90% ethanol. The supply air temperature is 60°C; the temperature of the compacts in the vessel is maintained at approximately 35°C. The amount of film coating sprayed on is 19 mg (dry weight) per compact.

Oxprenolol Retard Tablets

Manufacturing Directions

1. 15.6 kg of 3-(4-chloro-3-sulfamoylphenyl)-3-hydroxyisoindolin-1-one (chlortalidone), 3.0 kg of microcrystalline cellulose, 6.456 kg of dicalcium phosphate, 0.9 kg of cornstarch, 0.024 kg of iron yellow, and 0.120 kg of magnesium stearate are homogeneously mixed.
2. The pressing of the two active substance mixtures to form capsule-shaped tablets is carried out as described in Example 2. The tablets have a length of 18.0 mm, a width of 5.5 mm, a depth of approximately 5.6 mm, and a radius of curvature of 3.5 mm; the depth of the dividing notches provided on both sides is 1.47 mm in each case.

Oxybutynin Chloride Tablets (5 mg/10 mg) Ditropan

Each Ditropan XL extended-release tablet contains 5 or 10 mg of oxybutynin chloride USP, formulated as a once-a-day controlled-release tablet for oral administration. Ditropan XL also contains the following inert ingredients: cellulose acetate, hydroxypropyl methylcellulose, lactose, magnesium stearate, polyethylene glycol, polyethylene oxide, synthetic iron oxides, titanium dioxide, polysorbate 80, sodium chloride, and butylated hydroxytoluene.

Ditropan XL uses osmotic pressure to deliver oxybutynin chloride at a controlled rate over approximately 24 hours. The system, which resembles a conventional tablet in appearance, comprises an osmotically active bilayer core surrounded by a semipermeable membrane. The bilayer core is composed of a drug layer containing the drug and excipients, and a push layer containing osmotically active components. There is a precision-laser-drilled orifice in the semipermeable membrane on the drug-layer side of the tablet. In an aqueous environment, such as the gastrointestinal tract, water permeates through the membrane into the tablet core, causing the drug to go into suspension and the push layer to expand. This expansion pushes the suspended drug out through the orifice. The semipermeable membrane controls the rate at which water permeates into the tablet core, that in turn, controls the rate of drug delivery. The controlled rate of drug delivery into the gastrointestinal lumen is thus independent of pH or gastrointestinal motility. The function of Ditropan XL depends on the existence of an osmotic gradient between the contents of the bilayer core and the fluid in the gastrointestinal tract. Because the osmotic gradient remains constant, drug delivery remains essentially constant. The biologically inert components of the tablet remain intact during gastrointestinal transit and are eliminated in the feces as an insoluble shell.

Oxybutynin Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Oxybutynin hydrochloride	15.00
15.00	2	Polyvinylpyrrolidone	15.00
3.00	3	Silicon dioxide	3.00
100.00	4	Lactose	100.00
30.00	5	Fumaric acid	30.00
1.50	6	Sodium stearyl fumarate	1.50

Manufacturing Directions

1. Oxybutynin hydrochloride, fumaric acid, and lactose are placed in a fluidized bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1-mm mesh), and sodium stearyl fumarate is weighed, added, and blended in a drum mixer.
4. The resulting mixture is pressed into tablets (7-mm diameter and 7-mm curvature) with average hardness being between 60 and 120 N and a total weight of 164.50 mg.
5. These tablet cores are then coated with the following formulation: ethyl cellulose (Ethocel), 10.10; polyvinylpyrrolidone (Povidone), 5.50 mg; stearic acid, 2.40 mg; for total weight of 182.50 mg.
6. Ethocel, povidone, and stearic acid are first dissolved in denatured alcohol (180 g). The coating solution is then sprayed onto the tablet cores in a coating pan.

Oxybutynin Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Oxybutynin hydrochloride	10.00
15.00	2	Polyvinyl pyrrolidone	15.00
3.00	3	Silicon dioxide colloidal	3.00
100.00	4	Lactose	100.00
30.00	5	Fumaric acid	30.00
1.50	6	Sodium stearyl fumarate	1.50
–	7	Water, purified	85.00

Manufacturing Directions

1. Charge oxybutynin hydrochloride, fumaric acid, and lactose in fluidized-bed equipment.
2. Prepare in a separate container an aqueous PVP solution (in 85 g of water).
3. Spray the solution in step 2 into step 1 to form granules at a typical setting using a fluid-bed dryer: Airflow = 100 to 110 m^3/h; liquid flow (g/min) = 6 to 7 g/min; inlet temperature = 65; and spraying pressure = 2.8 bar.
4. Pass dried granules through a sieve (1-mm mesh). Sodium stearyl fumarate is weighed, added, and blended in a drum mixer.
5. Compress using 7-mm punches at 164 mg.
6. Coat the tablets using the following formula per tablet: ethylcellulose (Ethocel), 10.10; polyvinylpyrrolidone (Povidone), 5.50; stearic acid, 2.40; and the total weight (dry weight of coated tablet) is 182.50.

Oxycodone Hydrochloride and Acetaminophen Tablets (5 mg/325 mg) Percocet

Each tablet of Percocet contains acetaminophen, 325 mg, and oxycodone HCl, 5 mg (5 mg oxycodone HCl is equivalent to 4.4815 mg oxycodone.) The inactive ingredients are microcrystalline cellulose, povidone, pregelatinized starch, stearic acid, and other ingredients.

Oxycodone and Acetaminophen Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
325.00	1	Acetaminophen powder	325.00
4.48	2	Oxycodone, use oxycodone hydrochloride	5.00
6.00	3	Colloidal silicon dioxide	6.00
77.00	4	Microcrystalline cellulose	77.00
32.00	5	Croscarmellose sodium	32.00
13.00	6	Hydroxypropyl methylcellulose	13.00
62.00	7	Starch (maize)	62.00
2.00	8	Magnesium stearate	2.00
–	9	Water, purified	QS

Manufacturing Directions

1. Pass hydrocodone bitartrate through a #20 mesh, and pass acetaminophen and colloidal silicon dioxide (50%) through a Frewitt SG Turbo Sieve equipped with a 1.0-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-line collecting drum at speed setting 5 (approximately 1030 rpm).
2. Pass microcrystalline cellulose (50%), croscarmellose sodium (50%), cornstarch (66%), and hydroxypropyl methylcellulose through the Turbosieve at the same settings as in step 2. Charge screened powders into a Lodige MGT-600 mixer, and mix for 5 minutes with the plow speed at approximately 103 rpm and no choppers.
3. Add water to the mixer over a 10-minute period, using a stainless steel transfer container with a valve, while mixing with the plows at about 103 rpm and the choppers at slow speed.
4. Mix the wet mass for another 15 minutes until a Wattmeter reading of 15 to 16 MkW is reached.
5. Dry the material. Preheat a Glatt fluid-bed dryer by running it for 2.5 minutes at 60°C inlet air temperature at 3500 m^3/h. Set the exhaust blower bypass speed at about 40%, the filter shaking interval for about 2 minutes and the filter shake duration of 5 seconds. Transfer the material in the dryer for drying. Decrease the inlet air to 2500 m^3/h and the inlet air temperature to 55°C after 30 minutes. Dry the material until an LOD of less than 0.5% is reached.
6. Pass the dried granulation through a FitzMill using a #20 mesh wire screen, with knives forward, at medium speed.
7. Pass the remaining microcrystalline cellulose and the colloidal silicon dioxide through a sieve equipped with a 1-mm round-hole screen, an angle bar, a cloth skirt, and a polyethylene-lined collecting drum.
8. Add magnesium stearate, and mix for 3 minutes.
9. Compress using a 13/32 ± round tooling.

Oxycodone Hydrochloride Tablets (5 mg)

Each tablet contains oxycodone hydrochloride, 5 mg. The tablets also contain microcrystalline cellulose and stearic acid. The oral solution contains alcohol, FD&C Red No. 40, flavoring, glycol, sorbitol, water, and other ingredients.

Oxytetracycline Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Oxytetracycline hydrochloride	250.00
230.00	2	Ludipress	230.00
6.00	3	Magnesium stearate	6.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with very low-compression force.
2. Compress into 495-mg tablets, using 12-mm biplanar punches.

Pancreatin and Cholic Acid Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
130.00	1	Pancreatin	130.00
2.00	2	Cholic acid	2.00
127.00	3	Avicel™ PH101	127.00
56.00	4	Lactose monohydrate	56.00
2.00	5	Magnesium stearate	2.00
3.00	6	Aerosil® 200	3.00

Manufacturing Directions

1. Mix the components, and press with high-compression force.
2. Compress into 324-mg tablets, using 9-mm biconvex punches.
3. Coat by enteric coating. (See Appendix.)

Pancreatin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Pancreatin	30.00
308.00	2	Ludipress®	308.00
10.00	3	Kollidon® CL	10.00
2.00	4	Magnesium stearate	2.00

Manufacturing Directions

1. Mix the components, pass through an 0.8-mm sieve, and press with low-compression force.
2. Compress into 355-mg tablets, using 8-mm biconvex punches.
3. Coat by enteric coating. (See Appendix.)

Pancreatin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Pancreatin	300.00
290.00	2	Ludipress®	290.00
25.00	3	Kollidon® CL	25.00
3.00	4	Magnesium stearate	3.00

Manufacturing Directions

1. Mix the components, pass through an 0.8-mm sieve, and press to tablets with low-compression force.
2. Compress into 615-mg tablets, using 11-mm biconvex punches.
3. Coat by enteric coating. (See Appendix.)

Pantoprazole Tablets Protonix

Protonix is supplied as a delayed-release tablet for oral administration, available in two strengths. Each delayed-release tablet contains 45.1 or 22.6 mg of pantoprazole sodium sesquihydrate (equivalent to 40 or 20 mg of pantoprazole, respectively), with the following inactive ingredients: calcium stearate, crospovidone, hydroxypropyl methylcellulose, iron oxide, mannitol, methacrylic acid copolymer, polysorbate 80, povidone, propylene glycol, sodium carbonate, sodium lauryl sulfate, titanium dioxide, and triethyl citrate.

Pantoprazole Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Pantoprazole	10.00
200.00	2	Calcium glycerophosphate	200.00
400.00	3	Sodium bicarbonate	400.00
12.00	4	Croscarmellose sodium	12.00
3.00	5	Pregelatinized starch	3.00

Pantoprazole Tablets (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Pantoprozole	10.00
175.00	2	Calcium glycerophosphate	175.00
175.00	3	Calcium lactate	175.00
250.00	4	Sodium bicarbonate	250.00
20.00	5	Polyethylene glycol 6000	20.00
12.00	6	Croscarmellose sodium	12.00
3.00	7	Peppermint flavor	3.00
1.00	8	Magnesium silicate	1.00
1.00	9	Magnesium stearate	1.00

Pantoprazole Tablets, Chewable (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Pantoprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
250.00	4	Sodium bicarbonate	250.00
0.50	5	Aspartame calcium	0.50
12.00	6	Silicon dioxide colloidal	12.00
15.00	7	Starch (maize)	15.00
12.00	8	Croscarmellose sodium	12.00
10.00	9	Dextrose anhydrous	10.00
3.00	10	Peppermint flavor	3.00
3.00	11	Maltodextrin	3.00
3.00	12	Mannitol	3.00
3.00	13	Pregelatinized starch	3.00

Manufacturing Directions

1. Pass all ingredients through a 250-μm mesh, and blend in a suitable blender.
2. Compress into 672-mg tablets, using 15-mm biplanar punches. For 20-mg tablets, increase the quantity of item 1, and compress an additional 10 mg.

Pantoprazole Tablets, Rapid Dissolution (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Pantoprazole	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
500.00	4	Sodium bicarbonate	500.00
50.00	5	Calcium hydroxide	50.00
12.00	6	Croscarmellose sodium	12.00

Papain Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Papain	1.00
150.00	2	Lycasin	150.00
17.40	3	Hydrogenated vegetable oil	17.40
9.60	4	Water	9.60
5.8	5	Gelatin (40% solution)	5.8
17.4	6	Starch-coated dicalcium phosphate	17.4
1.60	7	Monodiglyceride mixture	1.60
0.60	8	Lecithin	0.60
0.10	9	Aspartame	0.10
0.10	10	Vanillin	0.10
0.20	11	Glycerin	0.20
0.20	12	Sodium bicarbonate	0.20
0.38	13	Mint flavor	0.38

Manufacturing Directions

1. Boil Isomalt, Lycasin, water, fat, mono- and diglyceride mixture, glycerin, and lecithin to 131°C.
2. Glycerin is added and the mixture is cooled to 60°C.
3. Thereafter sodium bicarbonate, papain, dicalcium phosphate, and the remaining ingredients are added.
4. Thereafter the mixture is cooled to room temperature and is ground into powder and compressed into a 205 mg tablet by using a tablet press.

Papaverine Hydrochloride Retard Tablet

Formulation: Cetyl alcohol, 10 g; hydroxyethyl cellulose, 5 g; papaverine hydrochloride, 75 g; talc, 10 g.

Manufacturing Directions

1. Melt cetyl alcohol in a jacketed vessel and incorporate papaverine hydrochloride, blend well, and granulate through a #16 standard mesh sieve. Dry at room temperature.
2. Hydrate the hydroxyethyl cellulose with 15 g of water.
3. Blend the granules obtained as a result of step 1 with the hydrated cellulose component of step 2 and mix well.
4. Granulate the whole through a #16 standard mesh sieve and dry.
5. Compress into tablets of suitable size and shape.

Para Amino Salicylic Acid Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Calcium para amino salicylic acid	500.00
280.00	2	Ludipress	280.00
35.00	3	Kollidon 35	35.00
–	4	Isopropyl alcohol	QS
5.00	5	Magnesium stearate	5.00
5.00	6	Talc	5.00

Manufacturing Directions

1. Granulate items 1 and 2 with a solution of items 3 and 4. Dry the granules, and lubricate with items 5 and 6.
2. Compress into 825-mg tablets, using 16-mm biplanar punches.

Paroxetine Hydrochloride Tablets (10 mg/20 mg/ 30 mg/40 mg) Paxil

1. Immediate-release tablets—Each film-coated Paxil® tablet contains paroxetine HCl equivalent to paroxetine as follows. *10 mg:* yellow; *20 mg:* pink (scored); 30 mg: blue; and *40 mg:* green. Inactive ingredients consist of dibasic calcium phosphate dihydrate, hydroxypropyl methylcellulose, magnesium stearate, polyethylene glycols, polysorbate80, sodium starch glycolate, titanium dioxide, and one or more of the following: D&C Red No. 30, D&C Yellow No. 10, FD&C Blue No. 2, and FD&C Yellow No. 6.
2. Controlled-release tablets—Each enteric, film-coated, bilayer, controlled-release Paxil tablet contains paroxetine HCl equivalent to paroxetine as follows: 12.5 mg and 25 mg. One layer of the tablet consists of a degradable barrier layer, and the other contains the active material in a hydrophilic matrix. The barrier layer is pale yellow and pink for the 12.5- and 25-mg strength tablets, respectively; the active layer is white. Inactive ingredients consist of hydroxypropyl methylcellulose, polyvinylpyrrolidone, lactose monohydrate, magnesium stearate, colloidal silicon dioxide, glyceryl behenate, methacrylic acid copolymer type C, sodium lauryl sulfate, polysorbate 80, talc, triethyl citrate, and one or more of the following colorants: yellow ferric oxide or red ferric oxide.

Paroxetine Hydrochloride Hemihydrate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Paroxetine hydrochloride hemihydrates	22.76
160.24	2	Dibasic calcium phosphate hemihydrates	160.24
8.00	3	Povidone anhydrous PVP K30	8.00
6.00	4	Sodium starch glycolate	6.00
3.00	5	Magnesium stearate	3.00
qs	6	Water	qs

Manufacturing Directions

1. Paroxetine hydrochloride hemihydrate, dibasic calcium phosphate anhydrous, sodium starch glycolate and povidone are premixed and granulated with water;
2. The granulate, after drying and milling through a 0.6-mm sieve, is mixed with dibasic calcium phosphate anhydrous and sodium starch glycolate in a dry state for 20 minutes. Then magnesium stearate is added, followed by mixing for a further 5 minutes;
3. Tablets are pressed (approximately 206 mg) from the resulting mixture, and coated with a coating suspension of Opadry containing the composition (%w/w) titanium dioxide, 31.250; hydroxypropyl methylcellulose, 29.875 (Methocel E3 Premium); Hydropropyl methylcellulose, 29.875 (Methocel E5 Premium); Polyethylene Glycol 400, 8.000; Polysorbate 80 (Tween), 1.000).

Paroxetine Hydrochloride Hemihydrate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
22.76	1	Paroxetine Hydrochloride 22.76	22.76
160.24	2	Hemihydrate Dibasic Calcium Phosphate Anhydrous	160.24
8.00	3	Anhydrous Povidone (PVP K-30)	8.00
6.00	4	Sodium starch Glycolate	6.00
3.00	5	Magnesium Stearate	3.00
QS	6	Purified water Q.S.	QS

Manufacturing Directions

1. Paroxetine hydrochloride hemihydrate, dibasic calcium phosphate anhydrous, sodium starch glycolate, and povidone are premixed and granulated with water;
2. The granulate, after drying and milling through a 0.6-mm sieve, is mixed with dibasic calcium phosphate anhydrous and sodium starch glycolate in a dry state for 20 minutes. Then magnesium stearate is added, followed by mixing for a further 5 minutes;
3. Tablets are pressed from the resulting mixture, and coated with a coating suspension of Opadry Coating Suspension (Opadry 6.0) Composition: (%w/w) titanium dioxide, 31.250%; hydroxypropyl methylcellulose, 29.875% (Methocel E3 Premium); hydropropyl methylcellulose, 29.875% (Methocel E5 Premium); polyethylene glycol 400, 8.000%; polysorbate 80 (Tween), 1.000%.
4. Tablet weight is for about 20 mg strength (approximately 206 mg).

Penicillin Chewable Tablets (125 mg)

Each tablet contains Penicillin V potassium equivalent to 250 mg (400,000 units) or 500 mg (800,000 units) Penicillin V. The tablets also contain lactose, magnesium stearate, povidone, starch, stearic acid, and other inactive ingredients.

Penicillin Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
277.16	1	Mannitol	277.16
53.00	2	Sugar	53.00
21.20	3	Sodium cyclamate	21.20
2.30	4	Saccharin sodium	2.30
125.00	5	Penicillin, use benzathine Penicillin V, 3% excess	172.83
–	6	Water, purified, ca	96.00 mL
5.50	7	Raspberry flavor	5.50
4.40	8	Polarcillin potassium (Amberlite IRP-88)	4.40
11.60	9	Talc	11.60
35.00	10	Magnesium stearate	35.00

Note: Adjust the weight of penicillin for potency, and alter the weight of mannitol to compensate. The weight of sodium citrate is 450 minus the weight of penicillin.

Manufacturing Directions

Note: Allergic reactions sometimes occur with penicillin. Avoid contact as much as possible, and use equipment dedicated to penicillin or cephalosporin products. The LOD limits are low, so use an air-conditioned area.

1. Granulation
   a. Mill mannitol, sugar, sodium cyclamate, and sodium saccharin through a 2.38-mm aperture screen using a suitable comminuting mill, with knives forward, at medium speed.
   b. Add the milled materials from step 1 to the mixer, and then add the penicillin. Mix for 10 minutes. Add the water slowly, cleaning the sides of the mixer as necessary. Mix for 10 minutes after the water is added. The final mass should have a sandy appearance.
   c. Transfer the wet granulation to the bowl of a fluid-bed dryer through a 6.7-mm aperture screen. Dry at 30°C for 20 minutes. Stir, then pass the granulation by hand through a 5.5-mm aperture screen. After that, transfer the granulation to the bowl of the fluid-bed dryer.
   d. Continue drying at 60°C, turning over after each 30 minutes, until the LOD is no more than 0.8% (drying time is approximately 60 minutes).
   e. Screen the dried granules through an 840-μm aperture screen on a suitable sieve shaker, and pass the coarse material through a 1.6-mm aperture screen on a comminuting mill, at low speed, with knives forward.
   f. Screen the flavor, polarcillin potassium, magnesium stearate, and talc through a 595-μm screen on a sieve shaker. Charge the screened powders into a suitable blender.
   g. Charge the screened and milled granules from step 5 into the blender, and blend for 30 minutes.
   h. Discharge the granulation into tared polyethylene-lined drums, and seal the bags. Weigh them for yield.
   i. Compress on 9.53-mm square punches. Note the weight according to the adjustments made (hardness: 10–12 kPa diagonally, 15–21 kPa flat).

Peptide Sublingual Tablets

Formulation: The individual component peptides each have a molecular weight of less than 20000 daltons. Thymosin fraction, 5%; water, 5.0%; sucrose/lactose, 69.5%; propylene glycol, 0.5%; silicon dioxide, 15.0%; methyl nicotinate, 0.5%.

Manufacturing Directions

The wetted mixture is formed into tablets of a desired weight and the tablets are then dried at 30°C for 36 hours.

Perfloxacin Tablets (400 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Perfloxacin, use perfloxacin mesylate	592.00
63.00	2	Lactose monohydrate	63.00
42.00	3	Dicalcium phosphate	42.00
52.00	4	Starch (maize)	52.00
22.00	5	Starch (maize)	22.00
1.00	6	Gelatin	1.00
15.60	7	Sodium starch glycolate	15.60
10.00	8	Talc	10.00
5.00	9	Magnesium stearate	5.00
3.00	10	Sodium starch glycolate	3.00
10.00	11	Starch (maize)	10.00
–	12	Water, purified	QS

Manufacturing Directions

1. Sift items 1 to 4 through a 250-μm sieve, and charge into a suitable vessel; mix it for 10 minutes.
2. In a separate vessel, charge items 5 to 7, and add hot item 12 to make a 30% starch paste.
3. Add the paste in step 2 to step 1, and form a wet mass suitable for granulating.
4. Pass the wet mass through a #8 sieve, and spread it on paper-lined trays.
5. Dry the granules at 50°C overnight until an LOD of not more than 3% is reached.
6. Pass the dried granules through a 1.19-mm sieve screen into a blending vessel.
7. Sift items 8 to 11 through a 250-μm sieve, and add to step 6. Blend for 2 minutes.
8. Compress into 815-mg tablets, using an 18.8 × 8.8-mm punch.
9. Coat the material with an HPMC methylene chloride coating. (See Appendix.)

Phenindione Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Phenindione	50.00
165.00	2	Ludipress®	165.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with low-compression force.
2. Compress into 230-mg tablets, using 8-mm biplanar punches.

Phenindione Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Phenindione	50.00
165.00	2	Ludipress	165.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 230-mg tablets, using 8-mm biplanar punches.

Phendimetrazin Tablets (35 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
35.00	1	Phendimetrazin	35.00
281.00	2	Ludipress	281.00
281.00	3	Starch (maize)	281.00
3.00	4	Magnesium stearate	3.00
3.00	5	Aerosil 200	3.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 604-mg tablets, using 12-mm biplanar punches. The amount of Ludipress and cornstarch may be reduced to obtain better disintegration times.

Phenoxymethyl Penicillin Potassium Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
58.10	1	Sodium citrate powder	68.10
250.00	2	Penicillin V acid, use phenoxymethyl potassium[a]	277.20
29.50	3	Povidone K 29–32	29.40
–	4	Alcohol SD 3A 200 proof, ca	100 mL
16.00	5	Starch (maize)	16.00
16.00	6	Talc	16.00
6.10	7	Magnesium stearate	6.10

[a]Adjust the quantity based on the factored potency and adjusted by sodium citrate. Starch must be dried. The amount of sodium citrate is 345.30-weight of item 2.

Manufacturing Directions

Note: Allergic reactions sometimes occur with penicillin. Avoid contact as much as possible, and use equipment dedicated to penicillin or cephalosporin products. The LOD limits are low, so use an air-conditioned area.

1. Granulation
   Note: Dried cornstarch must be used for lubrication. Dry the starch at 80°C for 36 hours prior to its use in manufacturing. Check the LOD of starch. The LOD must be less than 2%.
   a. Mill separately the sodium citrate through a 595-μm aperture screen using a suitable comminuting mill, at medium speed, with impact forward, and the penicillin through a 595-μm aperture screen with knives forward, at high speed. In a suitable mixer, mix them for 5 minutes.
   b. Dissolve Povidone in 100 mL of alcohol in a dry stainless steel bucket.
   c. Add PVP-alcohol slowly to the mixer, and mix for 30 minutes or until balls form in the sandy mixture. Add and record extra alcohol if required.
   d. Pass the mass through a 9.52-mm aperture screen, place into a fluid-bed dryer bowl, and dry at 50°C for 1 hour. Turn over as necessary. The LOD should not be more than 0.7%.
   e. Mill the granules through a 1.59-mm aperture screen using a suitable comminuting mill, with knives forward, at medium speed. Put the granules into tared polyethylene-lined drums, then seal, and weigh.
2. Lubrication
   a. Transfer the dried granulation to a suitable blender.
   b. Screen the dried starch and talcum through a 595-μm aperture screen on a sieve shaker, and add to the blender. Blend this mixture for 30 minutes.
   c. Screen the magnesium stearate through a 595-μm aperture screen on a sieve shaker, and add it to the blender. Blend this for 30 minutes.
   d. Discharge the granules into polyethylene-lined drums. Then, seal and weigh for yield.
3. Compression
   a. Compress using 10.32-mm round, standard concave punches.
   b. Compress to calculated weight after adjustments, with a variation not more than 3%; thickness between 4.4 and 4.6 mm (range not more than ±5%); hardness between 10 and 14 kPa, and disintegration time no more than 15 minutes in water.
4. Coating: Coat by a methocel subcoat, color coat, and polishing coat. (See Appendix.)

Phenolphthalein Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Phenolphthalein	200.00
150.00	2	Dibasic calcium phosphate	150.00
11.00	3	Kollidon® 30	11.00
–	4	Isopropanol or ethanol (96%)	QS
19.00	5	Kollidon® CL	19.00
3.00	6	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, mix with items 5 and 6, pass through an 0.8-mm sieve, and press with low-compression force.
2. Compress into 385-mg tablets, using 9-mm biconvex punches.

Phenolphthalein Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
90.00	1	Yellow phenolphthalein	90.00
64.80	2	Microcrystalline cellulose	64.80
187.20	3	Dicalcium phosphate	187.20
3.60	4	Croscarmellose sodium	3.60
3.60	5	Fumed silica	3.60
7.20	6	Stearic acid	7.20
3.60	7	Magnesium stearate	3.60

Manufacturing Directions

1. Screen items 6 and 7 through a 40-mesh sieve.
2. Blend items 1 and 5 in a V-blender for 3 minutes.
3. Add items 2 and 4 to the blender, and mix for 5 minutes.
4. Add item 3 to the blender, and mix for 12 minutes.
5. Add item 6 and blend for 3 minutes.
6. Add item 7 and mix for another 5 minutes.
7. Compress using 3/8- in., flat, bevel-edged punches to hardness of 10 kPa; average tablet weight is 360 mg.

Phenylpropanolamine and Bromopheniramine Fast-Dissolving Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.25	1	Phenylpropanomaine hydrochloride	6.25
1.00	2	Brompheniramine maleate	1.00
6.00	3	Citric acid	6.00
1.80	4	Magnasweet 135	1.80
4.50	5	Aspartame	4.50
3.60	6	Cherry flavor	3.60
21.00	7	Croscarmellose sodium	21.00
3.00	8	Lecitihin	3.00
30.00	9	Cornstarch	30.00
3.00	10	Silicon dioxide	3.00
2.10	11	Magnesium stearate	2.10
219.25	12	Fast-dissolving granulation (see below)	219.25

Manufacturing Directions

1. Fast-dissolving granulation is made by combining 400 g of melted PEG 900 with fructose powder (100 g) in a planetary mixer (low-shear mixer) and mixing until the granules formed.
2. The granulations are allowed to cool, and are then screened.
3. All ingredients are mixed in a V-blender.
4. Tablets are compressed (301.5 mg) at approximately 3 kN.
5. Tablet hardness is 0.2 to 0.5 kPa and disintegration time 10 seconds.

Phenylpropanolamine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Phenylpropanolamine hydrochloride, USP	60.00
180.00	2	Calcium sulfate dihydrate	180.00
—	3	Starch paste10%	QS
12.00	4	Starch 1500 (StarX)	12.00
6.00	5	Magnesium stearate	6.00

Manufacturing Directions

1. Add starch in 1:10 ratio to cold water, heat to boil with constant stirring until a thick, translucent white paste is formed.
2. Keep it for use in granulation below.
3. Mix the phenylpropanolamine hydrochloride with the calcium sulfate in a Sigma blade mixer for 15 minutes.
4. Add starch paste in sufficient quantity to form a suitable wet mass of desirable consistency.
5. Allow to mix for 30 minutes.
6. Pass the wet mass through a #14 screen and distribute on drying trays.
7. Dry in a forced-air oven at 49°C to 54°C or in a fluid-bed dryer.
8. Pass the dried granules through a #18 mesh screen.
9. Transfer granules to a twin-sell blender, add items 4 and 5, and blend for 6 to 8 minutes.
10. Compress the granulation in a rotary press using 3/8- in. standard punches. Tablet weight is 260 mg.

Phenylpropanolamine Hydrochloride Tablets (60 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Phenylpropanolamine hydrochloride	60.00
180.00	2	Calcium sulfate dihydrate	180.00
QS	3	Starch paste (10%)	QS
12.00	4	Starch 1500 (StaRx)	12.00
6.00	5	Magnesium stearate	6.00

Manufacturing Directions

1. Starch paste: Add starch with a 1:10 ratio to cold water. Heat to a boil, with constant stirring, until a thick, translucent white paste is formed. Keep it for use in step 2.
2. Granulation
   a. Mix the phenylpropanolamine hydrochloride with the calcium sulfate in a sigma blade mixer for 15 minutes.
   b. Add starch paste from step 1 in sufficient quantity to form a wet mass suitable of desirable consistency.
   c. Allow to mix for 30 minutes.
   d. Pass the wet mass through a #14 screen and distribute on drying trays.
   e. Dry in a forced-air oven at 120°F to 130°F or in a fluid-bed dryer.
   f. Pass the dried granules through a #18 mesh screen.
3. Lubrication
   a. Transfer granules to a twin-sell blender, add Starch 1500 and magnesium stearate, and blend for 6 to 8 minutes.
4. Compression: Compress the granulation in a rotary press using 9.5-mm standard punches. The tablet weight should be 260 mg.

Phenylbutazone Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Phenylbutazone	100.00
3.33	2	Lactose monohydrate	3.33
3.33	3	Mannitol	3.33
162.00	4	Starch (maize)	162.00
10.00	5	Starch (maize)	10.00
0.66	6	Polyvinylpyrrolidone potassium 30	0.66
0.28	7	Propyl paraben	0.28
0.28	8	Methyl paraben	0.28
5.00	9	Talc	5.00
3.00	10	Magnesium stearate	3.00
7.00	11	Sodium starch glycolate	7.00
–	12	Water, purified	QS

Manufacturing Directions

1. Sift items 1 to 4 through #40 mesh into a suitable mixing vessel. Mix for 10 minutes.
2. In a separate vessel, heat item 12 to boiling and add and dissolve items 7 and 8. Allow this blend to cool to 60°C, then add item 6, and dissolve. Finally, add item 5, and stir well to make a smooth paste of 30% starch.
3. Add the starch paste from step 2 into step 1, and mix to form a suitable wet mass.
4. Pass the wet mass in step 3 through #18 mesh onto trays. Then, dry at 60°C overnight to an LOD of not more than 2.8%. Transfer to a blending vessel.
5. Sift items 9 to 11 through a 250-μm sieve. Add to step 4, and blend for 1 minute.
6. Compress into 280-mg tablets, using a 5-mm punch.
7. Coat the tablets with a sealing coat and a color coat (HPMC). (See Appendix.)

Phenytoin Sodium Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Phenytoin sodium	100.00
235.00	2	Ludipress	235.00
10.00	3	Magnesium stearate	10.00
8.00	4	Kollidon CL	8.00
5.00	5	Aerosil 200	5.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 346-mg tablets, using 12-mm biplanar punches.

Phenytoin Sodium Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Phenytoin sodium	100.00
50.00	2	Dicalcium phosphate	50.00
45.00	3	Sucrose crystalline	45.00
10.00	4	Kollidon 25	10.00
–	5	Isopropyl alcohol + ethanol (1:1)	30.00
5.00	6	Kollidon CL	5.00
2.00	7	Magnesium stearate	2.00

Manufacturing Directions

1. Granulate the mixture of items 1 to 3 with a solution of items 4 and 5; dry. Pass through a 0.8-mm sieve, mix with items 6 and 7, and press with high-compression force.
2. Compress into 209-mg tablets, using 8-mm biplanar punches.

Phenytoin Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Phenytoin base	100.00
235.00	2	Ludipress	235.00
2.00	3	Magnesium stearate	2.00
2.00	4	Stearic acid	2.00
8.00	5	Kollidon CL	8.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 351-mg tablets, using 12-mm biplanar punches.

Pioglitazone Hydrochloride Tablets (15 mg/30 mg/ 45 mg) Actos

Actos is available as a tablet for oral administration containing 15, 30, or 45 mg of pioglitazone (as the base) formulated with the following excipients: lactose monohydrate NF, hydroxypropyl cellulose NF, carboxymethylcellulose calcium NF, and magnesium stearate NF.

Pipemidic Acid Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Pipemidic acid, use pipemidic acid trihydrate	236.00
16.00	2	Calcium carboxymethyl cellulose	16.00
4.00	3	Hydroxypropyl cellulose	4.00
8.00	4	Cellulose microcrystalline	8.00
2.40	5	Silicon dioxide colloidal	2.40
5.60	6	Magnesium stearate	5.60
QS	7	Water, purified, ca	80.00 mL

Manufacturing Directions

Caution: Wear a mask and gloves during all operations.

1. Granulation
   a. Pass pipemidic acid (item 1) and calcium carboxymethyl cellulose (item 2) through a 24-mesh (0.6-mm) screen attached to an oscillating granulator. Charge into a planetary mixer, and blend for 10 minutes.
   b. Dissolve the hydroxypropyl cellulose (item 3) in 80 mL of water, using continuous mechanical stirring.
   c. Add the binder solution to the mixed powder from step 1, and blend for 10 minutes to form a suitable mass. More water should be added, if necessary, to complete granulation and densification.
   d. The granules should then be screened through an 8-mesh (2-mm) screen.
   e. Spread the moist granules on trays, and dry at 50°C (122°F) for 16 hours or until moisture level is within the range of 11% to 16%.
2. Lubrication
   a. Using an oscillating granulator, pass the dried granules through a 12-mesh (1.4-mm) screen.
   b. Pass the cellulose microcrystalline (item 4), maize starch (item 5), silicon dioxide colloidal (item 6), and magnesium stearate (item 7) through a 12-mesh (1.4 mm) screen.
   c. Charge the items from step 2b into planetary blender. Add half of the dried granule from step 2a and blend for 5 minutes. Then add the remainder of the dried granule, and blend for an additional 15 minutes at a nominal speed of 30 rpm.
   d. Load the lubricated granule into tared, polyethylene-lined drums, and weigh for yield.
3. Compression: Compress on a suitable machine using ovaloid tooling, 12.5 mm × 6.5 mm; the compression weight is 280 mg. For 400-mg strength, 9.1 × 15.5-mm punches and 560-mg weight.
4. Coating: Coat using a methocel/ethocel coating. (See Appendix.)

Pipobroman Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Pipobroman	25.00
100.00	2	Lactose monohydrate powder	100.00
5.00	3	Povidone K 29–32	5.00
QS	4	Water, purified, ca	12 mL
2.00	5	Starch (corn)	2.00
1.10	6	Magnesium stearate	1.10

Manufacturing Directions

1. Granulation
   a. Pass pipobroman, lactose, and povidone through an 840-μm aperture screen using a FitzMill or something similar, with impact forward and high speed.
   b. Charge milled granulation into a mixer. Mix for approximately 5 minutes, and then add 12 mL of purified water to the mass. Pass granulation through a FitzMill or a similar method using a no. 5 (12.7-mm) band, with knives forward and at slow speed.
   c. Pass granulation thinly on paper-lined trays, set the oven at 50°C, and dry overnight, or until the LOD is less than 2% (1 hour Brabender at 105°C).
   d. Sift dried granulation through an 840-μm aperture screen and FitzMill the coarse granules through a 1-mm aperture screen, with knives forward, at a slow speed.
2. Lubrication
   a. Charge one-half of the base granulation into a Glen mixer or a similar mixing method.
   b. Mix cornstarch and magnesium stearate. Screen this mixture through a 595-μm aperture screen into a mixer.
   c. Charge the remaining granulation into the mixer. Blend for approximately 5 minutes.
   d. Discharge into polyethylene-lined drums. The theoretical lubricated weight is 133.1 g.
3. Compression: Compress using 9/32-in. standard concave punches, with a compression weight of 133 mg.

Piroxicam Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.40	1	Piroxicam	150.40
6.70	2	Sodium dodecyl sulfate	6.70
18.00	3	Sodium starch glycolate	18.00
44.90	4	Hydroxypropyl methyl cellulose	44.90
228.00	5	Cellulose lactose	228.00

Manufacturing Directions

1. Compress tablet.
2. Coat with co-polymer of the methacrylic acid triethylcitrate (150 mg) and simethicone 30% emulsion (15 mg).

Piroxicam Water-Dispersible Tablets (20 mg)

Formulation: Piroxicam, 20 g; cornstarch, 150 g; Ludipress, 50 g; Kollidon CL, 8 g; polyethylene glycol 6000 powder, 10 g; Aerosil 200, 1 to 2 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with low- to medium-compression force at 238 mg.

Placebo Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
299.70	1	Ludipress®	299.70
0.30	2	Magnesium stearate	0.30

Manufacturing Directions

1. Mix the components, sieve, and press.
2. For this formulation, compress 300 mg.
3. The compression force determines hardness and friability.
4. At 7 kN, the hardness is 45 N; at 22 kN, the hardness is 160 N.
5. The disintegration time increases from 1 to 4 minutes.

Placebo Tablets

Formulation: Ludipress, 99.9%; magnesium stearate, 0.1%.

Manufacturing Directions

1. Mix the components, sieve, and press.
2. Tablet weight is 300 mg.

Plaroxetine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Paroxetine, use paroxetine hydrochloride hemihydrate	22.67
83.34	2	Dicalcium phosphate (Ditab)	83.84
50.67	3	Microcrystalline cellulose (Avicel PH 102)	50.67
8.34	4	Sodium starch glycolate (Explotab)	8.34
1.67	5	Magnesium stearate	1.67

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Paroxetine, use paroxetine hydrochloride hemihydrate	34.00
125.00	2	Dicalcium phosphate (Ditab)	125.00
76.00	3	Microcrystalline cellulose (Avicel PH 102)	76.00
12.50	4	Sodium starch glycolate (Explotab)	12.50
2.50	5	Magnesium stearate	2.50

Manufacturing Directions

1. Pass item 2 through a screen, and weigh it into a planetary mixer.
2. Add 30-mesh paroxetine to the bowl.
3. Add 20-mesh Avicel and Explotab, and mix all the powders for 10 minutes.
4. Add magnesium stearate, and mix for 5 minutes.
5. Compress into pentagonal tablets using 9.5-mm punches for 30-mg tablets and 8.25 mg for 20-mg tablets. Compress 250 and 166.7 mg, respectively.

Potassium Bicarbonate-Coated Tablet

Manufacturing Directions

1. Preparation of potassium bicarbonate crystals: US Patent 5445805 describes how to prepare crystals of size within the range of 800 to 900 μm, a B.E.T. surface area of 0.004 to 0.01 m^2/g and particle distributions such that over 90% by weight of the crystals are within the range of 700 to 1000 μm. (At least 90% of the crystals are retained on a 25-mesh screen [707 μm] and less than 10% are retained on an 18-mesh screen [1000 μm]).
2. Preparation and application of controlled release coating lacquers—Coating lacquer composition: CUTINA HR, 23.45 g; ETHOCEL, 163.45 g; acetyl tributyl citrate, 8.75 g; isopropyl alcohol, 3304.35 g. Total = 3500.00 g.
3. Coating conditions: process air flow = 100 to 171 m^3/h; spray period = 135 minutes; spray temperature = 60.1°C to 68.1°C; spray pressure = 2.0 bars; liquid flow rate = 26 to 28 g/min; product temperature = 46°C to 52°C. Coated crystals: theoretical yield = 3191.1 g; actual yield around 98% giving w/w dry matter of 6.37% (coated/uncoated crystals).
4. Hydrogenated castor oil (CUTINA HR), ethylcellulose (ETHOCEL Standard 100 premium), and acetyl tributyl citrate are dissolved in isopropyl alcohol to provide the controlled release coating lacquers.
5. CUTINA HR, ETHOCEL, and acetyl tributyl citrate are dissolved in the isopropyl alcohol solvent by heating in a mixer equipped with a heating jacket set at 60°C to 70°C with vigorous agitation. The agitation is continued for about 1 hour. When dissolved, the mixture is clear to translucent.
6. The coating lacquer composition is maintained at temperatures of 60°C to 70°C.
7. The lacquers are coated on the potassium bicarbonate particles by co-current flow through a fluidized bed in which the moisture content is controlled. The coating lacquer is sprayed from a spray nozzle positioned at the bottom of a GLATT fluidized bed apparatus equipped with a Wurster tube.
8. The potassium bicarbonate crystals are fluidized and the warm coating lacquer is sprayed on the crystals in multiple coating cycles.
9. The process air flow rate is adjusted as necessary to provide adequate movement of the crystals through the fluidized bed as they are coated. During the coating process, the isopropyl alcohol solvent is flash-evaporated from the crystals as they cycled through the fluidized bed.
10. After completing the application of the coating lacquer to the crystals, any trace residual solvent remaining on the coated crystals is removed by cycling in the fluidized bed without lacquer spray for 10 minutes.
11. Following the residual solvent removal, the coated crystals are cooled in the bed.
12. The amount of coating lacquer applied on the crystals is calculated as the % w/w of the dry matter of the respective coatings, relative to the uncoated potassium bicarbonate crystals.
13. Compression: potassium 85.00% bicarbonate coated crystals, CUTINA HR 1.50%; AVICEL PH 7.68%, cornstarch 5.12%, SYLOID 0.40%, LUBRITAB 0.30%. Compress tablets of 1500 mg of potassium bicarbonate.

Potassium Chloride Retard Tablet

Formulation: Cetyl alcohol, 14.00 g; potassium chloride, 82.00 g; hydroxy ethyl cellulose, 4.50 g; talc, 1.50 g.

Manufacturing Directions

1. To 10 g of water at 50°C, contained in a suitable vessel, fitted with a stirrer, add the hydroxy ethyl cellulose. Blend until a uniformly hydrated granular mass is formed.
2. Add to the hydrated cellulose granules, with constant stirring, the potassium chloride. Continue mixing until a free-flowing uniform granule blend is obtained.
3. Dry the cellulose-potassium chloride granules for 30 minutes at 50°C. Granulate the dried granules through a No. 16 stainless steel standard mesh screen.
4. Melt the cetyl alcohol in a water jacketed tank fitted with an efficient stirrer. Hold the melt at 50°C to 60°C and incorporate the granules from step 3. Continue stirring until a free-flowing granular mass is obtained. Allow the mass to cool and granulate through a No. 16 standard mesh stainless steel screen.
5. Lubricate the granules with talc and compress into cores. Core Compression Data: Core weight, 750.0 mg; punch size, 7/16th in. deep concave
6. The cores are then pan-coated using normal coating techniques.

Potassium Chloride Tablets (30 mg), Klor

Potassium chloride extended-release capsules, USP, are a solid oral dosage form of potassium chloride containing 10 mEq (750 mg) of potassium chloride (equivalent to 10 mEq [390 mg] of potassium and 10 mEq [360 mg] of chloride) in a microencapsulated capsule. This formulation is intended to release potassium so that the likelihood of a high localized concentration of potassium chloride within the gastrointestinal tract is reduced. The inactive ingredients are calcium stearate, gelatin, pharmaceutical glaze, povidone, sugar spheres, and talc.

Klor-Con extended-release tablets, USP, are a solid oral dosage form of potassium chloride. Each contains 600 or 750 mg of potassium chloride equivalent to 8 or 10 mEq of potassium in a wax matrix tablet.

Potassium Chloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Potassium chloride	30.00
150.00	2	Gelatin powder	150.00
2.00	3	Croscarmellose sodium	2.00
5.00	4	Talc	5.00
3.00	5	Magnesium stearate	3.00

Manufacturing Directions

1. Accurately weigh potassium chloride, gelatin, croscarmellose sodium, talc, and magnesium stearate.
2. Add potassium chloride, gelatin, and croscarmellose sodium, one item at a time, in a suitable blender, and mix for 15 minutes. Add talc and magnesium stearate, and mix for an additional 5 minutes.
3. Compress into 200-mg tablets, using 6-mm punches.

Povidone–Iodine Effervescent Vaginal Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
350.00	1	Polyvinylpyrrolidone (PVP)–iodine 30/06, with excess	360.00
1450.00	2	Ludipress®	1450.00
360.00	3	Tartaric acid	360.00
265.00	4	Sodium bicarbonate	265.00
19.00	5	Talc	19.00
2.00	6	Calcium arachinate	2.00
2.00	7	Aerosil® 200	2.00

Manufacturing Directions

1. Dry the mixture of items 2 to 4 for 4 hours at 60°C, mix with item 1 and items 5 to 7, and press to tablets.
2. Compress into 2.5-g tablet, using 20-mm biplanar punches.
3. The tablet is dissolved in water to obtain a vaginal douche solution.

Povidone–Iodine Lozenges

Bill of Materials			
Scale (mg/Lozenge)	Item	Material Name	Quantity/1000 Lozenges (g)
5.00	1	Polyvinylpyrrolidone (PVP)–iodine 30/06	5.00
150.00	2	Sorbitol (crystallized)	150.00
4.00–5.00	3	Menthol (crystalline)	4.00–5.00
4.00–5.00	4	Eucalyptol (crystalline)	4.00–5.00
1.00	5	Aspartame, potassium	1.00
0.10	6	Saccharine sodium	0.10
1.00	7	Aerosil® 200	1.00
1.00	8	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with medium-compression force.
2. Compress into 176-mg tablets, using 8-mm biplanar punches.

Pravastatin Sodium Tablets (10–40 mg), Pravachol

Pravachol is available for oral administration as 10-, 20-, and 40-mg tablets. Inactive ingredients include croscarmellose sodium, lactose, magnesium oxide, magnesium stearate, microcrystalline cellulose, and povidone. The 10-mg tablet also contains red ferric oxide; the 20-mg tablet also contains yellow ferric oxide; and the 40-mg tablet also contains green lake blend (mixture of D&C Yellow No. 10 Aluminum Lake and FD&C Blue No. 1 Aluminum Lake).

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Pravastatin sodium	10.00
12.00	2	Crospovidone	12.00
77.00	3	Lactose, spray dried	77.00
1.00	4	Magnesium stearate	1.00

Manufacturing Directions

1. Charge pravastatin sodium and polyplasdone in a blender after passing through a 250-μm sieve.
2. Add item 3, and mix for 20 minutes at moderate speed.
3. Add item 4, and blend for 5 minutes at low speed.
4. Compress in a suitable punch, 100 mg for 10-mg strength, and proportionally for strengths up to 40 mg.

Pravastatin Tablets

Formulation: Pravastatin, 6.7%; lactose, 67%; microcrystalline cellulose, 20%; croscarmellose sodium, 2%; magnesium stearate, 1%; magnesium oxide, 3.3%.

Manufacturing Directions

1. Pravastatin, magnesium oxide, and a fraction (30%) of lactose are mixed together for 2 to 10 minutes employing a suitable mixer. The resulting mixture is passed through a #12 to #40 mesh size screen.
2. Microcrystalline cellulose, croscarmellose sodium, and the remaining lactose are added and the mixture is mixed for 2 to 10 minutes. Thereafter, magnesium stearate is added and mixing is continued for 1 to 3 minutes.
3. The resulting homogeneous mixture is then compressed into tablets each containing 5, 10, 20, or 40 mg of pravastatin. A dispersion of the tablets in water had a pH of about 10.

Prazosin Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Prazosin hydrochloride, anhydrous[a]	5.00
94.00	2	Ludipress	94.00
1.00	3	Magnesium stearate	1.00

[a]If using polyhydrate, increase the amount to 6.00, and adjust with item 2.

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force.
2. Compress into 109-mg tablets, using 8-mm biplanar punches.

Prednisolone Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Prednisolone	5.00
60.00	2	Lactose monohydrate	60.00
32.50	3	Starch (maize)	32.50
6.00	4	Starch (maize)	6.00
4.00	5	Starch (maize, dried)[a]	4.00
2.00	6	Talc (fine powder)	2.00
0.50	7	Magnesium stearate	0.50
–	8	Purified water	18.00

LOD: not more than 4.5% when dried at 120°C for 4 hours.

Manufacturing Directions

Precautions: The binding solution contains maize starch, and, therefore, it is possible to have microbiological growth. Thus, prepare the solution directly before the granulation process. Prednisolone is a potent corticosteroid, and, therefore, use a mask, gloves, and goggles during the whole process.

1. Preparation of binding solution
   a. Prepare an homogeneous slurry of item 4 using 8 g of item 8 (25–30°C). Check that it is free of lumps.
   b. Charge this slurry into 10 g of item 8 heated to 90°C in the vessel (Giusti). Stir until there is complete gelatinization.
   c. Check the weight. The theoretical weight is 24 g.
   d. Leave the starch paste to cool to 40°C to 50°C.
   Note: Compensate any loss of weight due to vaporization by adding item 8.
2. Dry mixing: Pass items 1 to 3 through a 630-μm sieve using a sifter. Load this powder to the mixer, and mix for 15 minutes at high speed.
3. Wet massing: Add starch paste cooled to 40°C to 50°C from step 1d. Mix for 10 minutes at high speed. Add purified water if required.
4. Pass the wet granules through sieve 24205 using the FitzMill.
5. Drying: Spread the wet granules onto the trays. Load the trolleys to the dryer. Dry the granules at 60°C for 14 hours.
6. Grinding: Pass the dried granules through a 1-mm sieve using a granulator.
7. Lubrication
   a. Pass items 5 and 6 through a 250-μm sieve using a sifter. Collect the material in a stainless steel drum.
   b. Load the sieved material from step 6 into the blender.
   c. Load the sieved lubricant powders from step 7a into the blender.
   d. Blend the powders for 5 minutes.
8. Blending
   a. Pass item 7 through a 250-μm sieve using a sifter. Load the sieved powder into the blender. Mix the powder for 1 minute.
   b. Unload the lubricated granules in stainless steel drums.
9. Check and record the weight of the granules.
10. Compression: Compress 110 mg of the granules using a rotary tabletting machine in 7.1-mm punches.

Prednisolone Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Prednisolone, use as prednisolone micronized	10.50
49.50	2	Microcrystalline cellulose (Avicel PH 102)	49.50
7.50	3	Sodium starch glycolate (Primojel)	7.50
105.00	4	Lactose (spray dried)	105.00
25.00	5	Starch (maize), dried	25.00
1.00	6	Colloidal silicon dioxide (Aerosil 200)	1.00
1.50	7	Magnesium stearate	1.50

Manufacturing Directions

See the manufacturing directions for the 5-mg strength tablet.

Prednisolone Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Prednisolone micronized	21.00
60.00	2	Microcrystalline cellulose (Avicel PH 102)	60.00
9.00	3	Sodium starch glycolate (Primojel)	9.00
127.00	4	Lactose (spray dried)	127.00
30.00	5	Starch (maize, dried)	30.00
1.00	6	Colloidal silicon dioxide (Aerosil 200)	1.00
2.00	7	Magnesium stearate	2.00

Manufacturing Directions

See the manufacturing directions for the 5-mg strength tablet.

Prednisolone Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Prednisolone	20.00
155.00	2	Lactose monohydrate	155.00
10.00	3	Kollidon VA 64	10.00
8.00	4	Kollidon CL	8.00
5.00	5	Magnesium stearate	5.00
2.00	6	Aerosil 200	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress into 212-mg tablets, using 8-mm biplanar punches.

Prednisone Tablets (10 mg)

Deltasone tablets contain prednisone, which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, that are readily absorbed from the gastrointestinal tract. Prednisone is a white to practically white, odorless, crystalline powder. It is very slightly soluble in water and slightly soluble in alcohol, in chloroform, in dioxane, and in methanol. The chemical name for prednisone is pregna-1,4-diene-3,11,20-trione,17,21-dihydroxy-. Its molecular weight is 358.43.

Deltasone tablets are available in five strengths: 2.5, 5, 10, 20, and 50 mg. The inactive ingredients are as follows. *2.5 mg:* calcium stearate, cornstarch, erythrosine sodium, lactose, mineral oil, sorbic acid, and sucrose; *5 mg:* calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, and sucrose; *10 mg:* calcium stearate, cornstarch, lactose, sorbic acid, and sucrose; *20 mg:* calcium stearate, cornstarch, FD&C Yellow No. 6, lactose, sorbic acid, and sucrose; *50 mg:* cornstarch, lactose, magnesium stearate, sorbic acid, sucrose, and talc.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Prednisone	10.00
208.00	2	Ludipress	208.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with low-compression force.
2. Compress into 223-mg tablets, using 8-mm biplanar punches.

Pregabaline-Coated Granule Fast-Crumbling Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Pregabaline	150.00
6.43	2	Corpovidone potassium	6.43
7.50	3	Acesulfam	7.50
4.28	4	Precipitated silicat	4.28
39.64	5	Ethylcellulose AGM	39.64
6.43	6	Crospovidone	6.43

Manufacturing Directions

1. A suspension is obtained by mixing ethylcellulose, 80% precipitated silica, and 50% acesulfamin ethyl alcohol, until a homogeneous suspension is obtained.
2. The powder mixture consisting of pregabaline, item 6, 70% aspartame, and 20% precipitated silica is then fluidized.
3. The granulation is then started by spraying the mixture for about 15 to 20 minutes at a spraying rate of 25 g/min and a suspension atomization pressure of 0.8 bar.
4. The actual coating is then performed by spraying the remainder of the mixture over about 1 hour 30 minutes at a spraying rate of 15 to 20 g/min and a suspension atomization pressure of 1.5 bar.
5. 15% of the mixture is sprayed during the granulation step, the remainder to 100% being sprayed during the coating step.
6. The granules obtained are then formulated as fast-crumbling multiparticulate tablets, the composition of which is as follows: Coated granules (150 mg), Mannitol (474 mg), Cropovidone (80 mg), aspartame (14 mg), flavoring (8 mg), and magnesium stearate (8 mg).

Probenecid Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Probenecid	500.00
130.00	2	Starch (maize)	130.00
10.00	3	Kollidon 30	10.00
–	4	Alcohol	70.00 mL
25.00	5	Kollidon CL	25.00
3.00	6	Aerosil 200	3.00
3.00	7	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate a mixture of items 1 and 2 with a solution of items 3 and 4. Pass this mixture through a 0.8-mm sieve. Add items 5 to 7, and press with low-compression force.
2. Compress into 674-mg tablets, using 12-mm biplanar punches.

Promethazine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Promethazine HCl	10.50
41.95	2	Lactose monohydrate	41.95
20.00	3	Maize starch	20.00
0.05	4	Sodium metabisulfite (sodium disulfite)	0.05
2.00	5	Povidone (PVP K-30)	2.00
5.00	6	Maize starch (dried)	5.00
0.50	7	Magnesium stearate	0.50
–	8	Alcohol (ethanol, 95%)	6.07
–	9	Purified water	8.67

Manufacturing Directions

Note: Avoid over-mixing of lubricants; otherwise, hardness will be reduced.

1. Mix items 9 and 8 in a stainless steel container.
2. Dissolve items 4 and 5 by slow stirring with stirrer until mixture becomes clear.
3. Sift items 1 to 3 through a stainless steel 500-μm sieve in sifter.
4. Load into mixer, and mix for 5 minutes at low speed.
5. Add binding solution at a rate of 5 to 7 g/min to the dry powders, while mixing at low speed.
6. After addition is complete, scrape sides and blades.
7. Mix further for 2 minutes using a mixer and chopper at low speed.
8. Scrape sides and blades.
9. Check for the end point of granulation, which is the point where the granulation consists of few or no lumps.
10. If required, add purified water.
11. Dry the wet granules with the air circulation heater off to expel alcohol for 2 hours.
12. Then, dry at 55°C for 14 hours.
13. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
14. Check the LOD (limit: 1.0–1.5%).
15. If required, dry further at 55°C for 2 hours.
16. Grind the dried granules through a 1.25-mm sieve using a granulator at medium speed.
17. Collect in stainless steel drums.
18. Load granules into the blender.
19. Sift item 6 material through a 500-μm sieve using a sifter, and add it into blender.
20. Mix for 3 minutes.
21. Sift item 7 through a 500-μm sieve, and add 1 to 2 g of granules from above.
22. Mix in polyethylene bag for 1 minute.
23. Add to blender.
24. Mix for 30 seconds.
25. Compress 0.80 g.
26. Coat using one of the HPMC coatings given in the Appendix.

Promethazine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Promethazine HCl	26.00
103.75	2	Lactose monohydrate	103.75
50.00	3	Maize starch	52.50
1.50	4	Sodium metabisulfite (sodium disulfite)	1.50
5.00	5	Povidone (PVP K-30)	5.00
12.50	6	Maize starch (dried)	12.50
1.25	7	Magnesium stearate	1.25
–	8	Alcohol (ethanol, 95%)	15.00
–	9	Purified water	21.67

Manufacturing Directions

Note: Avoid over mixing of lubricants; otherwise, hardness will be reduced.

1. Mix items 9 and 8 in a stainless steel container.
2. Dissolve items 4 and 5 by slow stirring with stirrer until mixture becomes clear.
3. Sift items 1 to 3 through a stainless steel 500-μm sieve in sifter.
4. Load into mixer, and mix for 5 minutes at low speed.
5. Add binding solution at a rate of 5 to 7 g/min to the dry powders, while mixing at low speed.
6. After addition is complete, scrape sides and blades.
7. Mix further for 2 minutes using a mixer and chopper at low speed.
8. Scrape sides and blades.
9. Check for the end point of granulation, which is the point where the granulation consists of few or no lumps.
10. If required, add purified water.
11. Dry the wet granules with the air circulation heater off to expel alcohol for 2 hours.
12. Then, dry at 55°C for 14 hours.
13. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
14. Check the LOD (limit: 1.0–1.5%).
15. If required, dry further at 55°C for 2 hours.
16. Grind the dried granules through a 1.25-mm sieve using a granulator at medium speed.
17. Collect in stainless steel drums.
18. Load granules into the blender.
19. Sift item 6 material through a 500-μm sieve using a sifter, and add it into blender.
20. Mix for 3 minutes.
21. Sift item 7 through a 500-μm sieve, and add 1 to 2 g of granules from above.
22. Mix in polyethylene bag for 1 minute.
23. Add to blender.
24. Mix for 30 seconds.
25. Compress 0.80 g.
26. Coat using one of the HPMC coatings in the Appendix.

Promethazine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Promethazine HCl[a]	10.50
41.95	2	Lactose monohydrate	41.95
20.00	3	Starch (maize)	20.00
0.05	4	Sodium metabisulfite (sodium disulfite)	0.05
2.00	5	Povidone (PVP K-30)	2.00
5.00	6	Starch (maize), dried[b]	5.00
0.50	7	Magnesium stearate	0.50
–	8	Alcohol (ethanol 95%)	6.07
–	9	Purified water	8.67

[a]0.5-mg promethazine HCl/tablet added extra, considering the assay and LOD of the material (assay 97–101.5%, calculated on the dried basis LOD NMT 0.5%).
[b]LOD: NMT 4.5% when dried at 120°C for 4 hours.

Manufacturing Directions

1. Avoid over mixing lubricants, or hardness may be reduced.
2. Mix items 9 and 8 in a stainless steel container.
3. Dissolve items 4 and 5 by slow stirring with a stirrer until the mixture becomes clear.
4. Sift items 1 to 3 through a stainless steel 500-μm sieve in a sifter. Load into a mixer, and mix for 5 minutes at low speed.
5. Add a binding solution 5 to 7 g/min to the dry powders while mixing at low speed. After addition is over, scrape sides and blades. Mix an additional 2 minutes using a mixer and chopper at low speed. Scrape sides and blades.
6. Check for the end point of granulation. The end point is the point of granulation that consists of little or no lumps. If required, add purified water.
7. Dry the wet granules with the air circulation heater off, to expel alcohol for 2 hours. Then dry at 55°C for 14 hours. After 4 hours of drying, scrape the semidried granules to break the lumps for uniform drying.
8. Check the LOD. The limit is 1% to 1.5%. If required, dry further at 55°C for 2 hours.
9. Grind the dried granules through a 1.25-mm sieve using a granulator at medium speed. Collect the granules in stainless steel drums.
10. Load the granules into the blender. Sift the item 6 material through a 500-μm sieve using a sifter, and add it into the blender. Mix the blend for 3 minutes.
11. Sift item 7 through a 500-μm sieve. Add 1 to 2 g granules from step 10. Mix in a polythene bag for 1 minute. Add to the blender. Mix for 30 seconds.
12. Compress 0.80 g. Coat using one of the HPMC coatings. (See Appendix.)

Promethazine Hydrochloride Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Promethazine HCl	26.00
103.75	2	Lactose monohydrate	103.75
50.00	3	Starch (maize)	52.50
1.50	4	Sodium metabisulfite (sodium disulfite)	1.50
5.00	5	Povidone (PVP K-30)	5.00
12.50	6	Starch (maize), dried	12.50
1.25	7	Magnesium stearate	1.25
–	8	Alcohol (ethanol 95%)	15.00
–	9	Purified water	21.67

Promethazine Hydrochloride Tablets (10 mg) Phenergan

Each tablet of phenergan contains 12.5, 25, or 50 mg of promethazine hydrochloride. The inactive ingredients present are lactose, magnesium stearate, and methylcellulose. Each dosage strength also contains the following: *12.5 mg*—FD&C Yellow No. 6 and saccharin sodium; *25 mg*—saccharin sodium; and *50 mg*—FD&C Red No. 40.

Propranolol Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
120.00	1	Propranolol hydrochloride	120.00
4.00	2	Polyvinylpyrrolidone	4.00
2.00	3	Silicon dioxide	2.00
80.00	4	Lactose	80.00
2.00	5	Sodium stearyl fumarate	2.00
QS	6	Water qs	QS

Manufacturing Directions

1. Propranolol hydrochloride and lactose are placed in a fluidized bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1-mm mesh) and sodium stearyl fumarate is weighed, added, and blended in a drum mixer.
4. The resulting mixture is pressed into tablets 208.00 mg.
5. These tablet cores are then coated with the following formulation: ethylcellulose (Ethocel) 10.10 polyvinylpyrrolidone (Povidone) 5.50 mg, stearic acid 2.40 mg.
6. Ethocel, povidone, and stearic acid are first dissolved in denatured alcohol (180 g). The coating solution is then sprayed onto the tablet cores in a coating pan.

Propranolol Hydrochloride Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Propranolol hydrochloride	10.00
490.00	2	Ludipress	490.00
2.50	3	Magnesium stearate	2.50

Note: For 50-mg and 100-mg strengths, adjust with item 2.

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force.
2. Compress 514 mg for 10-mg strength, 496 mg for 50-mg strength, and 505 mg for 100-mg strengths, using 12-mm biplanar punches.

Propranolol Hydrochloride Tablets (10 mg)

Propranolol HCl is available as 10-, 20-, 40-, 60-, and 80-mg tablets. The inactive ingredients contained in propranolol HCl tablets are lactose, magnesium stearate, microcrystalline cellulose, and stearic acid. In addition, propranolol HCl 10-mg and 80-mg tablets contain FD&C Yellow No. 6 and D&C Yellow No. 10; propranolol HCl 20-mg tablets contain FD&C Blue No. 1; propranolol HCl 40-mg tablets contain FD&C Blue No. 1, FD&C Yellow No. 6, and D&C Yellow No. 10; and propranolol HCl 60-mg tablets contain D&C Red No. 30.

Propranolol Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (kg)
10.00	1	Propranolol hydrochloride	10.00
2.00	2	Maize starch	2.00
4.00	3	Lactose	4.00
0.20	4	Soluble starch	0.20
15.00	5	Purified water	15.00
3.00	6	Primojel	3.00
9.00	7	Microcrystalline cellulose	9.00
0.50	8	Magnesium stearate	0.50

Manufacturing Directions

1. Pass items 1 to 3 through a FitzMill sieve 24228 at medium speed, and mix for 15 minutes.
2. Bring to boil 1.25 kg of purified water (item 5), and dissolve in it item 4. Add the remaining water and allow boiling for a few minutes, allowing the mixture to cool to room temperature.
3. Make a uniform mass of step 2 with step 1 solution, and pass it through a FitzMill sieve 24183, adding water if necessary.
4. Dry granules at 35°C for 14 hours. Pass the granules through a FitzMill sieve 24228 at low speed.
5. Pass items 6 to 8 through a FitzMill sieve 24228 and at medium speed.
6. Compress.
7. Coat in a pan at 25°C to 30°C under a flow of warm air using the Opaspary coating. (See Appendix.) After coating, polish the film-coated tablet.

Propranolol HCl Substained-Release Pellets Releasing Tablets (MUPS-Formulation)

Formulation (for 500 g of tablets): Propranolol HCl/ Kollicoat® SR 30D pellets, 250.0 g; microcrystalline cellulose Vivapur® 200, 250.0 g; magnesium stearate, 2.5 g

Manufacturing Directions

Mix the ingredients together, pass through a 0.8-mm sieve, and compress into tablets with a force of about 15kN at 400 mg.

Propranolol Tablets (40 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Propranolol	40.00
108.00	2	Ludipress	108.00
0.30	3	Magnesium stearate	0.30
0.40	4	Stearic acid	0.40

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high-compression force.
2. Compress into 150-mg tablets, using 8-mm biconvex punches.

Proton Pump Inhibitor Dispersible Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lansoprazole or another PPI equipotent	10.00
175.00	2	Calcium acetate	175.00
175.00	3	Calcium glycerophospate	175.00
250.00	4	Sodium bicarbonate	250.00
20.00	5	Polyethylene glycol	20.00
12.00	6	Croscarmellose sodium	12.00
3.00	7	Peppermint	3.00
1.00	8	Magnesium silicate	1.00
1.00	9	Magnesium stearate	1.00

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Lansoprazole or another PPI equipotent	10.00
175.00	2	Calcium lactate	175.00
175.00	3	Calcium glycerophosphate	175.00
250.00	4	Sodium bicarbonate	250.00
20.00	5	Polyethyle glycol	20.00
12.00	6	Croscarmellose sodium	12.00
3.00	7	Peppermint	3.00
1.00	8	Magnesium stearate	1.00
1.00	9	Magnesium silicate	1.00

Proton Pump Inhibitor Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00 (or equipotent)	1	Proton pump inhibitor	10.00 (or equipotent)
175.00	2	Calcium lactate	175.00
250.00	3	Sodium bicarbonate	250.00
175.00	4	Calcium glycerophosphate	175.00
0.50	5	Phenylalanine (aspartame calcium)	0.50
12.00	6	Colloidal silicon dioxide	12.00
15.00	7	Cornstarch	15.00
12.00	8	Croscarmellose sodium	12.00
10.00	9	Dextrose	10.00
3.00	10	Peppermint	3.00
3.00	11	Maltodextrin	3.00
3.00	12	Mannitol	3.00
3.00	13	Pregelatinized Starch	3.00

Manufacturing Directions

1. Compress.
2. May be used for 20 mg or equivalent quantity of the active without any change in other ingredients.

Pseudoephedrine Hydrochloride Fast-Disintegrating Tablets

1. To the vortex of a rapidly stirred vessel containing 345 g of deionized water is added 30 g of croscarmellose sodium.
2. This slurry is mixed for 10 minutes.
3. Concurrently, 300 g of pseudoephedrine hydrochloride and 300 g of microcrystalline cellulose (Avicel PH-101) are placed in the bowl of a mixer.
4. This mixture is stirred for 10 minutes.
5. At the conclusion of the mixing time, the slurry is added slowly to the contents of the mixing bowl, forming a granulation which is then placed in trays and dried in a 65°C oven for 3 hours.
6. The dried granulation is passed through a US Standard 16 mesh screen (1190 μm).
7. The dried granulation is then placed in a twin-shell blender, and 300 g of Avicel AC-815 (85% microcrystalline cellulose coprocessed with 15% of a calcium, sodium alginate complex) and 300 g of microcrystalline cellulose (Avicel PH-102) are added.
8. This is thoroughly blended for 10 minutes, after which 10.05 g of magnesium stearate is added and mixed for an additional 5 minutes.
9. Prior to being added to the blender the magnesium stearate had been passed through a US Standard 30 mesh screen.
10. The resulting blend is compressed into tablets using 6.35 mm (0.25 in.) round standard concave tooling to give average weight of 0.1299 g and an average thickness of 4.864 mm (0.1915 in.).
11. The hardness of these tablets averaged 1.38 kPa.
12. Friability is measured at 0.077% after 4 minutes.
13. The average disintegration time is 15 seconds in 10 mL of deionized water, forming a suspension with minimal shaking.

Pseudoephedrine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Pseudoephedrine HCl[a]	63.00
120.20	2	Lactose monohydrate	120.20
25.00	3	Maize starch	25.00
1.00	4	Povidone (PVP K-30)	1.00
4.00	5	Povidone (PVP K-30)	4.00
1.80	6	Magnesium stearate	1.80
–	7	Alcohol (ethanol, 95%)	29.00

[a]Pseudoephedrine HCl 3.0 mg/tab can be added in excess to compensate for moisture and handling loss.

Manufacturing Directions

Note: Avoid over-mixing of lubricants; otherwise, hardness is reduced.

1. Dissolve item 5 in item 7 while mixing at slow speed using a stirrer.
2. Sift items 1 to 4 through a 500-µm sieve.
3. Load into mixer, and mix for 5 minutes at low speed.
4. Add binding solution to the dry powders while mixing at low speed for 2 minutes.
5. After addition is complete, mix further for 1 minute using mixer and chopper at low speed.
6. Scrape sides and blade.
7. Check for the end point of granulation, which is when the granulation consists of wet granules with few or no lumps.
8. If required, add ethanol 95% to achieve desired granules.
9. Record extra quantity of ethanol 95% used.
10. Dry the wet mass at 55°C for 7 hours.
11. After 4 hours of drying, scrape the semidried granules to break the lumps to promote uniform drying.
12. Check the moisture content (limit: 1.5–2.5%).
13. Sift the dried granules through a 1.25-mm sieve using a granulator at medium speed.
14. Collect in stainless steel drums.
15. Load granules into the drum blender.
16. Sift item 6 through a stainless steel 250-µm sieve in sifter.
17. Add 8 to 12 g granules in mixer to sieved item 6.
18. Mix manually for 1 minute.
19. Add to drum blender, and blend for 1 minute.
20. Compress into 215-mg tablets, using 8-mm round punches.

Pseudoephedrine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	(+) Pseudoephedrine hydrochloride	60.00
95.00	2	Dicalcium phosphate (Di-Tab)	95.00
5.00	3	Kollidon® 30	5.00
–	4	Water	QS
20.00	5	PEG-6000 (powder)	20.00
2.00	6	Aerosil® 200	2.00

Manufacturing Directions

1. Granulate dicalcium phosphate with solution of items 3 and 4, dry, pass through an 0.8-mm sieve, and mix with item 1.
2. Add items 5 and 6, and press with low-compression force.
3. Compress into 192-mg tablets, using 8-mm biplanar punches.

Psyllium and Docusate Sodium Tablets

Formulation: Psyllium, 71.0%; ethylcellulose, 4.8%; isopropyl alcohol qs; microcrystalline cellulose, 16.7%; PVP crosslinked, 1.9%; carnuba wax, 2.3%; docusate sodium, 3.3%.

Manufacturing Directions

1. Soak ethylcellulose in isopropyl alcohol overnight.
2. Granulate psyllium with isopropyl/ethylcellulose mixture in mixer.
3. Dry at 49°C for 3 hours.
4. Mill through 12-mesh screen.
5. Mix in a mixer the following: psyllium, microcrystalline cellulose, and carnuba wax.
6. Compress the tablet per granulation specifications using a tabletting press.
7. Coat the core tablets.

Methylcellulose, polycarbophil, calcium polycarbophil, bran, malt soup extract, karaya, guar gum, or mixtures of these can be substituted for the psyllium. The amounts of psyllium and/or dioctyl sulfosuccinate can be varied. Dioctyl calcium sulfosuccinate, dioctyl potassium sulfosuccinate, can be substituted for the dioctyl sodium sulfosuccinate, or two or three of these can be combined.

Psyllium Husk Tablets

Manufacturing Directions

1. Raw, unmilled psyllium seed husk (2 g) is stirred with 0.2 N sodium hydroxide (400 mL) containing sodium borohydride (400 mg) in a nitrogen atmosphere at ambient temperature for 90 minutes.
2. The pH of the solution is from 10 to 11.
3. The solution is passed through a pasteurizer at a temperature of 100°C for a period of 50 seconds.
4. Once pasteurized, the mixture is centrifuged for 20 minutes at 23500 × *g*.
5. The supernatant is decanted from an insoluble fraction that settles out in the centrifuge bottle.
6. The insoluble fraction is mixed with fresh sodium hydroxide/sodium borohydride solution (100 mL) and recentrifuged for 15 minutes to increase yield of the soluble fraction.
7. The pH of the supernatant is adjusted to 5.5 by the addition of acetic acid at ambient temperature with stirring, forming a gel.
8. The gel is desiccated with isopropanol added with high shear mixing.
9. The isopropanol solution is then decanted from the gel.
10. The solids content of the gel is 30%.
11. The gel material is passed through an extruder and extruded into individual particles with an average particle size of 500 μm.
12. The extruded particles enter a fluidized bed dryer fitted with a cyclonic airflow screen, such as a Conidur screen.
13. The air temperature is maintained at 80°C.
14. The gel temperature remains below 70°C throughout the drying process.
15. The particles are dried to a powder, with 90% of the water being removed.
16. The yield of the gel-forming polysaccharide is 85%.
17. Chewable tablets, total weight 2.5 g, are manufactured while step 8 is dry blended with sorbitol for 10 minutes, each component having an average particle size of about 500 μm.
18. The premix, if desired, is added and the mixture is blended for an additional 10 minutes.
19. Magnesium stearate is added and the composition is blended for another 5 minutes.
20. The mixture is directly compressed into tablets using pressures of from 2000 to 4000 psi.
21. The final compositions comprise the following components by weight: gel-forming, 50.0%; polysaccharide sorbitol Neosorb P20, 48.16%; magnesium stearate, 0.5%; flavorant, 0.4%; colorant, 0.14%; citric acid, 0.8%.
22. Optionally, the coating can be applied directly to a chewable tablet containing the gel-forming polysaccharide.
23. Additionally, it may be desired to include a flavorant within the coating composition: ethanol, 94%; polyethylene glycol, 5%; flavorant, 1%

Pyrazinamide Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Pyrazinamide	500.00
134.50	2	Ludipress	134.50
12.00	3	Kollidon CL	12.00
3.50	4	Aerosil 200	3.50

Manufacturing Directions

1. Mix all components, sieve through a 0.8-mm screen, and press with medium-compression force.
2. Compress into 652-mg tablets, using 12-mm biplanar punches.

Pyrazinamide Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Pyrazinamide	500.00
50.00	2	Starch (maize)	50.00
20.00	3	Kollidon 30	20.00
–	4	Alcohol, ca	200 mL
5.00	5	Kollidon CL	5.00
6.00	6	Magnesium stearate	6.00

Manufacturing Directions

1. Granulate mixture items 1 and 2 with a solution of items 3 and 4. Pass through a 0.8-mm sieve, mix with items 5 and 6, and press with low-compression force.
2. Compress into 605-mg tablets, using 12-mm biplanar punches.
3. The quantity of items 5 can be increased to 10 mg if there is a problem in compressing tablets.

Pyrazinamide Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Pyrazinamide	500.00
125.00	2	Mannitol	125.00
–	3	Water, purified	50.00 mL
25.00	4	Starch (maize)	35.00
QS	5	Water, purified	150 mL
10.00	6	Talc	10.00
6.00	7	Magnesium stearate	6.00

Manufacturing Directions

Note: Carry out all operations subsequent to drying at a relative humidity below 50% and temperature below 26°C.

1. Granulation
   a. Pass the pyrazinamide and mannitol through a 1.2-mm aperture stainless steel screen on a sieve shaker, transfer them to a suitable mass mixer, and mix for 5 minutes.
   b. Add the starch to the water (item 3) and mix until a smooth slurry, free from lumps, is formed.
   c. Heat the water (item 5) to boiling. Reduce the heat, then, while mixing, add the slurry from step 1b. Continue mixing well, until a smooth translucent paste is formed. Allow this paste to cool to 50°C before using it in step 1d.
   d. Add one-half of the starch paste from step 1c to the blended powders in the mixer, and mix for 1 minute. Stop mixing, and scrape the blades and sides of the mixer. Add the second half of the starch paste and mix for another 1 minute. Stop mixing, scrape the blades and sides of the mixer, and examine the mass.
   e. If necessary, add more water at 50°C in small quantities, mixing for 1 minute after each addition, until a good, wet, holding mass is formed. Record extra water used. *Note:* Do not overwet or overmix the mass.
   f. Pass the wet mass through a 4.76-mm aperture stainless steel screen by hand, spread on paper-lined trays, and dry in a hot-air oven at 50°C, turning the granules every 20 minutes, to an LOD of 1% to 1.5% (3 hours at 60°C under maximum vacuum).
2. Lubrication
   a. Pass the granules through a 1.2-mm aperture stainless steel screen on a sieve shaker, and transfer the fines to a blender.
   b. Pass the coarse granules through an 840-μm aperture stainless steel screen on an oscillating granulator, and then transfer the granules to the blender.
   c. Screen the talc and sodium starch glycolate through a 595-μm aperture stainless steel screen on a sieve shaker, and add the mixture to the blender. Blend it for 15 minutes.
   d. Screen the magnesium stearate through a 595-μm aperture stainless steel screen on a siever shaker, and add to the blender. Blend for 2 minutes only.
   e. Discharge into polyethylene-lined drums, and then seal and weigh.
3. Compression: Compress using 12.5-mm round, concave bisected punches; disintegration time is not more than 15 minutes in water.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Pyridoxine hydrochloride	40.00
150.00	2	Lactose monohydrate	150.00
150.00	3	Avicel™ PH101	150.00
15.00	4	Kollidon® VA 64	15.00
10.00	5	Kollidon® CL	10.00
1.00	6	Magnesium stearate	1.00
1.00	7	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with high-compression force.
2. Compress into 361-mg tablets, using 12-mm biplanar punches; items marked with asterisk can be deleted when the compression weight becomes 340 mg.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40.00	1	Pyridoxine hydrochloride	40.00
300.00	2	Cornstarch	300.00
15.00	3	Kollidon® 30	15.00
80.00	4	Water + isopropanol	80.00
1.00	5	Magnesium stearate	1.00
2.00	6	Aerosil® 200	2.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, dry, pass through an 0.8-mm sieve, mix with items 5 and 6, and press with high-compression force.
2. Compress into 354-mg tablets, using 12-mm biplanar punches.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Pyridoxine hydrochloride	100.00
200.00	2	Tabletlose®	200.00
10.00	3	Kollidon® VA 64	10.00
3.00	4	Kollidon® CL	3.00
1.00	5	Magnesium stearate	1.00
1.00	6	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 363-mg tablets, using 12-mm biplanar punches.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Pyridoxine hydrochloride	100.00
150.00	2	Lactose monohydrate	150.00
83.00	3	Avicel™ PH101	83.00
10.00	4	Kollidon® VA 64	10.00
3.00	5	Kollidon® CL	3.00
1.00	6	Magnesium stearate	1.00
1.00	7	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix and press with medium-compression force.
2. Compress into 360-mg tablets, using 12 mm-biplanar punches.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Pyridoxine hydrochloride	250.00
100.00	2	Avicel™ PH101	100.00
12.00	3	Kollidon® VA 64	12.00
5.00	4	Magnesium stearate	5.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 361-mg tablets, using 12-mm biplanar punches.

Pyridoxine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Pyridoxine hydrochloride	300.00
100.00	2	Lactose monohydrate D 20	100.00
20.00	3	Kollidon® 30	20.00
QS	4	Isopropanol + water (1+1)	60.00
10.00	5	Kollidon® CL	10.00
2.00	6	Aerosil® 200	2.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 3 to 6, dry, and sieve through an 0.8-mm screen.
2. Press with medium-compression force.
3. Compress into 440-mg tablets, using 12-mm biplanar punches.

Pyridostigmine Bromide Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Pyridostigmine bromide	10.00
96.00	2	Starch (maize)	96.00
8.50	3	Silicic acid (Aerosil 200)	8.50
1.50	4	Prejel PA5	1.50
30.00	5	Lactose powder anhydrous	30.00
3.70	6	Talc	3.70
0.23	7	Magnesium stearate	0.23
QS	8	Water, purified, ca	39.70 mL

Manufacturing Directions

1. Mix 5% of item 2 and equal amounts of item 8 in a suitable vessel, at boiling. Mix and allow the paste to cool to 40°C.
2. Mix item 1 into the paste in step 1, in portions, and then add items 4 and 3, avoiding large lumps; mix to homogenous mix.
3. Add the following to item 5 (passed through a sieve), the balance of item 8 (at 40°C), and item 2, and mix to obtain a good mass; add more item 8 if necessary.
4. Pass the through a 10-mm screen in a granulator.
5. Dry the granules at 50°C until the relative humidity over the granules is 30% to 40%.
6. Crush granules in an oscillating granulator with 1-mm perforation place.
7. Blend the granules with items 6 and 7, and pass through a 1-mm sieve.
8. Blend for 10 minutes.
9. Compress to 150-mg weight.

Pyrilamine Tannate and Phenylephrine Tannate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Pyrilamine Tannate	60.00
25.00	2	Phenylephrine Tannate	28.75*
94.00	3	Starch	94.00
150.00	4	Methylcellulose USP 1500cps	150.00
32.00	5	Polygalactouronic acid	32.00
97.00	6	Calclium phosphate dehydrate	97.00
2.60	7	Magnesium stearate	2.60

*Manufacturing excess.

Quetiapine Fumarate Tablets (25 mg/100 mg/200 mg) Seroquel

Seroquel is supplied for oral administration as 25-mg (peach), 100-mg (yellow), and 200-mg (white) tablets. The inactive ingredients are povidone, dibasic dicalcium phosphate dihydrate, microcrystalline cellulose, sodium starch glycolate, lactose monohydrate, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol, and titanium dioxide. The 25-mg tablets contain red ferric oxide and yellow ferric oxide, and the 100-mg tablets contain only yellow ferric oxide.

Quinine Sulfate Tablets (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Quinine sulfate	300.00
20.00	2	Starch (maize)	20.00
25.00	3	Lactose monohydrate	25.00
5.00	4	Sodium starch glycolate	5.00
0.80	5	Methyl paraben	0.80
0.10	6	Propyl paraben	0.10
2.00	7	Gelatin	2.00
20.00	8	Starch (maize)	20.00
3.00	9	Talc	3.00
1.50	10	Aerosil 200	1.50
2.00	11	Magnesium stearate	2.00
–	12	Water, purified	QS

Manufacturing Directions

1. Sift items 1 to 4 through a 250-μm sieve into a suitable mixing vessel.
2. In a separate vessel, take the appropriate quantity of item 12, and heat it to a boil. Add and dissolve items 5 and 6. Cool to 50°C, and add items 7 and 8. Then mix to form a 30% starch paste.
3. Add the paste from step 2 into step 1, and mix the paste to form a suitable mass for granulation.
4. Pass the wet mass through a 2.38-mm sieve onto paper-lined trays; dry at 60°C overnight.
5. Pass the dried granules through #18 mesh into a blending vessel. Sift items 9 to 11 through a 250-μm sieve, and the pieces add to step 5, and blend for 2 minutes. Compress into 375-mg tablets, using 9.5-mm punches.
6. Coat the tablets using HPMC and methylene chloride. (See Appendix.)

Quinapril Hydrochloride Tablets (5 mg/10 mg/20 mg/40 mg) Accupril

Accupril tablets contain 5, 10, 20, or 40 mg of quinapril for oral administration. Each tablet also contains candelilla wax, crospovidone, gelatin, lactose, magnesium carbonate, magnesium stearate, synthetic red iron oxide, and titanium dioxide.

Quinapril Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Quinapril, use quinapril hydrochloride	22.00
108.00	2	Lactose monohydrate	108.00
55.00	3	Magnesium carbonate	55.00
10.50	4	Crospovidone	10.50
4.00	5	Povidone K-30	4.00
0.50	6	Magnesium stearate	0.50
QS	7	Purified water	QS

Manufacturing Directions

1. Sift quinapril hydrochloride, lactose monohydrate, magnesium carbonate, and crospovidone through a 0.9-mm sieve.
2. Load sifted powder from step 1 to a mixer granulator and mix for 5 minutes.
3. Dissolve povidone K-30 in purified water under slow stirring until the solution becomes clear.
4. Add the binding solution from step 3 to step 2, and mix for a few minutes until the proper granules are formed.
5. Unload the granules, and dry at 55°C in an oven to get the desired LOD of 2.5%.
6. Grind the dried granules to get granules of the desired particle size of #16 mesh.
7. Add crospovidone and magnesium stearate to ground granules in a blender, and blend for 3 minutes.
8. Compress 200 mg of the lubricated granules into tablets (12 mm).
9. Use appropriate coating materials (HPMC). (See Appendix.)

Quinolone Antibiotic Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Quinolone antibiotic[a]	100.00
23.50	2	Microcrystalline cellulose	23.50
15.00	3	Starch (maize)	15.00
6.50	4	L-Hydroxypropylcellulose	6.50
3.50	5	Magnesium stearate	3.50
1.50	6	Colloidal anhydrous silica (Aerosil 200)	1.50

[a]Applicable to most quinolone antibiotics.

Manufacturing Directions

1. The manufacturing process described is for the 100-mg tablet. Adjust the weights of all components based on the quantity used. When calculating, factor in for salt form, moisture, and activity.
2. Sift items 1 to 4.
3. Mix these (use two-thirds of item 4) at this stage in a blender. Add screened item 6, and mix at a slow speed.
4. Run the mixture through a compacting mill, and collect graded granules in a blender.
5. Add screened item 6 and the balance of item 4, and blend. Add the screened magnesium stearate in the rotating-shell blender. Mix at 6 rpm for 5 minutes. The final mixture is obtained.
6. Compress into 8-mm tablets or 10-mm tablets (for 200-mg tablets).
7. Coat using an HPMC coating. (See Appendix.)

Rabeprazole Sodium Tablets (20 mg) Aciphex

The active ingredient in Aciphex™ delayed-release tablets is rabeprazole sodium Aciphex is available for oral administration as delayed-release, enteric-coated tablets containing 20 mg of rabeprazole sodium. The inactive ingredients are mannitol, hydroxypropyl cellulose, magnesium oxide, low-substituted hydroxypropyl cellulose, magnesium stearate, ethylcellulose, hydroxypropyl methylcellulose phthalate, diacetylated monoglycerides, talc, titanium dioxide, carnauba wax, and ferric oxide (yellow) as a coloring agent.

Rabeprazole Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Rabeprazole	20.00
50.00	2	Precipitated calcium carbonate	50.00
40.00	3	Starch (maize)	40.00
73.40	4	Lactose monohydrate	73.40
6.00	5	Hydroxypropyl cellulose	6.00
2.00	6	Magnesium stearate	2.00
–	7	Water, purified	QS

Manufacturing Directions

1. Mix *R*(+) rabeprazole, precipitated calcium carbonate, cornstarch, lactose, and hydroxypropyl-cellulose together.
2. Add water, and knead the mixture. Then dry in vacuum at 40°C for 16 hours.
3. Pass the granules through a 16-mesh sieve to give granules.
4. Add item 6, and blend.
5. Compress.

Raloxifene Tablets (60 mg) Evista

Evista is supplied in a tablet dosage form for oral administration. Each Evista tablet contains 60 mg of raloxifene HCl, which is the molar equivalent of 55.71 mg of free base. Inactive ingredients include anhydrous lactose, carnauba wax, crospovidone, FD&C Blue No. 2 Aluminum Lake, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, modified pharmaceutical glaze, polyethylene glycol, polysorbate 80, povidone, propylene glycol, and titanium dioxide.

Raloxifene Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Raloxifene HCl	60.00
156.00	2	Lactose anhydrous	156.00
7.20	3	Polyvinyl pyrrolidone	7.20
7.20	4	Polysorbate 80	7.20
7.20	5	Cross-linked polyvinyl pyrrolidone	7.20
2.40	6	Magnesium stearate	2.40

Manufacturing Directions

1. Granulate the mixture of raloxifene HCl, lactose anhydrous, and cross-linked polyvinyl-pyrrolidone with an aqueous solution of polyvinylpyrrolidone and polysorbate 80.
2. Dry the granules, and reduce to a suitable size.
3. Mix and blend magnesium stearate.
4. Compress into 240-mg tablets.

Ranitidine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Ranitidine; use Ranitidine HCl	88.88
65.00	2	Microcrystalline cellulose, NF	65.00
1.12	3	Magnesium stearate, NF	1.12

Manufacturing Directions

1. Pass ranitidine and microcrystalline cellulose through a 595-μm screen, and transfer to a suitable mixer.
2. Mix for 10 minutes.
3. Screen magnesium stearate through a 400-μm screen and add to the blender.
4. Blend for 2 minutes.
5. Compress using slightly convex round punches at hardness 8 ppi and disintegration time of not more than 15 minutes in water.
6. Coat using a methocel-ethocel coating solution (see Appendix).

Ranitidine Hydrochloride Tablets (150 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Ranitidine, use ranitidine hydrochloride	167.68
129.75	2	Microcrystalline cellulose	129.75
9.00	3	Hydroxypropyl methyl cellulose 2910	9.00

Manufacturing Directions

1. Granulation: Pass ranitidine and microcrystalline cellulose through a 595-μm aperture screen, transfer to a suitable mixer, and mix for 10 minutes.
2. Lubrication
   a. Screen magnesium stearate through a 400-μm aperture screen and add to the blender. Blend for 2 minutes.
   b. Discharge the granule into polyethylene-lined drums. Seal the drums, and weigh for yield.
3. Compression: Compress using slightly convex round punches. The weight of 10 tablets should be about 2.07 g, with not more than 3% variation. Disintegration time is not more than 15 minutes in water.
4. Coating: Use opaque methocel–ethocel coating. (See Appendix.)

Ranitidine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Ranitidine	150.00
147.00	2	Ludipress	147.00
3.00	3	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm screen, and press with low-compression force.
2. Compress into 305-mg tablets, using 8-mm biconvex punches.
3. If the flowability of the tabletting mixture is not sufficient, add about 1% Aerosil 200. For 300-mg strength, use proportion weight, and increase fill weight; the use of 1% Aerosil 200 is required.

Ranitidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
167.39	1	Ranitidine HCl USP [Orchev Pharma]	167.39
78.28	2	Microcrystalline cellulose NF [Avicel® PH-102, FMC]	78.28
62.00	3	Pregelatinized starch NF [Starch 1500®, Colorcon]	62.00
1.55	4	Fumed silica NF [Aerosil® 200, Degussa AG]	1.55
0.78	5	Magnesium stearate NF [Peter Greven]	0.78

Manufacturing Directions

1. All materials, with the exception of magnesium stearate, are blended for 10 minutes in a blender.
2. Magnesium stearate is added and blended for an additional 2 minutes.
3. Tablets compressed at 310 mg.

Ranitidine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Ranitidine; use Ranitidine HCl[a]	85.00
95.00	2	Microcrystalline cellulose (Avicel™ PH102)	95.00
7.00	3	Croscarmellose sodium (Ac-Di-Sol)	7.00
6.60	4	Microcrystalline cellulose (Avicel™ PH102)	6.60
1.40	5	Magnesium stearate	1.40

[a]Ranitidine HCl (1.5%) is added to compensate LOD and process loss.

Manufacturing Directions

1. Process the product in an area where the relative humidity is 40% to 45% and temperature does not exceed 25°C.
2. Store the bulk tablets in polyethylene-lined stainless steel containers at a controlled relative humidity of 45% to 50% and temperature not exceeding 25°C.
3. Pass items 2, 3, and 1 through a sifter using a 900-μm sieve.
4. Load into a blender, and mix for 3 minutes.
5. Manually mix items 4 and 5 in a polyethylene bag for 1 minute.
6. Pass through a sifter using a 500-μm sieve.
7. Collect in a polyethylene bag.
8. Add to blender, and blend for 1 minute.
9. Check temperature and humidity before start of slugging (at a temperature not exceeding 25°C and a relative humidity of 40% to 45%).
10. Slug 240.0 g of mixed powder in a rotary tabletting machine.
11. Grind the slugs in a granulator using a 3.0-mm sieve followed by a 1.00-mm sieve.
12. Compress 195 mg using oblong biconvex punches.
13. Check temperature and humidity before start of compression (limit: temperature not exceeding 25°C and relative humidity of 40% to 45%).
14. Coat using a hydroalcoholic HPMC coating.

Ranitidine Tablets (75 mg)

Bill of Materials			
Scale(mg/tablet)	Item	Material Name	Quantity/1000 Tabs (g)
75.00	1	Ranitidine, use ranitidine HCl[a]	85.00
95.00	2	Microcrystalline cellulose (Avicel PH 102)	95.00
7.00	3	Croscarmellose sodium (Ac-Di-Sol)	7.00
6.60	4	Microcrystalline cellulose (Avicel PH 102)	6.60
1.40	5	Magnesium stearate	1.40

[a]Ranitidine HCl 1.5% is added as an extra to compensate LOD and process loss.

Manufacturing Directions

1. Process the product in an area where the RH is between 40% and 45%, and the temperature does not exceed 25°C. Store the bulk tablets in polythene-lined stainless steel containers at a controlled RH 45% to 50% and a temperature not exceeding 25°C.
2. Pass items 2, 3, and 1 through a sifter using a 900-μm sieve.
3. Load into blender, and mix for 3 minutes. Mix items 4 and 5 in a polythene bag manually for 1 minute. Pass through a sifter using a 500-μm sieve.
4. Collect in a polythene bag. Add to the blender, and blend for 1 minute.
5. Check temperature and humidity before starting to get sluggish. (Temperature not exceeding 25°C, RH 40–45%.)
6. Slug 240.0 g of mixed powder in a rotary tablet-ting machine. Grind the slugs in the granulator, using a 3-mm sieve followed by a 1-mm sieve.
7. Compress into 195-mg tablets, using oblong biconvex punches. Check the temperature and humidity before starting the compression. The limitation is that the temperature should not exceed 25°C, and the RH should be 40% to 45%.
8. Coat using a hydroalcoholic HPMC coating.

Ranitidine Tablets (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Ranitidine use as ranitidine HCl*	340.00
110.00	2	Microcrystalline cellulose (Avicel PH 102)	110.00
10.00	3	Croscarmellose sodium (Ac-Di-Sol)	10.00
16.00	4	Microcrystalline cellulose (Avicel PH 102)	16.00
4.00	5	Magnesium stearate	4.00

*Anhydrous; adjust for moisture.

Manufacturing Directions

Precautions: Process the product in an area where the relative humidity is between 40% and 45%, and the temperature should not exceed 25°C. Store the bulk tablets in polythene-lined stainless steel containers at a controlled relative humidity of 45% to 50% and at temperatures not exceeding 25°C.

1. Dry powder sieving and mixing: Pass items 2, 3, and 1 through a sifter, using a 900-μm sieve. Load into the blender, and mix for 3 minutes.
2. Lubrication
   a. Mix manually items 4 and 5 in a polythene bag for 1 minute. Pass through a sifter using a 500-μm sieve. Collect in a polythene bag. Add to the blender (step 1), and blend for 1 minute.
   b. Unload in stainless steel drums. Check and record the weight of powder mix.
3. Slugging
   a. Check the temperature and humidity before the start of slugging. Limits: temperature not exceeding 25°C; relative humidity of 40% to 45%.
   b. Slug 240.0 g of the mixed powder in a rotary tabletting machine using the following parameters. Keep the rest of the quantity in a stainless steel drum.
4. Grinding: Grind the slugs in a granulator using a 3-mm sieve followed by a 1-mm sieve.
5. Mixing: Ground granules, 240 g, from step 2, and 240 g of the lubricated granules from step 3a. Load into blender and mix for 1/2 minutes.
6. Compression: Check the temperature and humidity before starting compression. Limits: temperature not exceeding 25°C; relative humidity of 40% to 45%. Compress the granules using a rotary tabletting machine. Compress into 480-mg tablets, using 015.5 mm × 7 mm punches.

Ranitidine Tablets (150 mg), Zantac

Each Zantac 150 tablet for oral administration contains 168 mg of ranitidine HCl equivalent to 150 mg of ranitidine. Each tablet also contains the inactive ingredients FD&C Yellow No. 6 Aluminum Lake, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, titanium dioxide, triacetin, and yellow iron oxide.

Each Zantac 300 tablet for oral administration contains 336 mg of ranitidine HCl equivalent to 300 mg of ranitidine. Each tablet also contains the inactive ingredients croscarmellose sodium, D&C Yellow No. 10 Aluminum Lake, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, titanium dioxide, and triacetin.

Zantac 150 EFFERdose tablets and Zantac 150 EFFERdose granules for oral administration are effervescent formulations of ranitidine that must be dissolved in water before use. Each individual tablet or the contents of a packet contains 168 mg of ranitidine HCl equivalent to 150 mg of ranitidine and the following inactive ingredients: aspartame, monosodium citrate anhydrous, povidone, and sodium bicarbonate. Each tablet also contains sodium benzoate. The total sodium content of each tablet is 183.12 mg (7.96 mEq) per 150 mg of ranitidine, and the total sodium content of each packet of granules is 173.54 mg (7.55 mEq) per 150 mg of ranitidine.

Riboflavin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3.00	1	Riboflavin	3.00
195.00	2	Ludipress®	195.00
2.00	3	Magnesium stearate	2.00
1.00	4	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with very low-compression force (4 kN).
2. Compress into 202-mg tablets, using 8-mm biplanar punches.
3. This is a very low active ingredient formulation (3 mg).
4. If content uniformity is a problem, prepare a premix of the active ingredient with a small part of the Ludipress® or with lactose monohydrate before mixing with the other components of the formulation.

Riboflavin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Riboflavin	10.00
75.00	2	Lactose monohydrate	75.00
20.00	3	Cornstarch	20.00
15.00	4	Avicel™ PH101	15.00
5.00	5	Kollidon® 30	5.00
25.00	6	Water	25.00
0.80	7	Aerosil® 200	0.80
2.50	8	Talc	2.50
1.70	9	Hydrogenated castor oil	1.70

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with solution of items 5 and 6, dry, pass through an 0.8-mm sieve, mix with items 7 to 9, and press with low compressive force.
2. Compress into 134-mg tablets, using 8-mm biplanar punches.

Riboflavin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Riboflavin	75.00
375.00	2	Sorbitol (crystalline)	375.00
23.00	3	Kollidon® VA 64	23.00
4.00	4	Magnesium stearate	4.00
12.00	5	Aerosil® 200	12.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with low compressive force.
2. Compress into 493-mg tablets, using 12-mm biplanar punches.

Riboflavin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Riboflavin	100.00
250.00	2	Sorbitol (crystalline)	250.00
19.00	3	Kollidon® VA 64	19.00
5.00	4	Magnesium stearate	5.00
10.00	5	Aerosil® 200	10.00

Manufacturing Directions

1. Pass all components through an 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 384-mg tablets, using 12-mm biplanar punches.

Riboflavin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Riboflavin, with excess	156.00
150.00	2	Ludipress®	150.00
4.00	3	Magnesium stearate	4.00
2.00	4	Aerosil® 200	2.00

Manufacturing Directions

1. Mix all components, pass through an 0.8-mm sieve, and press with low compressive force.
2. Compress into 308-mg tablets, using 8-mm biplanar punches.

Rifampicin, Isoniazid, Ethambutol, and Pyridoxine Tablets (300 mg/200 mg/25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
–	1	Alcohol SD 3A, 200 proof	150.00 mL
3.00	2	Alcohol cetostearyl	3.00
300.00	3	Rifampicin powder	300.00
12.00	4	Hydroxypropyl methyl cellulose 2910, 50 cps	2.00
–	5	Alcohol SD 3A, 200 proof	QS
200.00	6	Isoniazid zisonicotinylhydrazine, 10% excess	220.00
25.00	7	Pyridoxine hydrochloride	25.00
400.00	8	Ethambutol hydrochloride	400.00
20.00	9	Povidone K 29–32	20.00
–	10	Water, purified	50.00 mL
–	11	Water, purified	QS
20.00	12	Talc	20.00
40.00	13	Sodium starch glycolate	40.00
10.00	14	Magnesium stearate	10.00

Manufacturing Directions

Note: Rifampicin and ethambutol hydrochloride are expensive raw materials, therefore, handle with care. The product should be manufactured in a separate, closed area, and all manufacturing equipment should be covered to minimize dust contamination.

1. Granulation I
   a. Charge the alcohol (item 1) into a container, and while stirring, gradually add the alcohol cetostearyl. Continue mixing until it all dissolves.
   b. Charge the rifampicin into the mixer (preferably a planetary mixer), followed by the hydroxypropyl methylcellulose. Mix together for 5 minutes.
   c. While mixing the blended powders from step 1b, pour in the alcoholic solution from this step. (Do not add too slowly or excessive evaporation will occur.) When all the solution is added, continue mixing for 1 minute.
   d. Stop the mixer, scrape the blades, walls, and bottom of the mixer, and then restart the mixer.
   e. While mixing, add extra alcohol (item 5) in portions, mixing for 30 seconds between each addition. Continue adding alcohol and mixing until the mass changes to a uniform dark reddish-brown color that exhibits good adhesion when squeezed and contains no dry powder. Stop mixing.
   f. Quickly scrape the blades, walls, and bottom of the mixer. Then pass the mass through a 4.76-mm aperture screen, spread on lined trays, and dry in a hot-air oven at 50°C to an LOD (60°C for 3 hours under vacuum) of not more than 2.5%.
   g. Sift the dried granules through a 1.2-mm screen on a sieve shaker.
   h. Pass the coarse granules from step 1g through a 1.7-mm screen. i. Transfer the siftings from step 1g and the granules from step 1h to a suitable blender.
2. Granulation II
   a. Pass successively, through a 1.2-mm aperture screen on a sieve shaker, the isoniazid followed by the pyridoxine hydrochloride. Charge the screened powders into a suitable mixer, and mix for 5 minutes.
   b. Pass the ethambutol hydrochloride through a 1.2-mm aperture screen, and transfer to the mixer. Blend all the powders together for 5 minutes.
   c. Add the water (item 10) to a stainless steel container, and add, while mixing, the povidone. Continue mixing until it all dissolves.
   d. While mixing the powders from step 2b add the aqueous solution from step 2c in a slow stream. When all the solution is added, continue mixing for 1 minute.
   e. Stop the mixer, and scrape the blades, wall, and bottom of the mixer. Start mixing again.
   f. Gradually add extra water until granulation is achieved with the formation of balls.
   g. Pass the mass through a 4.76-mm aperture screen, and spread on lined trays. Dry in a hot-air oven at 50°C for 4 hours, pass the granules through a 2.38-mm aperture screen, return to the oven, and continue drying to an LOD of less than 1% (60°C for 3 hours under vacuum).
   h. Sieve the dried granules through an 840-μm aperture screen on a suitable sieve shaker.
   i. Pass the coarse granules from step 2h through an 840-μm aperture screen.
   j. Transfer the fines from step 2h and the granules from step 2i to the blender (see step 1i).
3. Lubrication
   a. Pass the talc and sodium starch glycolate through a 595-μm aperture screen on a sieve shaker, and then transfer to the blender with Granulations I and II.
   b. Blend all the items together for 15 minutes, then stop the blender.

c. Pass the magnesium stearate through a 595- μm aperture screen on a sieve shaker, then transfer to the blender.
d. Blend the batch for 3 to 4 minutes, then stop the blender.
e. Discharge the contents of the blender into polyethylene-lined drums, and weigh.

4. Compression: Compress into 1.05-g tablets, using ovaloid punches (18.6 × 8.7 mm), with a disintegration time of not more than 20 minutes in water and a thickness of 8.4 to 8.8 mm.
5. Coating: Apply an organic methocel coating. (See Appendix.)

Rifampicin Tablets (300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
–	1	Alcohol SD 3A, 200 proof	150.00 mL
3.00	2	Alcohol cetostearyl	3.00
300.00	3	Rifampicin powder	300.00
12.00	4	Hydroxypropyl methylcellulose 2910 50 cps	12.00
–	5	Alcohol SD 3A, 200 proof	QS
8.00	6	Talc	8.00
16.00	7	Sodium starch glycollate powder	16.00
7.50	8	Magnesium stearate	7.50

Manufacturing Directions

Caution: (1) Rifampicin is an expensive raw material; handle with care. (2) The product should be manufactured in a separate closed area, and all manufacturing equipment should be covered so as to minimize dust contamination. (3) After use, wash the manufacturing area and equipment thoroughly with water and detergent. Personnel should take a cleansing shower after exposure during manufacturing.

1. Granulation
   a. Do not over fill the mixer, because this retards penetration of the alcohol to the bottom of the bowl, leading to excessive evaporation and inadequate massing.
   b. Charge the alcohol (item 1) into a container, and while stirring gradually, add the alcohol cetostearyl. Continue mixing until all has dissolved.
   c. Charge the rifampicin into the mixer (preferably a planetary mixer), followed by the hydroxypropyl methylcellulose. Mix together for 5 minutes.
   d. While mixing the blended powders from step 1b, pour in the alcoholic solution from step 1a. (Do not add too slowly or excessive evaporation will occur.) When all the solution is added, continue mixing for 1 minute.
   e. Stop the mixer; scrape the blades, walls, and bottom of the mixer well, and then restart the mixer.
   f. While mixing, add extra alcohol (item 5) in portions, mixing for 30 seconds between each addition. Continue adding alcohol and mixing until the mass changes to a uniform dark reddish-brown color that exhibits good adhesion when squeezed and contains no dry powder. Stop mixing.
   g. Quickly scrape the blades, walls, and bottom of the mixer, and then pass the mass through a 4.76-mm aperture screen; spread on lined trays, and then dry in a hot-air oven at 50°C to an LOD not more than 2.5% (60°C for 3 hours under vacuum). Request samples.
   h. Sift the dried granules through a 1.2-mm screen on a sieve shaker.
   i. Pass the coarse granules from step g through a 1.7-mm screen on a granulator or something similar.
   j. Transfer the siftings from steps g and \ through a 1.7-mm screen on a granulator.
2. Lubrication: Pass the talc and sodium starch glycolate through a 595-μm aperture screen on a sieve shaker, and then transfer to the blender.
3. Blend all the items together for 15 minutes, then stop the blender.
   a. Pass the magnesium stearate through a 595-μm aperture screen on a sieve shaker, then transfer to the blender.
   b. Blend the batch for 3 to 4 minutes, and then stop the blender.
   c. Discharge the contents of the blender into polyethylene-lined drums, and weigh. Record the batch weight.
4. Compression: Compress the tablets on a suitable rotary tabletting machine, using round punches of 10.32 mm. The tablet weight for 10 tablets is as follows: (3.465 × 100)/(100% LOD). Hardness is 6 to 8 kPa; disintegration time should be more than 15 minutes in water; and thickness should be 5.15 to 5.25 mm.
   a. For other strengths of rifampicin, 450 and 600 mg, scale up the formula. For 450-mg tablets, use ovaloid punches of 15.2 × 7.77 mm. The tablet weight for 10 tablets is (5.145 × 100)/(100% LOD); hardness is 9 to 15 kPa; the disintegration time is not more than 15 minutes in water; and the thickness is 6.55 to 6.65 mm. The coating solution will be 200 mL—optionally add coating solution gloss methocel, 90.00 mL. (See Appendix.)
   b. For 600-mg tablets, use ovaloid punches of 18.6 × 7.8 mm. The tablet weight for 10 tablets is (6.930 × 100)/(100% LOD); hardness is 9 to 15 kPa; the disintegration time is not more than 15 minutes in water; and the thickness is 6.35 to 6.45 mm. Use a coating solution of 250 mL. Optionally add coating solution gloss methocel, 90.00 mL. (See Appendix.)

Rifampicin Tablets (450 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
450.00	1	Rifampicin	450.00
58.00	2	Starch maize	58.00
9.00	3	Kollidon 90F	9.00
–	4	Isopropyl alcohol or alcohol, ca	50 mL
15.00	5	Kollidon CL	15.00
10.00	6	Stearic acid	10.00
2.00	7	Magnesium stearate	2.00
2.00	8	Aerosil 200	2.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4. Dry, sieve, and mix with items 5 to 8, and press with low-compression force to tablets.
2. Compress into 550-mg tablets, using 12-mm biplanar punches.

Risedronate Sodium Tablets (5 mg/30 mg) Actonel

The inactive ingredients are crospovidone, ferric oxide yellow (5-mg tablets only), hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, silicon dioxide, and titanium dioxide.

Risedronate Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
30.00	1	Risedronate sodium[a]	30.00
156.00	2	Lactose anhydrous	156.00
60.50	3	Microcrystalline cellulose	60.50
7.40	4	Crospovidone	7.40
1.10	5	Magnesium stearate	1.10

[a]This quantity of risedronate sodium is determined by assay and then adjusted to provide the designed dosage level of risedronate sodium on an anhydrous basis.

Manufacturing Directions

1. Charge the risedronate active ingredient with the microcrystalline cellulose in a twin-shell blender. Blend for 20 minutes.
2. Pass the blend through an oscillator equipped with a 60-mesh screen.
3. Return the milled blend to the shell blender, along with the lactose and crospovidone, and mix until uniform.
4. Add the magnesium stearate, and mix until adequate lubrication is achieved.
5. Compress 250 mg.
6. Coat. (See Appendix.)

Risperidone Tablets (4 mg) Risperdal

Risperdal tablets are available in 0.25-mg (dark yellow), 0.5-mg (red-brown), 1-mg (white), 2-mg (orange), 3-mg (yellow), and 4-mg (green) strengths. The inactive ingredients are colloidal silicon dioxide, hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, and starch (corn). Tablets of 0.25, 0.5, 2, 3, and 4 mg also contain talc and titanium dioxide. The 0.25-mg tablets contain yellow iron oxide; the 0.5-mg tablets contain red iron oxide; the 2-mg tablets contain FD&C Yellow No. 6 Aluminum Lake; the 3-mg and 4-mg tablets contain D&C Yellow No. 10; and the 4-mg tablets contain FD&C Blue No. 2 Aluminum Lake.

Risperidone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Risperidone	4.00
140.00	2	Lactose monohydrate	140.00
105.00	3	Microcrystalline cellulose (Avicel PH 102)	105.00
81.00	4	Maize starch	81.00
18.00	5	Maize starch, dried	18.00
1.00	6	Colloidal silicone dioxide (Aerosil 200)	1.00
1.00	7	Magnesium stearate	1.00
QS	8	Purified water	QS

Manufacturing Directions

1. Sift risperidone, lactose monohydrate, Avicel PH 102, and a part of the maize starch through a stainless steel 500-μm sieve.
2. Load the sifted powder into a mixer, and mix for 5 minutes.
3. Make a paste with the remaining part of the maize starch in purified water (80–90°C).
4. Knead the powder mix with the starch paste to get the desired granules.
5. Dry the granules in an air-circulating oven to a targeted LOD of not more than 2.5%.
6. Pass the dried granules through a 250-μm sieve into a blending vessel.
7. Lubricate with Aerosil 200, maize starch dried, and magnesium stearate previously sieved through a stainless steel 250-μm sieve. Blend for 1 minute.
8. Compress into tablets to get the labeled amount of risperidone per tablet using specified tools.
9. Coat the tablets using a hypermellose coating. (See Appendix.)

Rofecoxib Tablets (12.5 mg/25 mg/50 mg) Vioxx

Each tablet of Vioxx for oral administration contains 12.5, 25, or 50 mg of rofecoxib and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, lactose, magnesium stearate, microcrystalline cellulose, and yellow ferric oxide.

Rosiglitazone Maleate Tablets (2 mg/4 mg/8 mg) Avandia

Each pentagonal film-coated Tiltab" tablet contains rosiglitazone maleate equivalent to rosiglitazone, 2 mg, 4 mg, or 8 mg, for oral administration. Inactive ingredients are hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol 3000, sodium starch glycolate, titanium dioxide, triacetin, and one or more of the following: synthetic red and yellow iron oxides and talc.

Roxithromycin-Dispersible Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Roxithromycin base	150.00
22.50	2	Crospovidone	22.50
62.50	3	Croscarmellose sodium	62.50
3.80	4	Polysorbate	3.80
666.20	5	Microcrystalline cellulose	666.20
40.00	6	Aspartame	40.00
20.00	7	Saccharin sodium	20.00
20.00	8	Mint flavor	20.00
5.00	9	Colloidal silica	5.00
10.00	10	Magnesium stearate	10.00

Roxithromycin-Dispersible Tablets (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Roxithromycin	200.00
30.00	2	Ethylcellulose	30.00
12.80	3	Sodium croscarmellose	12.80
0.27	4	Isopropyl alcohol	270.00 mL
130.00	5	Dicalcium phosphate	130.00
4.40	6	Sodium lauryl sulfate	4.40
320.00	7	Starch (maize)	320.00
4.00	8	Magnesium stearate	4.00
4.00	9	Talc	4.00
28.00	10	Sodium starch glycolate	28.00
8.00	11	Aerosil 200	8.00
24.00	12	Aspartame	24.00
24.00	13	Flavor	24.00
–	14	Water, purified	QS

Manufacturing Directions

1. Sift items 1, 3, and 5 through a 250-μm sieve into a suitable mixing vessel.
2. In a separate vessel, add and mix items 2 and 4.
3. Add the binding solution in step 2 to step 1, and mix until a suitable mass is formed.
4. Pass the wet mass through a 2.38-mm sieve, and dry the granules in a dehumidified room.
5. Pass the dried granules through a 595-μm sieve into a blending vessel.
6. Pass items 6 and 7 through a 250-μm sieve into a blender, and mix for 15 minutes.
7. Prepare the paste with a portion of item 7 in hot water, and add to step 6. Mix until a proper mass is formed.
8. Dry the granules at 50°C overnight, and pass the dried granules through 595-μm sieve.
9. Lubricate the two granules mixed together with items 8 to 13.
10. Compress into 150-mg tablets, using 8-mm punches.
11. Coat using HPMC coating. (See Appendix.)

Saccharin Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Saccharin sodium	15.00
10.00	2	Tartaric acid	10.00
14.00	3	Sodium bicarbonate	14.00
2.00	4	Kollidon® VA 64	2.00
2.00	5	PEG-6000 (powder)	2.00

Manufacturing Directions

1. Dry saccharin sodium and tartaric acid for 1 hour at 100°C.
2. Mix all components, pass through an 0.8-mm sieve, and press with low compressive force.
3. Compress into 42-mg tablets, using 5-mm biplanar punches.

Saccharin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
37.50	1	Sodium cyclamate	37.50
17.00	2	Mannitol	17.00
6.35	3	Soda ash (light-milled powder, 58% Na_2O)	6.35
3.75	4	Saccharin sodium (dihydrated powder)	3.75
1.40	5	Povidone (PVP K-29–32)	1.40
8.00	6	Purified water	8.00
11.00	7	Tartaric acid	11.00
0.80	8	Soda ash (light-milled powder, 58% Na_2O)	0.80
1.00	9	Anhydrous sodium citrate	1.00
1.00	10	Sodium benzoate	1.00
0.20	11	PEG-8000	0.20

Manufacturing Directions

1. This product is hygroscopic and should be processed in a low-humidity area not exceeding 50% relative humidity at 24°C.
2. Maintain at 35% to 40% relative humidity at 24°C if possible.
3. If necessary, pass sodium cyclamate and mannitol (if used) through a FitzMill or similar type using a 420-μm or similar screen, then charge into a suitable mixer.
4. To this mixture, add soda ash (item 3) and blend for 30 minutes or until uniform.
5. Dissolve Povidone in 4 mL of warm purified water.
6. Dissolve saccharin sodium in 3 mL of warm purified water.
7. Add solutions from previous steps together plus sufficient purified water.
8. Mass with blended powders.
9. Blend for 1 hour or until uniform.
10. Pass the wet mass through a 4.76-mm or similar screen in an oscillating granulator, and spread onto trays.
11. Oven dry at 50°C to 55°C for 16 to 24 hours using a full oven load of trays (LOD NMT 0.9%).
12. Pass dried granulation through a 1.19-mm or similar screen in an oscillating granulator or through a 1.68-mm or similar screen using a comminuting mill (knives forward, slow speed).
13. Lubricants must meet LOD/moisture content before proceeding.
14. If lubricants fail, dry them at 80°C for 8 hours.
15. Use 60°C for tartaric acid.
16. Mill lubricants (except tartaric acid and granulated lactose, if used) through a 600-μm or similar screen in a comminuting mill (hammers forward, medium speed).
17. Load dried granulation, coated tartaric acid, lactose (if used), and milled lubricants into a suitable mixer and blend for 30 to 40 minutes.
18. Compress into 80-mg tablets, using 7/32-in. punches.

Saccharin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Saccharin sodium	15.00
31.00	2	Ludipress®	31.00
2.00	3	Kollidon® CL	2.00
0.30	4	Magnesium stearate	0.30
2.00	5	PEG-6000 (powder)	2.00
2.00	6	Lutrol F 68	2.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force.
2. Compress into 51-mg tablets (or 50 mg if items 5 and 6 are omitted), using 5-mm punches.

Salbutamol Tablets (2 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Salbutamol, use as salbutamol sulfate	2.40
80.00	2	Lactose monohydrate	80.00
33.60	3	Starch (maize)	33.60
3.30	4	Starch (maize)	3.30
0.10	5	FD&C Yellow No. 6	0.10
0.60	6	Magnesium stearate	0.60
–	7	Purified water	28.00

Manufacturing Directions

Note: The binding solution is susceptible to microbial growth, and so prepare the solution directly before use.

1. Sift item 4 through a 250-μm sieve using a sifter.
2. Manually make a homogeneous slurry of item 4 in 4 g of cold item 7 (25–30°C) in a stainless steel container. Check that it is free of lumps.
3. Add item 5 and the slurry of the starch paste (from step 2) into 24 g of item 7, heated to 85°C into a Giusti vessel. Stir until there is complete gelatinization. Cool to 50°C.
4. Sift items 1, 3, and 2 through a 630-μm sieve using a sifter. Collect in a stainless steel container.
5. Load sieved powders in the mixer. Mix for 15 minutes at high speed.
6. Add starch paste from step 4 to the mixer. Mix this for 10 minutes.
7. Pass the wet mass through a FitzMill using sieve no. 24205 at medium speed, knives forward.
8. Spread the wet granules onto the trays. Load the trolleys into the oven. Dry the granules at 55°C for 10 hours. Scoop the granules after 4 hours of drying, then put the upper trays to the down position and the down trays to the upper position for uniform drying. Check the moisture content—as a limit, there should not be more than 2.5%.
9. Grind the dried granules through a 1-mm sieve using a granulator. Collect in a stainless steel drum, and load to the blender. Sift item 6 through a 250-μm sieve using a sifter. Collect in a polythene bag. Mix 2 g of granules with this, and add to the blender. Mix this for 1 minute.
10. Compress the granules. The weight of 10 tablets is 1.20 g ± 3%; hardness is not less than 2 kPa.

Salbutamol Tablets (4 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Salbutamol, use as salbutamol sulfate	4.80
80.00	2	Lactose monohydrate	80.00
31.28	3	Starch (maize)	31.28
3.30	4	Starch (maize)	3.30
0.02	5	Red FD&C No. 3	0.02
0.60	6	Magnesium stearate	0.60
–	7	Purified water	28.00

Manufacturing Directions

See the manufacturing directions for the 2.0-mg strength.

Scopolamine Tablets

Manufacturing Directions

1. To 0.2 g of scopolamine hydrobromide, 29.4 g of calcium hydrogenphosphate (anhydrous) is added in small portions and well mixed in a mortar to form a triturate.
2. Triturate (29.6 g) is well mixed with fumaric acid (60 g) and calcium stearate (0.4 g) in a polyethylene bag to form a mixed powder A.
3. 25 g of fumaric acid, 9.8 g of potassium hydrogenphosphate (anhydrous), and 0.2 g of calcium stearate are intimately mixed in a polyethylene bag to make a mixed powder B.
4. To 0.1 g of scopolamine hydrobromide, 10 g of crystalline cellulose is added in small portions and mixed well in a mortar to make a triturate.
5. This triturate (10.1 g) is mixed well with 24.7 g of lactose and 0.2 g of calcium stearate in a polyethylene bag to make a mixed powder C.
6. Multilayer tabletting is performed on a single-punch machine equipped with a die (8 mm) and flat-faced punches: first, 90 mg of the mixed powder A is placed in the die and precompressed lightly; 35 mg of the mixed powder B is placed on the first fill and lightly precompressed; thereafter, 35 mg of the mixed powder C is placed on the second fill and compressed with a total pressure of about 1.2 tons.

Selegiline Tablets (5 mg)

Formulation: Selegiline HCI (BASF), 5 g; Ludipress, 94 g; Magnesium stearate, 1 g;

Manufacturing Directions

Mix all components intensively, pass through a 0.8-mm sieve and press with low-compression force at 99 mg.

Selegiline Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Selegiline	5.00
94.00	2	Ludipress®	94.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components intensively, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 99-mg tablets, using 6-mm biplanar punches.

Serratiopeptidase Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Serratiopeptidase	10.00
228.00	2	Ludipress	228.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix intensively, and press with low-compaction force (6 kN).
2. Compress into 238-mg tablets, using 8-mm biplanar punches.

Serratiopeptidase Tablets (10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Serratiopeptidase, 40% excess	14.00
70.00	2	Lactose monohydrate	70.00
50.00	3	Microcrystalline cellulose potassium	50.00
80.00	4	Starch (maize)	80.00
–	5	Isopropyl alcohol	100 mL
2.50	6	Magnesium stearate	2.50
5.00	7	Talc	5.00

Manufacturing Directions

1. Charge items 2 to 4 in a suitable vessel. Mix these items for 5 minutes.
2. Add item 5 and granulate the mass. Pass it through a 2.38-mm sieve onto paper-lined trays.
3. Dry the granules in a dehumidified area overnight.
4. Pass the granules through #18 mesh into a blending vessel.
5. Add item 1 to step 4, and mix well.
6. Sift items 6 and 7 through a 250-µm sieve, and add to step 5.
7. Compress into 225-mg tablets, using 7-mm punches.
8. Coat with HPMC organic coating. (See Appendix.)

Serratiopeptidase Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Serratio peptidase	10.00
228.00	2	Ludipress®	228.00
2.00	3	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix intensively, and press with low compressive force (6 kN).
2. Compress into 238-mg tablets, using 8-mm biplanar punches.

Sertraline Hydrochloride Tablets (25 mg/50 mg/ 100 mg) Zoloft

Zoloft is supplied for oral administration as scored tablets containing sertraline hydrochloride equivalent to 25, 50, and 100 mg and the following inactive ingredients: dibasic calcium phosphate dihydrate, D&C Yellow No. 10 Aluminum Lake (in the 25-mg tablet), FD&C Blue No. 1 Aluminum Lake (in the 25-mg tablet), FD&C Red No. 40 Aluminum Lake (in the 25-mg tablet), FD&C Blue No. 2 Aluminum Lake (in the 50-mg tablet), hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, synthetic Yellow iron oxide (in the 100-mg tablet), and titanium dioxide.

Sertraline L-Lactate Osmotic Tablet

Manufacturing Directions

1. Tablet cores comprising sertraline L-lactate (13.8 wt%), L-aspartic acid (11 wt%), calcium acetate (5 wt%), microcrystalline cellulose (29.5 wt%), and fructose (38.2 wt%) are blended, then run through a roller compactor and milled.
2. This milled material is then blended wish 2.5 wt% magnesium stearate to form the final blended material that is used to make tablets having a total weight of 470 mg on a conventional tablet press.
3. Semipermeable asymmetric membrane coatings comprised 10 wt% cellulose acetate 398-10, 2.5 wt% polyethylene glycol 3350, 15 wt% water, and 72.5 wt% acetone.
4. The coating solution is spray-coated onto the tablets at a rate of 20 g/min until a 10 wt% coating level on the tablets had been achieved.

Sertraline Hydrochloride Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
27.98	1	Sertraline hydrochloride equivalent to Sertraline 25.00 mg	27.98
52.52	2	Dibasic calcium phosphate dihydrate, DC Grade	52.52
15.00	3	Microcrystalline cellulose (Avicel PH102)	15.00
3.00	4	Sodium starch glycolate	3.00
0.50	5	Hydroxypropyl cellulose	0.50
1.00	6	Magnesium stearate	1.00
2.00	7	Hypromellose	2.00
0.40	8	Polyethylene glycol 4000	0.40
0.20	9	Polysorbate 80	0.20
0.60	10	Titanium dioxide	0.60
0.20	11	D & C Yellow #10 aluminum lake	0.20
0.30	12	FD & C Blue #1 aluminum lake	0.30
–	13	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1, 4, and 5 through 0.5-mm sieve and add to step 1.
3. Pass item 3 through 0.7-mm sieve and charge to step 1.
4. Mix step 1 for 20 minutes using tumbler.
5. Pass item 6 through 0.250-mm sieve and add to step 4.
6. Mix step 5 for 2 minutes.
7. Compress into 100-mg tablets, using a suitable punch (5.0 mm, round).
8. Charge item 13 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
9. Add items 8 to 12 to step 8 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
10. Load core tablets from step 7 in coating pan and apply coating dispersion from step 9 to get 2.5% to 3.0% weight gain.

Sertraline Hydrochloride Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
55.96	1	Sertraline hydrochloride equivalent to Sertraline 50.00 mg	55.96
105.04	2	Dibasic calcium phosphate dihydrate, DC grade	105.04
30.00	3	Microcrystalline cellulose (Avicel PH102)	30.00
6.00	4	sodium starch glycolate	6.00
1.00	5	Hydroxypropyl cellulose	1.00
2.00	6	Magnesium stearate	2.00
4.00	7	Hypromellose	4.00
0.80	8	Polyethylene glycol 4000	0.80
0.30	9	Polysorbate 80	0.30
1.20	10	Titanium dioxide	1.20
0.40	11	FD & C Red #40 aluminum lake	0.40
0.60	12	FD & C Blue #2 aluminum lake	0.60
–	13	Water, purified	60.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1, 4, and 5 through 0.5-mm sieve and add to step 1.
3. Pass item 3 through 0.7-mm sieve and charge to step 1.
4. Mix step 1 for 20 minutes using tumbler.
5. Pass item 6 through 0.250-mm sieve and add to step 4.
6. Mix step 5 for 2 minutes.
7. Compress into 200-mg tablets, using a suitable punch (6.5 mm × 10 mm, oblong).
8. Charge item 13 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hypromellose.
9. Add items 8 to 12 to step 8 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
10. Load core tablets from step 7 in coating pan and apply coating dispersion from step 9 to get 2.5% to 3.0% weight gain.

Sertraline Hydrochloride Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
111.92	1	Sertraline hydrochloride equivalent to Sertraline 100.00 mg	111.92
110.08	2	Dibasic calcium phosphate dihydrate, DC grade	110.08
60.00	3	Microcrystalline cellulose (Avicel PH102)	60.00
12.00	4	sodium starch glycolate	12.00
2.00	5	Hydroxypropyl cellulose	2.00
4.00	6	Magnesium stearate	4.00
6.00	7	Hypromellose	6.00
1.20	8	Polyethylene glycol 4000	1.20
0.40	9	Polysorbate 80	0.40
1.80	10	Titanium dioxide	1.80
0.20	11	Yellow iron oxide	0.20
–	12	Water, purified	90.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1, 4, and items 5 through 0.5-mm sieve and add to step 1.
3. Pass item 3 through 0.7-mm sieve and charge to step 1.
4. Mix step 1 for 20 minutes using tumbler.
5. Pass item 6 through 0.250-mm sieve and add to step 4.
6. Mix step 5 for 2 minutes.
7. Compress into 300-mg tablets, using a suitable punch (10 mm, round).
8. Charge item 12 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3% to 4 hours for saturation of hypromellose.
9. Add items 8 to item 11 to step 8 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
10. Load core tablets from step 7 in coating pan and apply coating dispersion from step 9 to get 2.5% to 3.0% weight gain.

Sildenafil Tablets (25 mg/50 mg/100 mg), Viagra

Viagra is formulated as blue, film-coated, rounded-diamond-shaped tablets equivalent to 25, 50, and 100 mg of sildenafil for oral administration. In addition to the active ingredient, sildenafil citrate, each tablet contains the following inactive ingredients: microcrystalline cellulose, anhydrous dibasic calcium phosphate, croscarmellose sodium, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, lactose, triacetin, and FD&C Blue No. 2 Aluminum Lake.

Sildenafil Citrate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Sildenafil, use sildenafil citrate	70.50
100.00	2	Avicel PH 102	100.00
131.00	3	Dibasic calcium phosphate anhydrous	131.00
9.00	4	Ac-Di-Sol	9.00
1.00	5	Aerosil 200	1.00
1.50	6	Magnesium stearate	3.50

Manufacturing Directions

1. Charge items 1 and 2 in a suitable blender or plastic bag after sifting through a 500-μm sieve. Mix them for 5 minutes.
2. Add item 3 to step 1 after sifting through a 500-μm sieve. Mix for 5 minutes.
3. Add items 4 to 6 after sifting them through a 500-μm sieve (item 6 through a 250-μm sieve). Blend this for 1 minute.
4. Compress into 315-mg tablets, using diamond-shaped 13.2 × 8.2-mm punches.
5. Coat using an HPMC coating. (See Appendix). Use dispersed Blue E, 132 1.4 mg/tab, to match the color of Viagra. Following is a proposed formulation of coating solution:

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Hypermellose	4.00
0.80	2	Triacetin	0.80
1.22	3	Talc	1.22
2.60	4	Titanium dioxide	2.60
0.46	5	Lactose monohydrate	0.46
1.41	6	Dispersed blue E112	1.41
0.40	7	Opadry OY-LS 29019 clear	0.40
QS	8	Water, purified	QS

Silimarin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
35.50	1	Silimarin	35.50
410.50	2	Ludipress®	410.50
4.50	3	Magnesium stearate	4.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force (about 10 kN).
2. Compress into 458-mg tablets, using 12-mm biplanar punches.

Silimarin Tablets (35 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
35.00	1	Silimarin	35.50
410.50	2	Ludipress	410.50
4.50	3	Magnesium stearate	4.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low-compression force (about 10 kN).
2. Compress into 458-mg tablets, using 12-mm biplanar punches.

Simethicone and Magnesium Carbonate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
16.00	1	Dextrose Monohydrate, USP25.0 kg	16.00
0.16	2	Yellow #10 D&C Dye Lake 250 g	0.16
0.06	3	Blue #1 FD&C Dye Lake 90.0 g	0.06
80.00	4	Simethicone Pwd GS (30%) 417 kg	266.40
64.00, 266.4	5	Magnesium Carbonate 100 kg	64.00, 266.4
128.00	6	Microcryst Cellulose 200 kg	128.00
175.68	7	Dextrates 275 kg	175.68
5.00	8	Stearic Acid 8.00 kg	5.00

Manufacturing Directions

1. Simethicone mix is processed by preblending magnesium carbonate and simethicone powder GS 30% in a V-blender.
2. This preblended mix is then dry granulated and placed in a V-shell blender.
3. Dextrates and microcrystalline cellulose are then added to the preblended mix in the V-shell blender and the preblended mix, dextrates and microcrystalline cellulose are blended for approximately 10 minutes.
4. Blue #1 FD&C dye lake, yellow #10 D&C dye lake and dextrose are combined in a drum roller, dry granulated and then placed in the V-shell blender with the preblended mix, dextrates and microcrystalline cellulose.
5. An additional amount of dextrose is dry granulated in the same granulator that the colorants are granulated in, for the purpose of rinsing the granulator after the dry granulation of the colorants.
6. This amount of dextrose is also added to the V-shell blender.
7. An amount of stearic acid is then passed through a 30-mesh screen and added to the V-shell blender.
8. The preblended mix, dextrates, microcrystalline cellulose, colorants, dextrose and stearic acid are then blended in the V-shell blender for 3 minutes.
9. A sample of the V-shell blender mix is then measured to test blend uniformity.
10. Upon meeting satisfactory blend uniformity requirements, the simethicone layer mix is transferred to tote bins and then compressed into 650 mg tablets.

Simethicone Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
70.00	1	Simethicone dry powder 25%	280.00
158.00	2	Sucrose, powder	158.00
7.00	3	Kollidon® 90F	7.00
3.50	4	Kollidon® 90F	3.50
QS	5	Isopropanol	QS
2.80	6	Aerosil® 200	2.80

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with solution of items 4 and 5, dry, pass through a 0.8-mm sieve, add item 6, mix thoroughly, and press with high compressive force.
2. Compress into 442-mg tablets, using 12-mm biplanar punches.

Simethicone Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
80.00	1	Simethicone (Wacker silicon oil, S184)	80.00
400.00	2	Sorbitol, (crystalline)	400.00
20.00	3	Aerosil® 200	20.00
390.00	4	Ludipress®	390.00
2.00	5	Menthol (powder)	2.00
8.00	6	Magnesium stearate	8.00

Manufacturing Directions

1. Mix items 2 and 3 with item 1, pass through a 0.8-mm sieve, add mixture of items 4 to 6, mix thoroughly, pass again through a 0.8-mm sieve, and press with high compressive force.
2. Compress into 870-mg tablets, using 16-mm biplanar punches.

Simethicone Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
70.00	1	Simethicone	70.00
71.40	2	Microcrystalline cellulose	71.40
71.40	3	Magnesium hydroxide	71.40
265.00	4	Mannitol	265.00
100.00	5	Lactose	100.00
395.10	6	Granular sugar	395.10
0.70	7	Menthol	0.70
10.00	8	Fumed silica	10.00
5.00	9	Fumed silica	5.00
10.00	10	Magnesium stearate	10.00

Manufacturing Directions

1. Blend item 2 and item 3 in a V-blender for 10 minutes.
2. Transfer to planetary mixer.
3. Slowly add weighted amount of item 1 to the mix, and mix slowly using a "B" flat beater blade; after thorough mixing, pass through a #20-mesh screen.
4. Add the balance of the ingredients, mix, and compress.

Simvastatin Fast-Melt Tablet

Manufacturing Directions

1. Mix simvastatin 15%, sodium bicarbonate 25%, citric acid anhydrous 25%, xylitol 12%, microcrystalline cellulose 15%, anhydrous lactose 6%, and crodesta F160 2%.
2. Dry the above ingredients at elevated temperature in the presence of a desiccant to significantly reduce the moisture content of each material.
3. Blend for 10 minutes and extrude in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix SV-EGF (30–80 mesh), 45%; Avicel PH113, 31%; Mannogen 3215, 15%; L-HPC LH-11, 5%; aspartame, 3%; redberry flavor, 0.25%; natural orange powder, 0.15%; magnesium stearate, 0.5%; fumed silicon dioxide, 0.1%.
5. Blend for 5 minutes prior to compression.
6. Simvastatin tablets are then compressed to a hardness of approximately 1 to 5 kPa (depending upon the dose of the drug) and tablets disintegrate in water in approximately 15 to 35 seconds.

Simvastatin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Simvastatin	10.10
55.23	2	Lactose monohydrate	55.23
15.000	3	Pregelatinized starch (Starch 1500)	15.00
0.02	4	Butylated hydroxy anisole	0.02
2.50	5	Ascorbic acid	2.50
1.25	6	Citric acid	1.25
15.00	7	Microcrystalline cellulose (Avicel PH 102)	15.00
0.60	8	Magnesium stearate	0.60
0.30	9	Colloidal silicon dioxide (Aerosil 200)	0.30
–	10	Purified water	12.00
–	11	Absolute alcohol (ethanol, dehydrated alcohol)	5.00

Manufacturing Directions

Note: Avoid overmixing lubricants, or hardness may be reduced.

1. Preparation of granulating solution
   a. Make a clear solution of item 4 in item 11 by slow stirring.
   b. Dissolve items 5 and 6 in item 10 under slow stirring by a stirrer.
2. Dry powder mixing: Sift items 1, 2, and 3 through a stainless steel 500-μm sieve in a sifter. Load into the mixer, and mix for 3 minutes at low speed.
3. Kneading
   a. Add a binding solution, 25 to 31 g/min, to the dry powders while mixing at low speed. After the addition is over, scrape the sides and blades. Mix further for 2 minutes using a mixer and chopper at low speed. Scrape sides and blades. Check for the end point of granulation. (End point of the granulation is the point when the wet mass consists of little or no lumps of granule.)
   b. If required, add purified water. Record the extra quantity of purified water added. Unload the wet granules onto stainless steel trays for drying.
4. Drying
   a. Dry the wet granules in an oven at 55°C for 6 hours. After 3 hours of drying, scrape the semidried granules to break the lumps for uniform drying.
   b. Check the LOD, with a limit of 1.0% to 1.5%.
   c. If required, dry further at 55°C for 1 hour. Check the LOD. Transfer the dried granules in a stainless steel drum.
5. Grinding: Grind the dried granules through a 1.25-mm sieve. Collect in a polyethylene bag.
6. Lubrication
   a. Sift items 7 and 9 through a 500-μm sieve, and add this to the double polyethylene bag used in step 5a. Mix manually for 1 minute.
   b. Sift item 8 through a 500-μm sieve. Add 6 to 12 g granules from bulk (step 5). Mix in a polythene bag for 1 minute. Add this mixture to the polyethylene bag in step 5. Mix manually for 30 seconds. Add the two loads in the polyethylene bag, and mix manually for 15 seconds.
   c. Unload into stainless steel drums.
7. Compression: Compress the granules using a rotary tabletting machine. The dimension should be 8.5 mm × 5-mm oval punches; 100 mg per tablet should be compressed.
8. Coating: Coat the tablets using an HPMC coating. (See Appendix.)

Simvastatin Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Simvastatin	20.200
110.460	2	Lactose monohydrate	110.460
30.000	3	Pregelatinized starch (Starch 1500)	30.000
0.040	4	Butylated hydroxy anisol	0.040
5.000	5	Ascorbic acid	5.000
2.500	6	Citric acid	2.500
30.000	7	Microcrystalline cellulose (Avicel PH 102)	30.000
1.200	8	Magnesium stearate	1.200
0.600	9	Colloidal silicon dioxide (Aerosil 200)	0.600
–	10	Purified water	24.000
–	11	Absolute alcohol (ethanol, dehydrated alcohol)	10.000

Simvastatin Tablets (10 mg) Zocor

Zocor® tablets for oral administration contain 5, 10, 20, 40, or 80 mg of simvastatin and the following inactive ingredients: cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxides, lactose, magnesium stearate, starch, talc, titanium dioxide, and other ingredients. Butylated hydroxyanisole is added as a preservative.

Sodium Fluoride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.50	1	Sodium fluoride	0.55
56.25	2	Sorbitol, crystalline	56.25
56.25	3	Dicalcium phosphate	56.25
2.20	4	Kollidon® VA 64	2.20
0.50	5	Magnesium stearate	0.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high compressive force.
2. Compress into 116-mg tablets, using 6-mm biplanar punches.
3. If the content uniformity is not sufficient, a premix of sodium fluoride and sorbitol or dicalcium phosphate should be prepared separately before mixing with the rest of the excipients.

Sodium Fluoride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.30	1	Sodium fluoride	1.30
76.70	2	Ludipress®	76.70
0.40	3	Magnesium stearate	0.40

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 78-mg tablets, using 5-mm biplanar punches.
3. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of Ludipress® or with lactose monohydrate before mixing with the other components of the formulation.

Sotalol Hydrochloride Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Sotalol hydrochloride	500.00
100.00	2	Microcrystalline cellulose or lactose anhydrous	100.00
80.00	3	Starch maize	80.00
30.00	4	Sodium starch glycolate	30.00
4.00	5	Magnesium stearate	4.00
4.00	6	Silicon dioxide colloidal	4.00
QS	7	Dyes	QS
—	8	Water, purified	QS

Manufacturing Directions

1. Charge items 1 to 3 in a granulating bowl, and mix for 20 minutes. (*Note:* For item 2, a choice of using cellulose or lactose, or a combination thereof, is available.)
2. Add a sufficient quantity of item 8 to form a wet mass.
3. Pass the wet mass in step 2 through #8 mesh onto paper-lined trays. Dry at 60°C for 12 hours to achieve an LOD of less than 5%.
4. Pass the dried granules through 16 or 20 mesh, and transfer to a blending vessel.
5. Add items 4 to 7, and blend for 5 minutes.
6. Compress an appropriate amount in a suitable punch.

Spiramycin-Dispersible Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
750.00	1	Spiramycin base	750.00
45.00	2	Crospovidone	45.00
85.00	3	Croscarmellose sodium	85.00
7.50	4	Polysorbate	7.50
762.50	5	Microcrystalline cellulose	762.50
160.00	6	Aspartame	160.00
80.00	7	Saccharin sodium	80.00
80.00	8	Mint flavor	80.00
10.00	9	Colloidal silica	10.00
20.00	10	Magnesium stearate	20.00

Spironolactone Tablets (25 mg/50 mg/100 mg) Aldactone

Aldactone oral tablets contain 25, 50, or 100 mg of spironolactone. Inactive ingredients include calcium sulfate, cornstarch, flavor, hydroxypropyl methylcellulose, iron oxide, magnesium stearate, polyethylene glycol, povidone, and titanium dioxide.

Spironolactone Tablets

Bill of Materials			
Scale(mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Spironolactone	25.00
175.00	2	Ludipress	175.00
1.50	3	Magnesium stearate	1.50

Manufacturing Directions

1. Mix all components.
2. Pass the mixture through a sieve, and press with medium-compression force.
3. Compress into 197-mg tablets, using 8-mm biplanar punches.

Spirulina Extract Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Spirulina extract (powder)	250.00
245.00	2	Ludipress®	245.00
25.00	3	PEG-6000 (powder)	25.00
5.00	4	Aerosil® 200	5.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium compressive force.
2. Compress into 495-mg tablets, using 12-mm biplanar punches.

Sucralfate and Sodium Alginate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Sucralfate	500.00
20.00	2	Sodium alginate	20.00
70.00	3	Cornstarch	70.00
20.00	4	Kollidon® 30	20.00
–	5	Ethanol (95%)	80.00 mL
30.00	6	Kollidon® CL	30.00
3.00	7	Magnesium stearate	3.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with solution of items 4 and 5, pass through a sieve, mix the dry granules with items 6 and 7, and press with low compressive force.
2. Compress into 660-mg tablets, using 12-mm biplanar punches.

Sulfadimidine Tablets (500 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Sulfadimidine	500.00
100.00	2	Lactose monohydrate	100.00
15.00	3	Kollidon 30	15.00
–	4	Water, purified, ca	200.00
25.00	5	Kollidon CL	25.00
2.40	6	Talc	2.40
0.30	7	Aerosil 200	0.30
0.30	8	Calcium arachinate	0.30

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with the solution of items 3 and 4. Dry, pass through a 0.8-mm sieve, mix with items 5 to 8, and press.
2. Compress into 610-mg tablets, using 12-mm biplanar punches.

Sulfamethoxazole and Trimethoprim Tablets (400 mg/80 mg; 800 mg/160 mg; 100 mg/20 mg)

Each DS tablet contains 160 mg of trimethoprim and 800 mg of sulfamethoxazole plus magnesium stearate, pregelatinized starch, and sodium starch glycolate. Each tablet contains 80 mg of trimethoprim and 400 mg of sulfamethoxazole, plus magnesium stearate, pregelatinized starch, sodium starch glycolate, FD&C Blue No. 1 Lake, FD&C Yellow No. 6 Lake, and D&C Yellow No. 10 Lake. Each teaspoonful (5 mL) of the pediatric suspension or suspension contains 40 mg of trimethoprim and 200 mg of sulfamethoxazole in a vehicle containing 0.3% alcohol, edetate disodium, glycerin, microcrystalline cellulose, parabens (methyl and propyl), polysorbate 80, saccharin sodium, simethicone, sorbitol, sucrose, FD&C Yellow No. 6, FD&C Red No. 40, flavors, and water.

Sulfamethoxazole and Trimethoprim Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
800.00	1	Sulfamethoxazole	800.00
160.00	2	Trimethoprim	160.00
70.00	3	Starch (corn)	70.00
5.00	4	Alginic acid	5.00
–	5	Water, purified, ca	320.00 mL
5.00	6	Magnesium stearate	5.00

Manufacturing Directions

1. Granulation
   a. Pass the following ingredients through a 595-µm aperture screen: sulfamethoxazole, trimethoprim, and starch (corn), and charge into a suitable blender. Blend for approximately 20 minutes.
   b. Add and dissolve alginic acid (60°C) and purified water. Cool the solution to 35°C.
   c. Add the solution from step 1b to blended powders, and blend until a suitable granulating mass is obtained. Add more purified water if needed.
   d. Pass the granulating mass through a 2.38-mm aperture screen.
   e. Oven dry the wet granules at 45°C for 16 hours until the LOD is not more than 0.9% (105°C for 1 hour).
2. Lubrication
   a. Pass the dried granulate through a 1.2-mm aperture screen on an oscillating granulator, and charge into a suitable blender.
   b. Add magnesium stearate, and mix well for approximately 10 minutes.
3. Compression
   a. Compress using a 19-mm caplet punch. The weight of 10 tablets is 10.4 g; the thickness is 7.4 to 8.2 mm; and the hardness is 14 to 22 kPa units.
   b. For 400/80 tablets, use an 11.5-mm diameter flat, beveled edge punch. The weight of 10 tablets is 5.20 g; the thickness is 4.2 to 4.6 mm; and the hardness is 13 to 24 kPa.
   c. For 100/20 tablets, use 7.5-mm diameter beveled edge punch. The weight of 10 tablets is 1.2 g; the thickness is 2.4 to 2.7 mm; and the hardness is 6 to 12 kPa.

Sulfamethoxazole and Trimethoprim Tablets (400 mg/80 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Sulfamethoxazole	400.00
80.00	2	Trimethoprim	80.00
15.00	3	Kollidon 30	15.00
–	4	Isopropyl alcohol	QS
24.00	5	Kollidon CL	24.00
2.00	6	Talc	2.00
8.00	7	Magnesium stearate	8.00

Manufacturing Directions

1. Granulate a mixture of items 1 and 2 with a solution of items 3 and 4. Pass this through a 0.8-mm sieve, dry, add items 5 to 7, and press with low-compression force.
2. Compress into 546-mg tablets, using 12-mm biplanar punches.

Sulfamethoxazole and Trimethoprim Tablets (800 mg/160 mg; 400 mg/80 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/500000 Tablets (kg)
800.00	1	Sulfamethoxazole	800.00
160.00	2	Trimethoprim	160.00
20.00	3	Povidone K30	20.00
24.20	4	Primojel (sodium carboxymethyl starch)	24.20
5.00	5	Magnesium stearate	5.00
0.20	6	Dioctyl sodium sulfosuccinate	0.20

Manufacturing Directions

1. First prepare the PVP solution sufficient for the above batch divided into four lots.
2. In a suitable stainless steel container, take 30 kg of deionized water, heat it to 70°C, and add to it while stirring item 4 gradually.
3. After complete dissolution, continue to stir, and add 140 kg of deionized water, item 3. Stir until completely dissolved.
4. Let stand overnight.
5. In a separate container, take one-fourth of items 1 and 2, and mix. Then add, in small portions, the PVP solution made in step 1, 45.1 kg each, until a moist mass with granular lumps is obtained. Pass the granules through a centrifugal granulator using a 10-mm sieve.
6. Spread the granules on trays, and dry at 60°C for 28 hours. The relative humidity should be 15% to 20%.
7. Pass the granules through an oscillating granulator with 2-mm perforations at a rate of 2 to 2.5 kg/min.
8. Charge the granules in a V-type blender from each of the four lots, mix for 5 minutes, and transfer to a drum. Then add item 5 and the balance of Primojel (12.1 kg). Mix in a tumble mixer for 10 minutes.
9. Charge the mixture in a V-blender, and mix for 1 hour. The relative humidity should be 20% to 25%.
10. Compress at 4- to 5-ton pressure. The weight of one tablet is 1.010 mg. This is the formula for a double-strength tablet. Adjust quantities and fill the weight for 400/80 strength.

Sulfamethoxazole and Trimethoprim Tablets, Dispersible (800 mg/160 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
800.00	1	Sulfamethoxazole powder	800.00
160.00	2	Trimethoprim micronized	160.00
80.00	3	Starch (maize)	90.00
3.00	4	Sodium lauryl sulfate	3.00
15.00	5	Gelatin	15.00
25.00	6	Starch (maize)	25.00
8.00	7	Magnesium stearate	8.00
9.00	8	Guar gum	9.00
–	9	Purified water	300.00

Manufacturing Directions

Note: The binding solution is liable to microbiological growth, so prepare the solution fresh, before the granulation process.

1. Preparation of starch paste: Manually make a slurry of item 6 in 40 g of item 9 (40°C). Then add 110 g of item 9 into the vessel, and heat to 80°C. Add the slurry of item 6 to it, and mix until it swells and is translucent.
2. Add item 5 slowly to 150 g of item 9 (70°C) using a stirrer. Avoid lumps and excessive foam formation. Add the gelatin solution to the starch paste in step 1, and mix for 10 minutes.
3. Dry powder mixing: Load items 1, 2, 3, and 4 in the mixer. Mix and chop at high speed for 6 minutes.
4. Wet massing: Add starch paste from step 2 to the dry powders in the mixer, while mixing and chopping at low speed. When the addition is over, mix further for 5 minutes or until a satisfactory mass is obtained. *Note:* Avoid lumps or a ball formation that is too big.
5. Drying
   a. Dry the granules in a fluid-bed dryer at 55°C for 1 hour.
   b. Check the moisture content. The limit is 1% to 1.5%. *Note:* Moisture control is a very important step. It affects the microbial quality of this product.
6. Grinding: Grind the dried granules through a 1.5-mm sieve first, and then through a 1.25-mm sieve fitted on a dry granulator. Collect the granules in a stainless steel drum. Load the granules to the blender.

7. Lubrication
   a. Mix items 7 and 8 in a polythene bag. Pass the mix through a 250-μm sieve using a sifter. Collect in a polythene bag. Add 10 g granules from step 6. Mix for 1 to 2 minutes, add to the blender, and mix for 2 minutes.
   b. Unload into stainless steel drums.
8. Compression: Compress the granules using a rotary tabletting machine with 19 × 8.8-mm oblong punches. Each tablet will be 1100 mg.

Sulfathiazole Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Sulfathiazole	250.00
237.00	2	Lactose monohydrate or dicalcium phosphate	237.00
12.00	3	Kollidon 30	12.00
–	4	Water, purified	QS
12.00	5	Kollidon CL	12.00
2.00	6	Magnesium stearate	2.00

Manufacturing Directions

1. Granulate a mixture of items 1 to 3 with item 4, pass through a 0.8-mm sieve, dry, add items 5 and 6, and press with low-compression force.
2. Compress into 504-mg tablets (512 mg if using dicalcium phosphate), using 12-mm biplanar punches.

Sumatriptan Succinate Fast-Melt Tablets

Manufacturing Directions

1. Mix sumatriptan succinate 15%, sodium bicarbonate 27%, citric acid anhydrous 26%, microcrystalline cellulose 11%, anhydrous lactose 9%, xylitol 10%, and sucrose stearate 2%.
2. The above ingredients are dried at elevated temperatures to significantly reduce the moisture content of the materials.
3. Blend for approximately 10 minutes and extruded in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) and to form granules containing the effervescent ingredients.
4. Mix SS-EGF (30–60 mesh) 50%, microcrystalline cellulose 31%, Mannitol 10%, L-HPC LH-11 5%, aspartame 3%, redberry flavor 0.3%, natural orange powder 0.1%, magnesium stearate 0.5%, and fumed silicon dioxide 0.1%.
5. Screen and blend for 5 minutes prior to compression.
6. Surnatriptan succinate tablets are then compressed to a hardness of approximately 1 to 5 kPa (depending upon the dose of the active) and tablets disintegrate in water in approximately 15 to 35 seconds.

Sumatriptan Succinate Tablets (25 mg/50 mg) Imitrex

Each Imitrex tablet for oral administration contains 35 or 70 mg of sumatriptan succinate equivalent to 25 or 50 mg of sumatriptan, respectively. Each tablet also contains the inactive ingredients croscarmellose sodium, lactose, magnesium stearate, microcrystalline cellulose, and titanium dioxide dye.

Sumatriptan Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
140.00	1	Sumatriptan, use*	140.00
154.00	2	Lactose monohydrate	154.00
17.00	3	Microcrystalline cellulose	17.00
3.30	4	Sodium croscarmellose	3.30
1.70	5	Magnesium stearate	1.70
–	6	Water, purified, ca	12.50 mL

*For 25 mg strength, use 35 mg of sumatriptan succinate.

Manufacturing Directions

1. Sift items 1 and 2 through a 0.6-mm mesh sieve screen into a fluid-bed granulator.
2. Granulate by spraying item 6 with an inlet temperature of 75°C; allow granules to dry.
3. Pass granules through a granulator fitted with a 0.8-mm mesh screen.
4. Transfer granules to a blender, add item 5, and mix for 5 minutes.
5. Compress about 320 mg in a suitable punch.

Tamoxifen Tablets (10 mg/20 mg), Nolvadex

Nolvadex tablets are available as follows. *10-mg tablets:* each 10-mg tablet contains 15.2 mg of tamoxifen citrate, which is equivalent to 10 mg of tamoxifen; *20-mg tablets:* each 20-mg tablet contains 30.4 mg of tamoxifen citrate, which is equivalent to 20 mg of tamoxifen. The inactive ingredients are carboxymethyl-cellulose calcium, magnesium stearate, mannitol, and starch.

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Tamoxifen, use tamoxifen citrate	15.30
114.50	2	Lactose monohydrate	114.50
38.00	3	Starch (maize)	38.00
3.50	4	PVP K30	3.50
0.75	5	Magnesium stearate	0.75
3.00	6	Ac-Di-Sol	3.00
–	7	Water, purified, ca	30 mL

Manufacturing Directions

1. Charge items 1 to 3 after sifting them through a 500-μm sieve in a suitable mixer. Mix this for 5 minutes at low speed.
2. In a separate vessel, add and dissolve item 4 in item 7 at a slow speed.
3. Add step 2 into step 1, and knead and mix for 5 minutes, and then again, long enough to achieve a suitable wet mass.
4. Dry the wet mass on trays at 55°C for 5 hours to an LOD of not more than 1 to 1.5%. If required, dry for another hour.
5. Pass the dried granules through a 1.25-mm sieve, and transfer to a blender.
6. Add items 5 and 6 (sifted through a 500-μm sieve) to step 5, and blend for 1 minute.
7. Compress into 175-mg tablets, using 8-mm round, plain concave punches. For 20-mg tablet, use appropriate fill weight in 10-mm punches.

Tamsulosin Hydrochloride Buccal Tablets

Directions

1. 80 g of tamsulosin hydrochloride and 80 g of hydroxypropylmethyl cellulose (TC5E) are dissolved in a mixture of 304 g purified water and 2736 g methanol.
2. 4000 g of Celphere 102 (mean particle diameter of approximately 127 μm, particle diameter of approximately 50 to approximately 150 μm) is introduced to a fluidized bed granulator and coated with this solution by the side spraying method (spraying liquid volume 100 g/min, spraying air pressure 4 kg/cm^2, product temperature 40°C, inlet temperature 80°C) to obtain tamsulosin hydrochloride particles.
3. Separately, 533 g of ethyl cellulose and 187 g of hydroxypropylmethyl cellulose (TC5E) are dissolved in a mixture of 698 g purified water and 22582 g methanol.
4. Tamsulosin hydrochloride (4000 g) particles are introduced to a fluidized bed granulator and coated with this solution by side spraying (spraying liquid volume of 40 g/min, spraying air pressure of 4 kg/cm^2, product temperature of 50°C, inlet temperature of 60°C) to obtain sustained-release fine particles.
5. These sustained-release fine particles (4000 g) are introduced to a fluidized bed granulator and coated with a mixture of 2000 g of Aquacoat, 4000 g of Eudragit L30D55, 667 g of Eudragit NE30D, and 6667 g of purified water (spraying liquid volume of 40 g/min, spraying air pressure of 4 kg/cm^2, product temperature of 40°C, inlet temperature of 60°C) to obtain enteric sustained-release fine particles.
6. Then 368 g of these enteric sustained-release fine particles, 2560 g mannitol, and 640 g lactose are granulated (spraying liquid volume 200 g/min, spraying air pressure of 1.5 kg/cm^2, product temperature of 29°C, inlet temperature of 80°C, spraying cycle of 10 seconds spraying to 30 seconds drying) with an aqueous 40% w/w solution containing 400 g maltose in a fluidized bed granulator to obtain the final composition.
7. After further mixing 32 g calcium stearate with the composition that is obtained, 200 mg tablets containing 0.2 mg tamsulosin hydrochloride per tablet are made under a tabletting pressure of 100 kg/punch and an initial hardness of 1.0 kPa using a rotary tabletting machine.
8. Next, these tablets are kept for 18 hours while heating and humidifying at 25°C/75% RH using a thermostatic chamber at constant humidity.
9. Then they are dried for 3 hours at 30°C and 40% RH. The tablets that are obtained showed a hardness of 5.9 kPa ($n = 5$), friability of 0.8% (100 rounds) and disintegration time in the buccal cavity of 20 seconds.

Tannin–Crospovidone Complex Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
55.00	1	Tannic acid	55.00
230.00	2	Water	230.00
230.00	3	Kollidon® CL	230.00
33.00	4	Avicel™ PH101	33.00
2.60	5	Talc	2.60
0.30	6	Aerosil® 200	0.30
0.30	7	Calcium arachinate	0.30

Manufacturing Directions

1. Prepare solution of items 1 and 2, suspend item 3, and filter the formed insoluble tannin–crospovidone complex.
2. Wash with water until the water is clear, pass the solids through a 0.8-mm sieve, and dry.
3. Add items 4 to 7, and press with low compressive force.
4. Compress into 323-mg tablets, using 12-mm biplanar punches.

Tegaserod Maleate Tablets 2 mg

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.77	1	Tegaserod maleate equivalent to Tegaserod 2 mg	2.77
87.73	2	Lactose Spray Dried	87.73
3.00	3	Crospovidone	3.00
5.00	4	Poloxamer	5.00
0.50	5	Hypromellose	0.50
1.00	6	Glyceryl behenate	1.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass item 1, item 4 and item 5 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 5% (=2.2 g) powder from step 1 to step 3 and mix well.
5. Add 15% (=6.6 g) powder from step 1 to step 4 and mix well.
6. Transfer step 5 into step 2.
7. Pass item 3 through 0.5-mm sieve and add to step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 6 through 0.250-mm sieve and charge in step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).

Tegaserod Maleate Tablets 6 mg

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
8.31	1	Tegaserod maleate equivalent to Tegaserod 2 mg	8.31
127.44	2	Lactose spray dried	127.44
4.50	3	Crospovidone	4.50
7.50	4	Poloxamer 188	7.50
0.75	5	Hypromellose	0.75
1.50	6	Glyceryl behenate	1.50

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, and 5 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 10% (=6.3 g) powder from step 1 to step 3 and mix well.
5. Transfer step 4 into step 2.
6. Pass item 3 through 0.5-mm sieve and add to step 2.
7. Transfer balance quantity of step 1 into step 2.
8. Mix step 2 for 20 minutes using tumbler.
9. Pass item 6 through 0.250-mm sieve and add to step 8.
10. Mix step 9 for 2 minutes.
11. Compress into 150-mg tablets, using a suitable punch (5.5 mm × 7.0 mm, modified oval).

Temafloxacin Hydrochloride Tablets (200 mg/300 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Temafloxacin hydrochloride, excess 10%	220.00
112.50	2	Lactose monohydrate	112.50
40.00	3	Sodium starch glycolate	40.00
12.50	4	Hydroxypropyl cellulose	12.50
100.00	5	Cellulose microcrystalline	100.00
5.00	6	Magnesium stearate	5.00
10.00	7	Talc	10.00
QS	8	Water, purified, ca	186.00 mL

Manufacturing Directions

1. Granulation
   a. Dissolve hydroxypropyl cellulose in two-thirds volume of purified water (item 8).
   b. Pass lactose, temafloxacin hydrochloride, and the sodium starch glycolate through an approximately 765-μm aperture screen, if necessary, and charge into a mixer and mix. Add hydroxypropyl cellulose solution from step 1a, mix, and granulate. Add more water, if needed, until a granule mass is formed.
   c. Pass the wet mass through an approximate 4.8-mm aperture screen, and dry in a dryer at 45°C to 52°C to an LOD of not more than 1.5%. Pass the dried granules through an approximately 1.18-mm screen. If necessary, screen the microcrystalline cellulose (and crospovidone for 400- and 600-mg tablets) through an approximate 500-μm aperture screen. Add to the dried granules, and blend for 10 minutes.
   d. Pass magnesium stearate and talc through a 500-μm aperture screen. Add to the bulk from step 1c, and blend for 5 to 10 minutes.
   e. Compress as follows: 200 mg, 7.32 × 15.19 mm; 500 mg and 300 mg, 8.5 × 17.5 mm; 750 mg.
   f. Coat the compressed tablets by spraying with a color coat and then apply gloss. (See Appendix.)

Tenoxicam Tablets (20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
20.00	1	Tenoxicam	20.00
90.00	2	Lactose monohydrate	90.00
84.00	3	Maize starch	84.00
4.00	4	Talc	4.00
2.00	5	Magnesium stearate	2.00
–	6	Water, purified, ca	50.00 mL

Manufacturing Directions

1. Charge item 6 and item 3 (20%) in a mixer heated to 40°C, and mix for 10 minutes. Heat at 70°C to 80°C until a homogenous paste is formed. Cool to 50°C.
2. In a separate vessel, charge item 2, the balance of item 3, and item 1. Mix well.
3. Add the paste from step 1 into step 2, and mix for 15 minutes until a loose, moist mass is obtained.
4. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
5. Spread over paper-lined trays, and dry at 45°C overnight (the relative humidity over the granules should be 20–35%).
6. Pass the dried granules through a 1.5-mm sieve granulator.
7. Transfer the granules to a tumbler, add item 4 and then item 5, and mix for 20 minutes.
8. Compress into 200-mg tablets, using a suitable punch (11.5 × 6.0 mm).

Terazosin Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Terazosin hydrochloride	1.10
98.00	2	Ludipress	98.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix intensively, and press with low-compression force (10 kN).
2. Compress 98.1 mg for 1-mg and 97.6 mg for 5-mg strength, using 6-mm biplanar punches.
3. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.
4. For 5-mg strength, adjust with item 2.

Terazosin Tablets (1 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
128.560	1	Lactose	128.530
1.000	2	Terazosin, use terazosin monohydrate	1.187
7.500	3	Starch (maize)	7.500
6.000	4	Starch (maize)	6.000
–	5	Water, purified, ca	25 mL
6.000	6	Talc	6.000
1.123	7	Magnesium stearate	1.120

Manufacturing Directions

1. Granulation
   a. Mix the terazosin and a portion of lactose. Mill the mixture through a 425-μm (or similar) aperture screen using a comminuting mill, with impact forward, at high speed.
   b. If necessary, mill the remainder of lactose.
   c. Add the powders (step 1a and 1b) and starch (item 3) to the mixer. and blend for 20 minutes.
   d. Disperse starch (item 4) in purified water, and heat to make a paste.
   e. Add starch paste to powder blend, and blend for 5 to 7 minutes, adding extra purified water. Record any additional volume.
   f. If necessary, pass the granule through a 4.76mm aperture on an oscillating granulator or a 12.7-mm aperture screen on a comminuting mill, with knives forward, at slow speed.
   g. Dry at 49°C to an LOD of not more than 2% (105°C for 1 hour).
   h. Pass granules through a 1.18-mm aperture screen on an oscillating granulator.
   i. Add one-half of the granules to a suitable blender.
   j. Blend the magnesium stearate and talc with a portion of the granules. Pass through a 1.18-mm aperture screen, and add to the bulk.
   k. Add the remainder of granule, and blend for 10 minutes. 2. Compression: Use 7.14-mm or other similar size punches. For 2-mg, 5-mg, and 10-mg strengths, adjust with item 1 and any dye added to differentiate tablets.

Terbinafine Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Terbinafine (used as terbinafine hydrochloride)	250.00
10.00	2	Hypromellose (hydroxy propyl methyl cellulose)	10.00
105.00	3	Avicel PH 102 (microcrystalline cellulose)	105.00
2.50	4	Ac-Di-Sol (croscarmellose sodium)	2.50
1.50	5	Magnesium stearate	1.50
QS	6	Purified water	QS

Manufacturing Directions

1. Sift terbinafine hydrochloride and Avicel through a 250-μm sieve.
2. Dissolve hydroxy propyl methyl cellulose in purified water to make a granulating solution.
3. Knead the powder mix in step 1 with the granulation solution to get the desired wet mass. Pass the mass through a #8 sieve onto drying trays.
4. Dry granules at 60°C for 12 hours to an LOD of not more than 2%.
5. Pass the granules through #16 mesh into the blending vessel.
6. Pass croscarmellose sodium and magnesium stearate through a 250-μm sieve, and add to step 5. Blend for 3 minutes.
7. Compress into 400-mg tablets, using a suitable punch.

Terfenadine Chewable Tablets

Manufacturing Directions

1. Terfenadine, 10.00% (micronizer or powdered); PVP K-90, 3.00%; block co-polymer poloxomer 188, 1.00%; Maltodextrin QD M500 fine, 10.00%; Sorbitol INSTANT, 30.00%; aspartame, 0.50%; Mannitol or xylitol, 44.50%; magnesium stearate, 0.50%; spray-dried flavor, 0.50%.
2. Terfenadine, block-copolymer, aspartame, spray-dried flavor, and PVP are premixed in a cube blender for a time period of 10 minutes.
3. The sorbitol INSTANT is added, and the resulting admixture is mixed for another 10-minute time period.
4. The maltodextrin and mannitol or xylitol are added, and the resulting composition is mixed for a further 10 minutes. The magnesium stearate lubricant is then added and mixed into the composition for a further 3 minutes.
5. The lubricated admixture is then made into tablets by compression to a hardness of 9 to 12 kPa (12–18 Strong Cobb units) using 3/8-in. standard concave punches or an appropriate punch/die set.

Terfenadine Tablets (60 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Terfenadine	60.00
235.00	2	Ludipress	235.00
6.00	3	Kollidon CL	6.00
1.00	4	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with very low-compressive force.
2. Compress into 301-mg tablets, using 8-mm biplanar punches.

Testosterone and Norethindrone Buccal Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Testosterone	50.00
35.00	2	Norethindrone	35.00
14.80	3	Polyethylene oxide	14.80
0.20	4	Magnesium stearate	0.20

Manufacturing Directions

1. All components (i.e., testosterone, norethindrone, polyethylene oxide and magnesium stearate, as set forth in the above table) are thoroughly mixed prior to tablet formation using aqueous fluid-bed granulation to provide a homogeneous mixture of active agents and excipients.
2. The individual dosage units are then made by applying approximately 10 to 15 mg of the mixture into the punch die of a tablet press, and compressing the mixed components using a pressure in the range of approximately 500 to 2000 psi. Tablets having a diameter of approximately 4 mm and a height of 1 mm are prepared. The tablet is removed from the punch die and the weight and dimensions of the tablet are measured.

Testosterone, Estradiol, and Progesterone Buccal Tablet

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.50	1	Testosterone	1.50
0.30	2	Estradiol	0.30
4.70	3	Progesterone	4.70
2.48	4	Polyethylene oxide (Polyox WSR-303)	2.48
1.00	5	Carbopol	1.00
0.02	6	Magnesium Stearate	0.02

Manufacturing Directions

1. All components (i.e., testosterone, estradiol, polyethylene oxide, carbomer, and magnesium stearate) are thoroughly mixed prior to tablet formation using aqueous fluid-bed granulation to provide a homogeneous mixture of active agents and excipients.
2. The individual dosage units are then made by applying 10 mg of the mixture into the punch die of the tablet press, and compressing the mixed components using a pressure in the range of approximately 500 to 2000 psi. Tablets having a diameter of approximately 4 mm and a height of 1 mm are prepared.

Tetracycline Tablets (125 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
125.00	1	Tetracycline hydrochloride	125.00
100.00	2	Ludipress	100.00
42.00	3	Microcrystalline cellulose (Avicel PH 101)	42.00
3.00	4	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press to tablets with very low-compression force.
2. Compress into 278-mg tablets, using 8-mm biplanar punches.

Tetracycline Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Tetracycline hydrochloride	250.00
175.00	2	Lactose monohydrate	175.00
15.00	3	Kollidon 30	15.00
25.00	4	Kollidon CL	25.00
28.00	5	Talc	28.00
3.50	6	Aerosil 200	3.50
3.50	7	Calcium arachinate	3.50

Manufacturing Directions

1. Pass items 1 to 4 through a 0.5-mm sieve, add the mixture of items 6 and 7, and press with low-compression force.
2. Compress into 505-mg tablets, using 12-mm biplanar punches.

Tetrazepam Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Tetrazepam	50.00
113.00	2	Microcrystalline cellulose (Avicel PH 101)	113.00
30.00	3	Starch 1500 (Colorcon)	30.00
5.00	4	Kollidon VA 64	5.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Pass the components through a 0.5-mm sieve, and press with low-compression force.
2. Compress into 208-mg tablets, using 8-mm biplanar punches.

Theophylline and Ephedrine Tablets (130 mg/15 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
130.00	1	Theophylline (0.1–0.4 mm)	130.00
15.00	2	Ephedrine hydrochloride	15.00
150.00	3	Ludipress	150.00
2.00	4	Aerosil 200	2.00
2.00	5	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with very low-compression force.
2. Compress into 302-mg tablets, using 8-mm biplanar punches.

Theophylline Sustained-Release Tablets (500 mg) DC

Formulation: Theophylline, granular type (BASF), 500 g; Kollidon SR, 125 g; Ludipress LCE, 225 g; magnesium stearate, 3 g.

Manufacturing Directions

Mix all components, pass through a sieve of 0.8 mm, and press with medium-compression force at 853 mg.

Theophylline Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Theophylline (0.1–0.4 mm)	100.00
147.00	2	Ludipress	147.00
3.00	3	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with low-compression force.
2. Compress into 247-mg tablets, using 8-mm biplanar punches.

Theophylline Tablets

Manufacturing Directions

1. Theophylline, 200 mg; crystalline PVA homopolymer, 200 mg; magnesium stearate, 5 mg. Total = 405 mg.
2. Mix in a geometric dilution.

Compress on 2.7×10^6 kg/m^2 pressure with 3/8-in. (9.53 mm) diameter standard concave tooling to form tablets with average hardness of 12SCU.

Theophylline Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Theophylline	100.00
70.62	2	Starch 1500	70.62
72.50	3	Microcrystalline Cellulose (50 μm)	72.50
5.00	4	Stearic Acid	5.00
1.25	5	Fumed Silica	1.25
0.63	6	Magnesium Stearate	0.63

Manufacturing Directions

1. All ingredients except magnesium stearate are blended for 10 minutes in a twin-shell blender.
2. Magnesium stearate is added and blended for an additional 5 minutes.
3. Tablets are compressed at 250 mg.

Theophylline Tablets (100 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Theophylline	100.00
137.10	2	Lactose anhydrous	137.10
60.00	3	Carbopol® 971P	60.00
1.50	4	Cab-o-Sil®	1.50
1.50	5	Magnesium stearate	1.50

Manufacturing Directions

1. Pass all items through a 250-μm mesh, and charge items 1 to 3 in a suitable blender. (item 3 can be used granulated in a fluid-bed.)
2. Add items 4 and 5, and blend for 3 minutes.
3. Compress into 300-mg tablets, using a suitable punch.

Theophylline Tablets CR (200 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Theophylline powder	200.00
2.00	2	Sodium lauryl sulfate	2.00
2.00	3	Calcium stearate	2.00
35.00	4	Ethyl cellulose	35.00
3.60	5	Cetanol	3.60
1.60	6	Sodium lauryl sulfate	1.60
148.00	7	Triethyl citrate	148.00
–	8	Water, purified	QS

Manufacturing Directions

1. Charge items 1 to 3 in a suitable mixer, and mix for 10 minutes.
2. Granulate step 1 by passing the items through a compactor or dry granulator.
3. Pass the compact material from step 2 through #16 to #32 mesh.
4. In a separate vessel, add items 4 to 7, and make a solution with item 8 to 200 g.
5. Transfer step 3 into a fluid-bed granulator, and apply the solution in step 4 to coat the granules.
6. Compress.

Theophylline Tablets (100 mg)

Formulation: Theophylline granules 0.1/0.4 mm (BASF), 100 g; Ludipress, 147 g; magnesium stearate, 3 g.

Manufacturing Directions

Mix all components, pass through a sieve, and press with low-compression force at 247 mg.

Thiamine and Caffeine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Thiamine hydrochloride	500.00
100.00	2	Caffeine	100.00
30.00	3	Cornstarch	30.00
20.00	4	Kollidon® VA 64	20.00
15.00	5	Kollidon® VA 64	15.00
QS	6	Ethanol (96%)	QS
35.00	7	PEG-6000 (powder)	35.00

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with solution of item 5 and 6, dry, sieve, mix with item 7, and press with low compressive force.
2. Compress into 698-mg tablets, using 16-mm biplanar punches.

Thiamine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine HCl with excess	110.00
43.50	2	Lactose monohydrate	43.50
4.00	3	Crospovidone (Kollidon® CL)	4.00
5.50	4	Povidone (PVP K-90)	5.50
5.50	5	Crospovidone (Kollidon® CL)	5.50
32.00	6	Microcrystalline cellulose (Avicel™ PH112)	32.00
5.60	7	Talc (fine powder)	5.60
3.70	8	Glyceryl behenate (glyceryl monostearate)	3.70
0.20	9	Magnesium stearate	0.20
–	10	Alcohol (ethanol, 95%)	50.67

Manufacturing Directions

1. Sift items 1, 2, and 3 through a stainless steel 630-μm sieve.
2. Load into mixer.
3. Mix for 5 minutes at high speed.
4. Dissolve item 4 in item 10 under slow stirring by stirrer.
5. Add the binding solution while mixing at high speed over a period of 2 minutes. Scrape sides and blades.
6. Mix and chop at high speed for 2 minutes.
7. Check the end point of granulation.
8. If required, add additional item 10 to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Dry wet granules in oven at 55°C for 8 hours.
9. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
10. Check the LOD (limit: 1.0–1.5%).
11. If required, dry at 55°C for an additional hour.
12. Check the LOD again.
13. Grind the dried granules through a 1.25-mm sieve with the granulator set at medium speed.
14. Collect in stainless steel drums.
15. Load the granules into blender.
16. Sift items 5 and 6 through a 500-μm sieve, and add to blender.
17. Mix for 2 minutes (do not overmix).
18. Sift items 8 and 9 through a 500-μm sieve.
19. Add 1.33 to 2.67 g of granules.
20. Mix in a polyethylene bag for 1 minute.
21. Add to blender.
22. Blend for 1 minute.
23. Check temperature and humidity before start of compression (limit: temperature should not exceed 25°C; relative humidity, 45–50%).
24. Compress using 8-mm, round, beveled, concave punches.

Thiamine Hydrochloride Tablets, Sugar-Coated

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine hydrochloride monohydrate (with excess)	110.00
110.00	2	Lactose	110.00
5.00	3	Luviskol® K-98	5.00
1.00	4	Magnesium stearate	1.00
40.00	5	Ethyl alcohol (denatured)	40.00
251.44	6	Sugar (crystalline)	251.44
1.40	7	Sugar powder	1.40
14.50	8	Maize starch	14.50
14.81	9	Talcum	14.81
21.00	10	Copolymer lacquer	21.00
0.40	11	Paraffin (solid)	0.40
0.16	12	Gum acacia	0.16
0.228	13	Ethyl alcohol (denatured)	0.228
0.01	14	Paraffin (liquid)	0.01
QS	15	Purified water	QS

Manufacturing Directions

1. In a suitable stainless steel vessel, add denatured ethyl alcohol and Luviskol; mix until homogeneous mixture is obtained. Set aside.
2. Pass lactose through a #2-mesh sieve, add thiamine, and mix for 10 minutes in an appropriate mixer.
3. Slowly add to this mixture the solution made earlier, and stir until slightly lumpy mass is obtained.
4. If required, add ethyl alcohol to the mixture.
5. Pass the wet mass through an oscillating granulator with a 7.00-mm perforated sieve.
6. Spread the granules over paper-lined trays, and dry at 40°C for 5 hours in a drying oven.
7. The relative humidity of the granules should be 15% to 25%.
8. Pass magnesium stearate and talcum through a 1-mm hand sieve.
9. Compress on a rotary tablet machine at about 4 to 5 tons of pressure; the weight of each tablet should be about 230 mg.
10. In a suitable container, add purified water and acacia gum; pass the resulting solution through a 0.8-mm sieve.
11. Charge the compressed tablets into a coating pan and apply the copolymer lacquer in ten portions; after the last application, apply neutral spray (crystalline sugar in demineralized water).
12. Dry the insulated tablets in a drying oven overnight at 45°C (minimum 14 hours); the tablet weight should be around 236 mg each.
13. In an electric, jacketed kettle, put demineralized water, crystalline sugar, maize starch, and talcum; mix by stirring until homogeneous.
14. Pass through a sieve of mesh size 0.8 mm (pH, 6.0–8.0; density, 1.335–1.356).
15. Coat the tablets to 400 mg weight using the coating solution and a sugar-coating pan; set pans at slow speed, open air inlets, and set air inflow at 80°C and maximum contact temperature set at 42°C.
16. Roll tablets to reach this temperature.
17. Turn pan to fast speed, close the inlet air flap, and make first application of syrup.
18. When all tablets are wet and distribution of syrup is uniform, open the air inlet flap and allow 80°C air to blow (tablet temperature falls 1–2°C for a short time and then slowly rises to 42°C).
19. The next application of the syrup cycle begins.
20. Coat the tablets with color solution as described above to 495-mg weight.
21. Set the air inflow temperature at 25°C, and reduce the size of application with the falling temperature, whereby tablets are evenly and lightly moistened after each application; the temperature drops from 42°C to 32°C.
22. Turn the coating pans slowly during the drying phase; for the last three applications, keep the pan lids closed, as well as the air intake and outflow during this phase.
23. Drying only with outlet air may be extended for the last three applications up to 10 to 15 minutes.
24. Immediately after the last application of syrup has dried slightly, begin the polishing step.
25. The polishing paste is prepared in a suitable boiling vessel by adding stock gum solution, crystalline sugar, and demineralized water.
26. Boil until temperature reaches 106°C with stirring.
27. In a steam kettle, melt solid and liquid paraffin, and pour melted paraffins into the mixture of gum; make up the weight with demineralized water.
28. Polishing paste ready for use contains 0.75 kg of paste and 0.113 kg of ethyl alcohol.
29. Tablet temperature is 28°C to 32°C.
30. Shut off the inlet flaps and outlet flaps, set the pans at the fast speed, and add polishing paste (about 0.3% of tablet weight).
31. Close the pans with inner lids and allow them to rotate at fast speed for 90 seconds for even distribution.
32. Remove the inner lid of the pan, and set it on slow speed.
33. Open the outlet air for 3 minutes, blow the inlet air at 40°C for 6 to 8 minutes until a good sheen appears.
34. Set the pans on automatic system for overnight, with intermission time of 5 minutes off and 10 seconds on.

Thiamine, Pyridoxine, and Cyanocobalamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
110.00	1	Thiamine mononitrate	110.00
210.00	2	Pyridoxine hydrochloride	210.00
76.82	3	Lactose monohydrate	76.82
10.00	4	Crospovidone (Kollidon® CL)	10.00
18.50	5	Povidone (PVP K-90)	18.50
0.30	6	Cyanocobalamin	0.30
85.00	7	Microcrystalline cellulose (Avicel™ PH102)	85.00
14.00	8	Crospovidone (Kollidon® CL)	14.00
10.00	9	Glyceryl behenate (glyceryl monostearate)	10.00
0.49	10	Magnesium stearate	0.49
15.00	11	Talc (fine powder)	15.00
–	12	Alcohol (ethanol, 95%)	88.90

Manufacturing Directions

1. Dissolve item 5 in item 12 by using a stirrer to make a clear solution.
2. Dissolve item 6 carefully in the solution.
3. Sift items 1 to 4 through a 630-μm sieve.
4. Load the material into a mixer.
5. Mix and chop at high speed for 5 minutes.
6. Add binding solution from previous step to the dry powder in the mixer while mixing and chopping at high speed for 2 minutes.
7. Check for satisfactory wet mass.
8. Add additional item 12, if required, to obtain a satisfactory wet mass.
9. Do not allow big lumps.
10. Record the additional quantity of ethanol 95%.
11. Spread the granules onto stainless steel trays to a thickness of 1/4th of the tray thickness, and load the trays onto a trolley.
12. Load the trolley into an oven.
13. Keep the door open, switch on the oven with air circulation, heater turned off for 2 hours.
14. Dry the granules at 55°C for 12 hours.
15. Check the LOD of dried granules (limit: NMT 0.7%).
16. Grind the dried granules through a 1.25-mm sieve using a granulator.
17. Collect in a stainless steel drum.
18. Load into the blender.
19. Sift items 7, 8, and 9 through a 500-μm sieve.
20. Collect in stainless steel container.
21. Load the sieved powder into the blender.
22. Blend for 3 minutes.
23. Sift items 11 and 10 through a 500-μm sieve.
24. Collect in a polyethylene bag.
25. Add 4.44 to 6.67 g of granules from earlier step, and mix manually for 1 minute.
26. Add this mixture to the blender, and mix for 1 minute.
27. Compress the granules using a rotary tabletting machine.
28. Compress into 550-mg tablets, using round, binconvex punches at 9 to 16 kp.
29. Coat tablets using an HPMC coating (see Appendix).

Thiamine, Pyridoxine, and Cyanocobalamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine mononitrate (powder)	115.00
50.00	2	Pyridoxine hydrochloride	50.00
9.75	3	Anhydrous Citric Acid (powder)	9.75
20.10	4	Monohydrate lactose (powder, regular)	20.10
1.67	5	Saccharin sodium	1.67
0.24	6	Dye	0.24
0.009	7	Dye	0.009
0.02	8	Dye	0.02
2.00	9	Cornstarch	2.00
QS	10	Purified water	18.00 mL
50.00 μg	11	Vitamin B12; use vitamin B12 oral powder cobalamin conc	62.50
12.50	13	Monohydrate lactose (powder, regular)	12.50
1.50	14	Oil orange terpeneless	1.50
3.50	15	Magnesium stearate	3.50
1.50	16	Talc (powder)	1.50
17.70	17	Corn starch, Light Coral Red 6 LA	17.70

Manufacturing Directions

1. Pass thiamine mononitrate, pyridoxine HCl, citric acid, lactose (item 4), and saccharin sodium through a #30-mesh (595-μm or similar) screen.
2. Charge into mixer, and dry mix.
3. Dissolve the dyes in purified water.
4. Add the starch (item 9) to this dye solution with stirring.
5. Heat and continue stirring until a thick paste is formed.
6. Cool to room temperature before using.
7. (*Note*: Use 7.5 g of colored starch paste for the vitamin B1 and B6 blend and 12.5 g of colored starch paste for the vitamin B12 blend.) Add 7.5 g of colored starch paste to powder blend, and mix until mass is formed.
8. Pass through a #6-mesh (3.36-mm or similar) screen, and air dry for 3 to 4 hours.
9. Screen vitamin B12 oral powder and lactose (item 12) through a #30-mesh (595-μm or similar) screen.
10. Charge into mixer, and dry mix.
11. Add 12.5 g colored starch paste to powder blend, and mix until mass is formed.
12. Pass through #6-mesh (3.36-mm or similar) screen, and air dry for 3 to 4 hours.
13. Dry granulations from the two steps separately at 49°C overnight or until LOD is less than 1%.
14. Mill the two dried granulations through a #16-mesh (1.2-mm or similar) screen (knives forward, medium speed), and combine.
15. Sift a small quantity of granulation from the steps above over a #30-mesh (595-μm or similar) screen, and add the orange oil to the fines.
16. Add magnesium stearate, talc powder, and Light Coral Red starch to mixture, and pass through a #30-mesh (595-μm or similar) screen.
17. Charge base granulation and lubricants into a blender, and blend thoroughly.
18. Compress using 11/32-in. concave punches.

Thiamine, Pyridoxine, and Cyanocobalamin Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine hydrochloride	100.00
10.00	2	Pyridoxine hydrochloride	10.00
0.10	3	Cyanocobalamin (gelatin coated, 1%)	10.00
277.00	4	Ludipress®	277.00
3.00	5	Magnesium stearate	3.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with low compressive force.
2. Compress into 394-mg tablets, using 12-mm biplanar punches.

Thiamine, Pyridoxine, and Cyanocobalamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine mononitrate	100.00
200.00	2	Pyridoxine hydrochloride	200.00
0.10	3	Cyanocobalamin (gelatin coated, 1%)	10.00
250.00	4	Ludipress®	250.00
45.00	5	PEG-6000 (powder)	45.00
5.00	6	Aerosil® 200	5.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 609-mg tablets, using 12-mm biplanar punches.

Thiamine, Pyridoxine, and Cyanocobalamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.00	1	Thiamine mononitrate	250.00
250.00	2	Pyridoxine hydrochloride	250.00
75.00	3	Lactose monohydrate	75.00
25.00	4	Kollidon® 30	25.00
QS	5	Isopropanol	QS
1.00	6	Cyanocobalamin (gelatin coated, 1%)	100.00
25.00	7	Kollidon® CL	25.00
2.00	8	Magnesium stearate	2.00
2.00	9	Talc	5.00

Manufacturing Directions

1. Granulate mixture items 1 to 3 with solution of items 4 and 5, dry, pass through a 0.8-mm sieve, mix with items 6 to 9, and press with low compressive force, applying a vibrating hopper.
2. Compress into 730-mg tablets, using 12-mm biplanar punches.

Thiamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Thiamine hydrochloride or thiamine mononitrate	50.00
293.00	2	Ludipress®	293.00
5.00	3	Magnesium stearate	5.00
2.00	4	Aerosil® 200	2.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with medium compressive force.
2. Compress 357 mg, if hydrochloride salt is used, or 347 mg, if mononitrate salt is used, with 12-mm biplanar punches.

Thiamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Thiamine hydrochloride or thiamine mononitrate	50.00
150.00	2	Lactose monohydrate	150.00
150.00	3	Avicel™ PH101	150.00
15.00	4	Kollidon® CL	15.00
2.00	5	Aerosil® 200	2.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with high compressive force.
2. Compress 344 mg, if hydrochloride salt is used, or 373 mg, if mononitrate salt is used, with 12-mm biplanar punches.

Thiamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine hydrochloride or thiamine mononitrate	110.00 (or 100.00)
190.00	2	Ludipress®	190.00
100.00	3	Lactose monohydrate	100.00
100.00	4	Avicel™ PH 101	100.00
9.00	5	Kollidon® CL	9.00
3.00	6	Aerosil® 200	3.00
2.00	7	Magnesium stearate	2.00

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with medium compressive force.
2. Compress 302 mg, if hydrochloride salt is used, or 320 mg, if mononitrate salt is used, with 8-mm biplanar punches.

Thiamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Thiamine hydrochloride	100.00
200.00	2	Lactose monohydrate	200.00
10.00	3	Kollidon® 30	10.00
60.00	4	Isopropanol	60.00
10.00	5	Kollidon® CL	10.00
2.00	6	Magnesium stearate	2.00
1.00	7	Aerosil® 200	1.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, dry, and sieve through a 0.8-mm screen, mix with items 5 to 7, and press to tablets.
2. Compress into 330-mg tablets, using 8-mm biplanar punches.

Thiamine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Thiamine mononitrate	300.00
100.00	2	Dicalcium phosphate (Di-Tab)	100.00
15.00	3	Kollidon® 30	15.00
QS	4	Isopropanol	~50.00
10.00	5	Kollidon® CL	10.00
4.00	6	Magnesium stearate	4.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 2 and 3, dry, and sieve through a 0.8-mm screen.
2. Mix with items 5 and 6, and compress into 430-mg tablets, using 12-mm biplanar punches.

Tibolone Tablets (0.3 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.30	1	Tibolone (Org GD 14)	0.30
1.95	2	Hydroxypropyl cellulose	1.95
32.50	3	Starch (maize)	32.50
0.32	4	Magnesium stearate	0.32
29.93	5	Lactose anhydrous	29.33
–	6	Water, purified	QS

Manufacturing Directions

1. Charge items 3 and 5 in a suitable blender, and mix for 1 minute after passing them through a 250-μm sieve.
2. In a separate vessel, charge items 1 and 2; add a sufficient amount of item 6 to make a uniform solution.
3. Add step 2 into step 1 gradually, and granulate for 2 minutes.
4. Pass the wet mass through #8 mesh, and dry at 40°C for 4 hours.
5. Screen the granules through a 710-μm sieve into a blender.
6. Add item 4, and blend for 1 minute.
7. Compress into 65-mg tablets, using a suitable punch.

Ticlopidine Hydrochloride Tablets (250 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
250.0	1	Ticlopidine HCl	250.0
72.0	2	Starch, maize	72.0
68.8	3	Microcrystalline cellulose (Avicel)	68.8
6.0	4	Polyvinylpyrrolidone (PVP K30)	6.0
1.2	5	Colloidal silicon dioxide (Aerosil 200)	1.2
2.0	6	Magnesium stearate	2.0
–	7	Water, purified	QS

Manufacturing Directions

1. Blend ticlopidine HCl, maize starch, Avicel, and PVP K-30 after passing through a 350-μm sieve.
2. Charge item 3 in a separate vessel, and prepare a paste using item 7.
3. Add step 2 into step 1. Knead to make a suitable wet mass.
4. Pass the wet mass through #8 mesh onto drying trays. Dry at 60°C for 12 hours. The LOD should not be more than 2.5%.
5. Pass the dried granules through #16 mesh into a blending vessel.
6. Blend with Avicel, Aerosil, and magnesium stearate previously sieved through a 500-μm sieve.
7. Compress into 400-mg tablets, using 15-mm punches.
8. Coat the tablets with hypermellose solution. (See Appendix.)

Tinidazole Controlled Release Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Tinidazole	1000.00
17.50	2	Methocel K15 MCR	17.50
10.00	3	Methocel K4 MCR	10.00
50.00	4	Lactose	50.00
25.00	5	Polyvinylpyrrolidone K30	25.00
10.00	6	Talc	10.00
5.00	7	Colloidal silicon dioxide	5.00
31.50	8	Sodium stearyl fumarate	31.50
1.00	9	Magnesium stearate	1.00

Manufacturing Directions

1. The drug is blended with the two polymers and lactose and granulated with a solution of polyvinylpyrrolidone in water.
2. The granules are dried, sized lubricated, and compressed to tablets at 1148 mg.

Tolterodine Tablets (1 mg/2 mg) Detrol

Detrol® tablets contain tolterodine tartrate. Detrol tablets for oral administration contain 1 or 2 mg of tolterodine tartrate. The inactive ingredients are colloidal anhydrous silica, calcium hydrogen phosphate dihydrate, cellulose microcrystalline, hydroxypropyl methylcellulose, magnesium stearate, sodium starch glycolate (pH 3.0–5.0), stearic acid, and titanium dioxide.

Topiramate Tablets (100 mg/200 mg), Topamax

Topamax (topiramate) tablets contain the following inactive ingredients: lactose monohydrate, pregelatinized starch, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, purified water, carnauba wax, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, synthetic iron oxide (100- and 200-mg tablets), and polysorbate 80.

Tosufloxacin Tosylate Tablets (75 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Tosufloxacin tosylate monohydrate	75.00
37.40	2	L-Aspartic acid	37.50
21.45	3	Cellulose, crystalline	21.45
34.50	4	Starch (maize)	34.50
7.50	5	Silicon dioxide, hydrated	7.50
2.25	6	Hydroxypropyl cellulose	2.25
1.80	7	Magnesium stearate	1.80

Manufacturing Directions

1. Pass items 1 and 2 through a 790-μm sieve into a suitable blender.
2. Blend for 2 minutes.
3. Add items 3 to 6, passing each item through a 500-μm sieve.
4. Blend for 5 minutes.
5. Pass item 7 through #100 mesh into step 4.
6. Blend for 1 minute.
7. Compress into 180-mg tablets, using 8-mm punches.

Tramadol Sustained-Release Tablets (100 mg)

Formulation: Tramadol-HCI (Chemagis), 100.0 g; Kollidon SR, 150.0 g; silicon dioxide, colloidal, 2.5 g; magnesium stearate, 1.5 g.

Manufacturing Directions

All ingredients are passed through a 0.8-mm sieve, blended for 10 minutes in a mixer, and then compressed with medium-compression force at 254 mg.

Tramodol Hydrochloride Matrix Tablets

Manufacturing Directions

1. Tramadolhydrochloride (100 mg), methylhydroxypropylcellulose type 2208, 100000 mPas (85 mg), calcium hydrogen phosphate (62 mg), colloidal silicon dioxide (5 mg), and magnesium stearate (3 mg).
2. Sieve all components through a 0.63-mm sieve, mixing in a cube blender for 10 minutes and pressing into tablets having a diameter of 9 mm, a radius of curvature of 8.5 mm and a mean weight of 255 mg.

Trazodone Hydrochloride Tablets (100 mg)

Trazodone HCl is supplied for oral administration in 50-mg, 100-mg, 150-mg, and 300-mg tablets. Trazodone HCl tablets, 50 mg, contain the following inactive ingredients: dibasic calcium phosphate, castor oil, microcrystalline cellulose, ethylcellulose, FD&C Yellow No. 6 Aluminum Lake, lactose, magnesium stearate, povidone, sodium starch glycolate, and starch (corn).

Trazodone HCl tablets, 100 mg, contain the following inactive ingredients: dibasic calcium phosphate, castor oil, microcrystalline cellulose, ethylcellulose, lactose, magnesium stearate, povidone, sodium starch glycolate, and starch (corn).

Trazodone HCl tablets, 150 mg, contain the following in active ingredients: microcrystalline cellulose, FD&C Yellow No. 6 Aluminum Lake, magnesium stearate, pregelatinized starch, and stearic acid.

Trazodone HCl tablets, 300 mg, contain the following inactive ingredients: microcrystalline cellulose, yellow ferric oxide, magnesium stearate, sodium starch glycolate, pregelatinized starch, and stearic acid.

Triamcinolone Tablets (4 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.00	1	Triamcinolone	4.00
191.00	2	Ludipress	191.00
2.00	3	Kollidon CL	2.00
2.00	4	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with low-compression force.
2. Compress into 206-mg tablets, using 8-mm biplanar punches.
3. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

Triametrene and Hydrochlorothiazide Tablets

Manufacturing Directions

1. First mixture—triamterene, 75 mg; Avicel, PH-102, 125 mg, Rexcel, 38 mg; Ac-Di-Sol, 10 mg; magnesium stearate/sodium lauryl sulfate (94/6), 6 mg; sodium lauryl sulfate, 4 mg; Cab-O-Sil, M-5, 2 mg.
2. Second mixture—hydrochlorothiazide, 50 mg; Avicel, PH-102, 80 mg; Ac-Di-Sol, 5 mg; magnesium stearate/sodium lauryl sulfate (94/6), 1 mg; Cab-O-Sil, M-5, 1 mg; D & C Yellow #10 Lake, 1 mg.
3. After the separate granules are prepared, 250 g of magnesium stearate/sodium lauryl sulfate (94/6) are added and the final mixture thoroughly blended and then formed into tablets (or capsules) by customary methods.

Trifluoperazine Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Trifluoperazine hydrochloride	5.00
194.00	2	Ludipress	194.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through a sieve, and press with very low-compression force.
2. Compress into 204-mg tablets, using 8-mm biplanar punches.
3. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

Trimebutine and Ranitidine Hydrocloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Trimebutine	200.00
150.00	2	Ranitidine hydrochloride	150.00
122.00	3	Microcrystalline cellulose PH102	122.00
20.00	4	Lactose monohydrate	20.00
1.65	5	Magnesium stearate	1.65

Manufacturing Directions

1. In a suitable vessel, the trimebutine, ranitidine HCL, microcrystalline cellulose, and lactose monohydrate are milled to a suitable size and mixed until homogeneous.
2. The magnesium stearate is added and the mixture is mixed until homogeneous.
3. The mixture is then discharged and compressed using conventional tablet tooling to a suitable hardness (e.g., 10–12 kPa) to target a net tablet weight of 500 mg.

Triprolidine and Pseudoephedrine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.60	1	Triprolidine HCl (4% excess)	2.70
60.00	2	Pseudoephedrine HCl (5% excess)	63.00
122.40	3	Lactose monohydrate	122.40
25.50	4	Maize starch	28.00
1.00	5	Povidone (PVP K-30)	1.00
4.00	6	Povidone (PVP K-30)	4.00
–	7	Alcohol (ethanol, 95%)	28.00
1.50	8	Magnesium stearate	1.50

Manufacturing Directions

1. Dissolve item 6 in item 7 using a stirrer.
2. Avoid loss of ethanol by evaporation.
3. Pass items 1 to 5 through a 630-μm sieve using sifter.
4. Collect in a stainless steel drum.
5. Load the sieved powders into a mixer.
6. Mix and chop for 5 minutes at low speed.
7. Add PVP solution to the mixer at medium rate while mixing.
8. Start the chopper at low speed when half of the solution is added.
9. Mix and chop at low speed until the satisfactory mass is obtained.
10. Spread the wet granules onto the trays.
11. Keep the trolleys in the open air for about 1 hour.
12. Load the trolleys into the oven, and start the air circulation at room temperature for 2 hours.
13. Dry the granules at 55°C with air circulation for 5 hours.
14. Scoop the granules after 2 hours of drying; move the upper trays down and the lower trays up for uniform drying.
15. Check the moisture content (limit: NMT 1.5%).
16. Pass the dried granules through a 1-mm sieve using a granulator.
17. Collect in a stainless steel drum and load into the blender.
18. Pass item 8 through a 250-μm sieve using a sifter.
19. Collect in a polyethylene bag.
20. Mix 2 g of granules with this mixture, and add to the blender.
21. Mix for 1 minute.
22. Unload the lubricated granules in a stainless steel drum.
23. Compress into 220-mg tablets, using 8.5-mm, round, concave punches.

Tulobuterol Hydrochloride Tablets (1 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.00	1	Tulobuterol hydrochloride	1.00
44.96	2	Lactose monohydrate	44.96
40.00	3	Blue dye	40.00
28.00	4	Starch (maize)	28.00
2.00	5	Acacia	2.00
3.00	6	Calcium carboxymethyl cellulose	3.00
–	7	Water, purified, ca	20 mL
1.00	8	Magnesium stearate	1.00

Manufacturing Directions

Caution: Tulobuterol is a low-dose bronchodilator. Operators should wear a mask and gloves during all stages of manufacture.

1. Blending
   a. Cross feed tulobuterol, blue dye, and lactose through a comminuting mill fitted with a 790-μm screen, with high speed knives.
   b. Blend the maize starch, acacia, and calcium carboxymethyl cellulose. Put the tulobuterol blend in a suitable mixer/blender for 20 minutes, and disintegrate.
2. Granulation: Load the blended ingredients from Blend A or B into a suitable planetary mixer. While mixing, add water in a slow steady stream. Continue massing for 5 minutes after all the water is added. Proceed to the drying step.
3. Drying
   a. Pass the wet mass through a 4-mm aperture screen onto paper-lined trays. Dry at 50°C to 55°C. The final LOD should be between 1.5% and 5% (105°C for 1 hour).
   b. Pass the dried granule through an oscillating granulator fitted with a 720-μm aperture screen.
4. Lubrication: Load the dried granules into a suitable blender. Pass the magnesium stearate and an equal portion of dried granule through a 600-μm aperture screen. Add to a blender, and blend for 5 minutes.
5. Compression
   a. Compress using a rotary machine fitted with 7/32-in. flat bevel-edged punches. The weight should be 80 mg ± 3%.
   b. For a 2-mg dose, adjust with lactose.

Valacyclovir Hydrochloride Tablets (500 mg/1 g), Valtrex

Each caplet contains valacyclovir hydrochloride equivalent to 500 mg or 1 g of valacyclovir and the inactive ingredients carnauba wax, colloidal silicon dioxide, crospovidone, FD&C Blue No. 2 Lake, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, povidone, and titanium dioxide. The blue, film-coated caplets are printed with edible white ink.

Valdecoxib Tablets (10 mg/20 mg) Bextra

Bextra tablets for oral administration contain 10 or 20 mg of valdecoxib. Inactive ingredients include lactose monohydrate, microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol, polysorbate 80, and titanium dioxide.

Valeriana and Passiflora Extract Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
44.00	1	Valeriana extract, powder	44.00
33.00	2	Passiflora extract, powder (with excess)	36.00
120.00	3	Avicel™ PH101	120.00
11.00	4	Kollidon® CL	11.00
3.60	5	Aerosil® 200	3.60
7.30	6	Magnesium stearate	7.30

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with low compressive force.
2. Compress into 231-mg tablets, using 9-mm biconvex punches.

Valproate Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
576.00	1	Sodium Valproate	576.00
20.00	2	Cab-o-Sil	20.00
266.00	3	A-tab	266.00
154.00	4	Carbomer 971P	154.00
10.00	5	Magnesium stearate	10.00

Manufacturing Directions

1. Sodium valproate, CARBOPOL 971 carbomer, and nonhygroscopic additives are admixed and blended in V-blender for about 5 minutes.
2. The blend from step 1 is comminuted through a 0.250-in. screen.
3. The mixture from step 2 is passed through 20 mesh vibrating sieve.
4. The sifted material from step 3 is blended in a V-blender for an additional 15 minutes.
5. Magnesium stearate is passed through a 50-mesh sieve.
6. The sieved magnesium stearate from step 5 is added to the resulting granulate from step 4 and blended for 5 minutes.
7. The blend from step 6 is compressed into caplets.

Valproate Sodium Tablets (500 mg), Depakote

Depakote tablets are supplied in three dosage strengths containing divalproex sodium equivalent to 125, 250, or 500 mg of valproic acid. The inactive ingredients are cellulosic polymers, diacetylated monoglycerides, povidone, pregelatinized starch (contains cornstarch), silica gel, talc, titanium dioxide, and vanillin. In addition, individual tablets contain the following. *125-mg tablets:* FD&C Blue No. 1 and FD&C Red No. 40; *250-mg tablets:* FD&C Yellow No. 6 and iron oxide; *500-mg tablets:* D&C Red No. 30, FD&C Blue No. 2, and iron oxide.

Valproate Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Valproate sodium	500.00
80.00	2	Starch (maize)	80.00
20.00	3	Kollidon 30	20.00
—	4	Isopropyl alcohol, ca	60 mL
5.00	5	Kollidon CL	5.00
5.00	6	Magnesium stearate	5.00

Manufacturing Directions

1. Granulate the mixture of items 1 and 2 with a solution of items 3 and 4. Pass through a sieve, mix the dry granules with items 5 and 6, and press with low-compression force.
2. Compress into 607-mg tablets, using 12-mm biplanar punches. *Note:* The powder mixture easily develops electric charge.

Valsartan and Hydrochlorothiazide Tablets (80 mg/12.5 mg; 160 mg/25 mg), Diovan HCT

Diovan HCT tablets are formulated for oral administration to contain valsartan and hydrochlorothiazide, USP 80/12.5 mg, 160/12.5 mg, and 160/25 mg. The inactive ingredients of the tablets are colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, iron oxides, magnesium stearate, microcrystalline cellulose, polyethylene glycol, talc, and titanium dioxide.

Valsartan and Hydrochlorothiazide Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
80.00	1	Valsartan	80.00
12.50	2	Hydrochlorothiazide	12.50
1.50	3	Colloidal silica anhydrous (Aerosil 200)	1.50
31.50	4	Microcrystalline cellulose (Avicel PH 102)	31.50
20.00	5	Polyvinyl pyrrolidone crospovidone	20.00
4.50	6	Magnesium stearate	4.50

Manufacturing Directions

1. Blend all components (use only 50% of magnesium stearate) in a container mixer.
2. Sieve the blended material, and mix again.
3. Compact using a roller compactor such as Bepex Pharmapaktor L 200/50 P, Hosokawa Micron Group by applying a compaction force of 25 to 65 kN and a roller speed of 1.3 to 7.5 rpm.
4. Sieve the compacted material and the remaining portion of the magnesium stearate, and blend again for 2 minutes.
5. Compress into 150-mg tablets.

Venlafaxine Hydrochloride Tablets (25 mg/37.5 mg/50 mg) Effexor

Compressed tablets of Effexor® contain venlafaxine hydrochloride equivalent to 25, 37.5, 50, 75, or 100 mg of venlafaxine. Inactive ingredients consist of cellulose, iron oxides, lactose, magnesium stearate, and sodium starch glycolate.

Effexor XR is formulated as an extended-release capsule for once-a-day oral administration. Drug release is controlled by diffusion through the coating membrane on the spheroids and is not pH dependent. Capsules contain venlafaxine hydrochloride equivalent to 37.5, 75, or 150 mg of venlafaxine. Inactive ingredients consist of cellulose, ethylcellulose, gelatin, hydroxypropyl methylcellulose, iron oxide, and titanium dioxide.

Venlafaxine Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Venlafaxine	25.00
90.00	2	Microcrystalline cellulose	90.00
100.30	3	Pregelatinized starch	100.30
7.00	4	Croscarmellose	7.00
0.20	5	Magnesium stearate	0.20

Manufacturing Directions

1. Sieve the active ingredient through a suitable sieve, and blend with the excipients until a uniform blend is formed.
2. Screen the dry blend, and blend with the magnesium stearate.
3. Compress and adjust weight for different strengths.

Verapamil Sustained-Release Tablets (220 mg)

Formulation: Verapamil hydrochloride, 240.0 g; Ludipress LCE, 230.0 g; Methocel K15M (Dow), 75.0 g; Talc, 75.0 g; magnesium stearate, 5.0 g; Aerosil 200, 2.5 g.

Manufacturing Directions

Mix all components, pass through a 0.8-mm sieve, and press with low-compression force using a vibrating hopper at 628 mg.

Verapamil Tablets

Manufacturing Directions

1. Verapamil hydrochloride 240 mg, Sodium alginate (300 cps) 135 mg, hydroxypropylmethyl cellulose (methocel E4M viscosity of 4000 cps) 45 mg, Avicel pH 101 33.2 mg, lactose 8.3 mg, hydroxypropylmethyl E5 9.0 mg, magnesium stearate 4.5 mg, purified water q.s.
2. Verapamil hydrochloride, hydroxypropylmethyl cellulose, sodium alginate, microcrystalline cellulose and lactose are dry blended for 5 minutes in a suitable blender. The powders are then wet massed using binder in aqueous solution and the mix passed through a 10# screen. The granules are dried and the magnesium stearate added thereto.
3. The so-formed mixture is then thoroughly mixed and compressed into tablets each weighing 475 mg.

Verapamil Tablets (120 mg), Calan

Calan is available for oral administration in film-coated tablets containing 40, 80, or 120 mg of verapamil HCl. The inactive ingredients are microcrystalline cellulose, cornstarch, gelatin, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxide colorant, lactose, magnesium stearate, polyethylene glycol, talc, and titanium dioxide. Sustained-release/extended-release tablets are designed for sustained release of the drug in the gastrointestinal tract. Sustained-release characteristics are not altered when the tablet is divided in half.

Verpamil Hydrochloride Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
120.00	1	Verapamil hydrochloride	120.00
270.00	2	Ludipress	270.00
3.00	3	Magnesium stearate	3.00
3.00	4	Aerosil 200	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium-compression force.
2. Compress into 400-mg tablets, using 12-mm biplanar punches.

VESIcare Tablet 5 mg Film-Coated Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Solifenacin succinate	5.00
74.30	2	Lactose spray dried	74.30
5.00	3	Cornstarch	5.00
5.00	4	Starch 1500	5.00
0.70	5	Magnesium stearate	0.70
2.00	6	Hydroxylpropylmethyl cellulose	2.00
0.40	7	Polyethylene glycol 8000	0.40
0.30	8	Talc	0.30
0.60	9	Titanium dioxide	0.60
0.20	10	Yellow ferric oxide	0.20
–	11	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 3, and item 4 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 5% (=1.9 g) powder from step 1 to step 3 and mix well.

5. Add 15% (=5.7 g) powder from step 1 to step 3 and mix well.
6. Transfer step 5 into step 2.
7. Transfer balance quantity of step 1 into step 2.
8. Mix step 2 for 20 minutes using tumbler.
9. Pass item 5 through 0.250-mm sieve and add to step 8.
10. Mix step 9 for 2 minutes.
11. Compress into 90-mg tablets, using a suitable punch (5.5 mm, round).
12. Charge item 11 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxylpropylmethyl cellulose.
13. Add items 7 to 10 one by one to step 12 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
14. Load core tablets from step 11 in coating pan and apply coating dispersion from step 13 to get 2.5% to 3.0% weight gain.

VESIcare Tablet (10 mg) Film-Coated

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Solifenacin succinate	10.00
122.20	2	Lactose Spray Dried	122.20
8.33	3	Cornstarch	8.33
8.33	4	Starch 1500	8.33
1.20	5	Magnesium stearate	1.20
3.00	6	Hydroxylpropylmethyl cellulose	3.00
0.75	7	Polyethylene glycol 8000	0.75
0.50	8	Talc	0.50
1.00	9	Titanium dioxide	1.00
0.30	10	Red ferric oxide	0.30
–	11	Water, purified	45.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 3, and 4 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 5% (=3 g) powder from step 1 to step 3 and mix well.
5. Add 15% (=9.1 g) powder from step 1 to step 3 and mix well.
6. Transfer step 5 into step 2.
7. Transfer balance quantity of step 1 into step 2.
8. Mix step 2 for 20 minutes using tumbler.
9. Pass item 5 through 0.250-mm sieve and add to step 8.
10. Mix step 9 for 2 minutes.
11. Compress into 150-mg tablets, using a suitable punch (7.5 mm × 6.0 mm, oval).
12. Charge item 11 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxylpropylmethyl cellulose.
13. Add items 7 to 10 one by one to step 13 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
14. Load core tablets from step 11 in coating pan and apply coating dispersion from step 13 to get 2.5% to 3.0% weight gain.

VIRACEPT 250-mg Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
292.00	1	Nelfinavir mesylate equivalent to Nelfinavir 250 mg	292.00
158.00	2	Lactose Monohydrate	158.00
25.00	3	Povidone	25.00
–	4	Water, purified	50.00
20.00	5	Crospovidone	20.00
5.00	6	Magnesium stearate	5.00
10.00	7	Hypromellose	10.00
2.00	8	Triacetin	2.00
0.30	9	FD& C blue #2	0.30
–	10	Water, purified	100.00

Manufacturing Directions

1. Dissolve item 3 in item 4 in a stainless steel container.
2. Pass items 2 and 1 and 20% of item 5 (4 g) through 0.7-mm sieve and mix well.
3. Charge step 2 in a granulator.
4. Knead step 3 with solution of step 1 for 5 to 10 minutes until a loose, moist mass is obtained.
5. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
6. Spread step over paper-lined trays and dry at 50°C to 55°C for 8 hours (the relative humidity over the granules should be 20–35%).
7. Pass the dried granules through a 1.25-mm sieve granulator.
8. Transfer the granules to a tumbler.
9. Pass the remaining quantity of item 5 through 0.5-mm sieve and add to step 8 and mix for 15 minutes.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 500-mg tablets, using a suitable punch (14.5 mm, round).
13. Charge item 10 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
14. Add item 8 and item 9 one by one to step 12 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
15. Load core tablets from step 12 in coating pan and apply coating dispersion from step 14 to get 1.5% to 2.0% weight gain.

VIRACEPT 625-mg Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
730.00	1	Nelfinavir mesylate equivalent to Nelfinavir 650 mg	730.00
62.00	2	Lactose Monohydrate	62.00
45.00	3	Povidone	45.00
–	4	Water, purified	100.00
45.00	5	Crospovidone	45.00
9.00	6	Colloidal Silicon Dioxide	9.00
9.00	7	Magnesium stearate	9.00
15.00	8	Hypromellose	15.00
3.00	9	Triacetin	3.00
0.50	10	FD& C blue #2	0.50
–	11	Water, purified	150.00

Manufacturing Directions

1. Dissolve item 3 in item 4 in a stainless steel container.
2. Pass item 2, item 1, and 20% of item 5 (9 g) through 0.7-mm sieve and mix well.
3. Charge step 2 in a granulator.
4. Knead step 3 with solution of step 1 for 5 to 10 minutes until a loose, moist mass is obtained.
5. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.

6. Spread step over paper-lined trays and dry at 50°C to 55°C for 8 hours (the relative humidity over the granules should be 20–35%).
7. Pass the dried granules through a 1.25-mm sieve granulator.
8. Transfer the granules to a tumbler.
9. Pass the remaining quantity of item 5 and the item 6 through 0.5-mm sieve and add to step 8 and mix for 15 minutes.
10. Pass item 7 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 900-mg tablets, using a suitable punch (16.5 mm, round).
13. Charge item 11 in a stainless steel vessel. Add item 8 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
14. Add item 9 and item 109 one by one to step 13 with stirring. Stir for 10 minutes. Homogenize for
15. minutes. Pass the coating dispersion through 180-mm sieve (if required).
16. Load core tablets from step 12 in coating pan and apply coating dispersion from step 14 to get 1.5 % to 2.0% weight gain.

Vitamin A and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
33000 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	69.00
70.00	2	Vitamin E acetate (dry powder)	70.00
146.00	3	Mannitol (granulated) with 10% of Kollidon® 30	146.00
17.00	4	Kollidon® CL	17.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with high compressive force.
2. Compress into 300-mg tablets, using 12-mm biplanar punches.

Vitamin A Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100000 IU	1	Vitamin A acetate (dry powder, 325000 IU/g)	350.00
350.00	2	Mannitol	350.00
25.00	3	Kollidon® VA 64	25.00
5.00	4	Magnesium stearate	5.00
3.00	5	Aerosil® 200	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with medium compressive force.
2. Compress into 750-mg tablets, using 12-mm biplanar punches.

Vitamin A Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50000 IU	1	Vitamin A acetate (dry powder, 500000 IU/g)	110.00
100.00	2	Avicel™ PH102	100.00
10.00	3	Kollidon® VA 64	10.00
5.00	4	Kollidon® CL	5.00
1.00	5	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with low compressive force.
2. Compress into 231-mg tablets, using 9-mm binconvex punches.

Vitamin A Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5000	1	Vitamin A acetate (dry powder, 500,000 IU/g)	110.00
189.00	2	Ludipress®	189.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 306-mg tablets, using 8-mm punches.

Vitamin A Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50,000	1	Vitamin A acetate (dry powder, 500000 IU/g)	120.00
120.00	2	Ludipress®	120.00
10.00	3	Avicel™ PH101	10.00
1.00	4	Magnesium stearate	1.00
1.00	5	Aerosil® 200	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 277-mg tablets, using 8-mm punches.

Vitamin A Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50,000	1	Vitamin A acetate (dry powder, 500000 IU/g)	110.00
154.00	2	Avicel™ PH101	154.00
10.00	3	Kollidon® VA 64	10.00
4.00	4	Kollidon® CL	4.00
1.00	5	Aerosil® 200	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press with low compressive force.
2. Compress into 250-mg tablets, using 8-mm punches.

Vitamin A Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25000 IU	1	Vitamin A acetate (dry powder, 500000 IU/g)	55.00
572.00	2	Dicalcium phosphate (granulated) (Di-Tab) with 3% of Kollidon® 30	572.00
28.00	3	Polyethylene glycol, powder	28.00
19.40	4	Kollidon® CL	19.40
5.60	5	Aerosil® 200	5.60

Manufacturing Directions

1. Granulate the dicalcium phosphate with Kollidon 30, dissolved in isopropanol or water, and pass through a 0.5- to 12-mm screen sieve using a vibrating hopper.
2. Mix the obtained dried granules with the other components, sieve, and press with high compressive force.
3. Compress into 680-mg tablets, using biplanar punches.

Vitamin A, Vitamin B6, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
40000 IU	1	Vitamin A acetate (dry powder, 500000 IU/g)	80.00
40.00	2	Pyridoxine hydrochloride	40.00
35.00	3	Vitamin E acetate (dry powder, SD 50)	75.00
395.00	4	Ludipress®	395.00
4.00	5	Magnesium stearate	4.00
5.00	6	Aerosil® 200	5.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high compressive force.
2. Compress into 583-mg tablets, using 12-mm biplanar punches.

Vitamin A, Vitamin C, and Vitamin D3 Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2000/200 IU	1	Vitamin A and vitamin D3 (dry powder, 500000 and 50,000 IU/g, respectively)	4.00
30.00	2	Ascorbic acid (powder)	33.00
300.00	3	Sucrose (crystalline)	300.00
300.00	4	Sorbitol (crystalline)	300.00
300.00	5	Mannitol	300.00
300.00	6	Ludipress®	300.00
5.00	7	Stearic acid	5.00
0.10	8	Saccharin sodium	0.10
30.00	9	Cyclamate sodium	30.00
30.00	10	Flavor mixture (Firmenich)	30.00
20.00	11	PEG-6000, powder	20.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high compressive force.
2. Compress into 1290-mg tablets, using 16-mm biplanar punches.

Vitamin A, Vitamin C, and Vitamin E Tablets (1200 IU/60 mg/30 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets
1200 IU	1	Vitamin A acetate (dry powder, 500000 IU/g)	2.40
60.00	2	Ascorbic acid (powder)	60.00
30.00	3	Vitamin E acetate (dry powder, 50%)	60.00
105.00	4	Lactose monohydrate	105.00
30.00	5	Avicel™ PH101	30.00
20.00	6	Kollidon® 25	20.00
5.00	7	Talc	5.00
1.00	8	Aerosil® 200	1.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 285-mg tablets, using 8-mm biplanar punches.

Vitamin B-Complex and Carnitine Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
95.00	1	Thiamine mononitrate	95.00
20.00	2	Riboflavin	20.00
100.00	3	Nicotinamide	100.00
50.00	4	Calcium D-pantothenate	50.00
2.00	5	Folic acid	2.00
0.20	6	Biotin	0.20
0.005	7	Cyanocobalamin (gelatin coated, 1%)	0.50
50.00	8	Carnitine hydrochloride	50.00
100.00	9	Inositol	100.00
2.00	10	Adenosine phosphate	2.00
15.70	11	Kollidon® 30	15.70
70.00	12	Isopropanol	70.00
26.00	13	Kollidon® CL	26.00
122.00	14	Lactose monohydrate	122.00
14.00	15	PEG-6000, powder	14.00

Manufacturing Directions

1. Granulate mixture of items 1 to 10 with solution of items 11 and 12.
2. Dry, pass through a 0.8-mm sieve, mix with items 13 and 15, and press with low compressive force.
3. Compress into 708-mg tablets, using 13-mm biplanar punches.

Vitamin B-Complex and Folic Acid Dragees

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
4.35	1	Calcium D-pantothenate (granulate, 67%)	6.50
2.60	2	Thiamine mononitrate (10.4%)	25.00
20.00	3	Magnesium oxide (light)	20.00
45.75	4	D-mannitol (powder)	45.75
100.00	5	DL-methionine	100.00
2.30	6	Riboflavin	2.30
6.30	7	Nicotinamide	6.30
2.40	8	Pyridoxine HCl	2.40
4.00	9	Magnesium stearate	4.00
0.1150	10	D-biotin	0.1150
0.46	11	Folic acid	0.46
100.00	12	Choline tartarate	100.00
28.00	13	Silicic acid (precipitated)	28.00
0.87 mcg	14	Vitamin B12 (as 0.1% water soluble form)	0.871
3.15	15	Vitamin E (50%)	6.30
30.00	16	Sodium carboxymethyl starch	30.00
116.66	17	Isopropyl alcohol	116.66
22.00	18	Povidone (PVK K-90) (Luviskol®)	22.00

Manufacturing Directions

1. Incorporate in mixer PVP K-90 and isopropyl alcohol, and make a solution with continuous stirring.
2. Place in mixer choline tartarate, DL-methionine, D-mannitol powder, magnesium oxide (previously sieved), silicic acid, and sodium carboxymethyl starch, and mix for 15 minutes.
3. Add the solution of isopropyl alcohol and alcohol in first step for 10 minutes until moist mass is obtained.
4. Granulate the moist mass through a centrifugal granulator with a 10-mm screen.
5. Spread the granules on paper-lined trays, and dry overnight in a drying oven at 50°C.
6. Crush the granules through a 1.5-mm sieve.
7. Vitamin granulate: Tumble D-biotin, vitamin B12, folic acid, riboflavin, and pyridoxine hydrochloride in mixer for 5 minutes.
8. Combine in the mixer nicotinamide, vitamin E, thiamine mononitrate/gelatin/mannitol granulate, D-mannitol powder, and sodium carboxymethyl starch, then add the vitamin mixture, and mix for 10 minutes.
9. Pass through a 1-mm sieve if lumpy.
10. In a mixer, make a separate solution of PVP K-90 and isopropyl alcohol.
11. Place in the mixer the solution of isopropyl alcohol and PVP, then knead until an evenly moist homogeneous mass is obtained.
12. Add calcium-D-pantothenate granules, and mix for 3 to 5 minutes.
13. Pass the granules through a centrifugal granulator with a 10-mm screen, and spread on paper-lined trays.
14. Keep overnight in a drying oven at 50°C; the relative humidity of the granules should be 10% to 20%.
15. Crush the dried granules through an oscillator with a 1.5-mm sieve.
16. Put the granulate mixture in the mixing drum—the choline tartarate and the two lots of vitamin granules.
17. Mix, and then add the magnesium stearate.
18. Check to be sure that the relative humidity of the mixture is 10% to 20%.
19. Compress, and apply a sealer coat (lacquer), sugar coat, and finishing coating.

Vitamin B-Complex and Vitamin C Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
33.00	1	Thiamine mononitrate	33.00
4.00	2	Riboflavin	4.00
10.00	3	Pyridoxine hydrochloride	10.00
66.00	4	Nicotinamide	66.00
17.00	5	Calcium D-pantothenate	17.00
350.00	6	Tartaric acid (powder)	350.00
450.00	7	Sodium bicarbonate	450.00
750.00	8	Sucrose, crystalline	750.00
30.00	9	Kollidon® 30	30.00
QS	10	Isopropanol	QS
500.00	11	Ascorbic acid (crystalline)	500.00
3.00 g	12	Riboflavin	3.00
10.00	13	Cyanocobalamin (gelatin coated, 0.1%)	10.00
10.00	14	Orange flavor	10.00
2.00	15	Saccharin sodium	2.00
5.00	16	Cyclamate sodium	5.00
50.00	17	PEG-6000 (powder)	50.00

Manufacturing Directions

1. Granulate mixture of items 1 to 9 with solvent item 10, dry, pass through a 0.8-mm sieve, mix with items 13 to 17, and press with high compressive force at a maximum of relative atmospheric humidity of 30%.
2. Compress into 2315-mg tablets, using 20-mm biplanar punches.

Vitamin B-Complex and Vitamin C Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Thiamine mononitrate	5.00
5.00 g	2	Riboflavin	5.00
5.00	3	Pyridoxine hydrochloride	5.00
0.50	4	Folic acid	0.50
30.00	5	Niacin	30.00
0.10	6	Biotin	0.10
10.00	7	Calcium D-pantothenate	10.00
150.00	8	Ascorbic acid (crystalline/powder)	150.00
172.40	9	Ludipress®	172.40
20.00	10	Kollidon® VA 64	20.00
2.00	11	Magnesium stearate	2.00

Manufacturing Directions

1. Mix all ingredients and pass through a 0.8-mm sieve, and then mix.
2. Use medium to low compressive force to compress 400 mg in 10-mm biplanar punches.

Vitamin B-Complex and Vitamin C Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Thiamine hydrochloride	15.00
2.00	2	Riboflavin	2.00
5.00	3	Pyridoxine hydrochloride	5.00
25.00	4	Choline bitartrate	25.00
10.00	5	Nicotinamide	10.00
100.00	6	Ascorbic acid (crystalline/powder)	100.00
220.00	7	Ludipress®	220.00
8.00	8	Stearic acid	8.00

Manufacturing Directions

1. Mix all ingredients and pass through a 0.8-mm sieve, and mix.
2. Use medium to low compressive force to compress 411 mg in 12-mm biplanar punches.
3. The thiamine mononitrate formulation is more stable compared with the thiamine hydrochloride formulation (above).

Vitamin B-Complex Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Thiamine mononitrate or hydrochloride	25.00
25.00	2	Riboflavin	25.00
80.00	3	Nicotinamide	80.00
40.00	4	Calcium D-pantothenate	40.00
16.00	5	Pyridoxine hydrochloride	16.00
0.16	6	Cyanocobalamin (gelatin coated, 0.1%)	16.00
282.00	7	Avicel™ PH101	282.00
16.00	8	Kollidon® 30	16.00
3.00	9	Aerosil® 200	3.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix.
2. Compress using 12-mm biplanar punches with medium- to high-compression force.
3. The mononitrate formulation is preferred for stability reasons.

Vitamin B-Complex Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.30	1	Thiamine mononitrate	2.30
2.60	2	Riboflavin	2.60
2.30	3	Nicotinamide	2.30
2.20	4	Calcium D-pantothenate	2.20
2.70	5	Pyridoxine hydrochloride	2.70
0.024	6	Cyanocobalamin (gelatin coated, 0.1%)	2.40
280.00	7	Ludipress®	280.00
14.00	8	Flavor (Firmenich)	14.00
0.050	9	Saccharin sodium	0.05
4.00	10	Cyclamate sodium	4.00
5.00	11	Magnesium stearate	5.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and 8-mm biplanar punches.
2. Compress into 314-mg tablets, using low-compression force.
3. According to European Commission, this formulation is classified as dietary food.

Vitamin B-Complex Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Microcrystalline cellulose (Avicel™ PH102)	15.00
0.20	2	Colloidal silicon dioxide (Aerosil® 200)	0.20
3.00	3	Calcium pantothenate	3.00
9.33	4	Powdered cellulose	9.33
35.60	5	Lactose (spray-dried)	35.60
0.91	6	Magnesium stearate	0.91
20.00	7	Nicotinamide	20.00
2.10	8	Pyridoxine hydrochloride	2.10
2.00	9	Riboflavin base	2.00
0.80	10	Talc (fine powder)	0.80
2.10	11	Thiamine mononitrate	2.10

Manufacturing Directions

1. Riboflavin base is a fine powder that tends to form globules while mixing.
2. Disperse the base with Aerosil and lactose carefully.
3. Mix items 9 and 2 and 6.67 g of item 5 in the drum of a drum mixer for 10 minutes.
4. Pass the mix two times through a 500-μm sieve using a sifter.
5. Pass items 11, 8, and 3 and 6.67 g of item 5 through a granulator fitted with a 1.0-mm sieve.
6. Pass items 7, 1, and 4 and 22.27 g of item 5 through a granulator fitted with a 1.0-mm sieve.
7. Pass items 10 and 6 through a sifter fitted with a 500-μm sieve.
8. Load sieved material from previous step to the blender.
9. Load sieved material to the blender.
10. Blend the powders for 15 minutes.
11. Load lubricant powders into the blender, and mix for an additional 5 minutes.
12. Compress into 91-mg tablets at low relative humidity (55–60%).
13. Coat tablets with a sealing coat, color coat, and polishing coat.

Vitamin B-Complex, Choline, and Bile Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
60.00	1	Acid dehydrochloric (powder)	60.00
100.00	2	Choline dihydrogen citrate	100.00
20.00	3	Niacinamide (white powder)	20.00
100.00	4	Inositol	100.00
2.50	5	Riboflavin (2% excess)	2.55
0.50	6	Pyridoxine hydrochloride	0.50
30.00	7	Povidone (*K* value, 29– 32)	30.00
100.00	8	Racemethionine (crystals)	100.00
60.00	9	Ox bile extract (powder, #30-mesh) (Bilein)	60.00
–	10	Alcohol dehydrated (200 proof)	26.00
3.0 μg	11	Cyanocobalamin (oral powder in gelatin, 1000 μg/g)	3.30
3.00	12	Thiamine hydrochloride (powder, regular)	3.60
8.40	13	Magnesium stearate (impalpable powder)	8.40
8.40	14	Stearic acid (fine powder)	8.40

Manufacturing Directions

1. Mill dehydrochloric acid, choline dihydrogen citrate, nicotinamide, inositol, and methionine through a 600-μm screen.
2. Charge milled mixture from first step with riboflavin, pyridoxine hydrochloride, Povidone, and ox bile extract in mass mixer.
3. Add alcohol QS (approximately 26 g or 32.7 mL) very slowly to the mass.
4. Mass for approximately 45 minutes in mixer.
5. Scrape all material from the mass mixer as much as possible.
6. Rinse mass mixer between runs.
7. Granulate through a comminuting or similar mill or a 4.76-mm screen.
8. Dry at 49°C to less than 1% LOD.
9. Sift through an 840-μm screen in a shaker and grind coarsely through a comminuting mill (knives forward, medium speed).
10. Charge one half of the base granulation through a 1.68-mm screen into a blender, if necessary.
11. Mix cyanocobalamine oral powder with an equal volume of base granulation, and charge into a blender through a 1.68-mm screen.
12. Blend thiamine hydrochloride, magnesium stearate, and stearic acid.
13. Then hand-screen mixture through a 600-μm screen.
14. Load into a blender through a 1.68-mm screen with the remainder of the base granulation, and blend for 20 minutes.
15. Compress and coat tablets using an appropriate formulation to render required color and sealing of tablet.

Vitamin B-Complex, Vitamin A, Vitamin C, and Vitamin D Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.00	1	Thiamine mononitrate (20% excess)	2.40
1.00	2	Riboflavin (10% excess)	1.10
74.50	3	Lactose (spray-dried)	74.50
15.00	4	Nicotinamide	15.00
300 IU	5	Vitamin D3 (dry powder, 100000 IU/g)	3.60
3000 IU	6	Vitamin A palmitate (250000 IU/g)	18.00
36.00	7	Cellulose (microcrystalline) (Avicel™ PH102)	36.00
20.00	8	Ascorbic acid (90%) (33% excess)	26.60
1.00	9	Silicon dioxide (colloidal) (Aerosil® 200)	1.00
1.80	10	Magnesium stearate	1.80

Manufacturing Directions

1. Mix items 1 and 2 and 13.33 g of item 3 in a drum using a drum mixer for 10 minutes.
2. Pass the mix through a 250-μm sieve using a sifter.
3. Collect in a stainless steel drum, and load into the blender.
4. Pass items 4 to 7 and 61.17 g of item 3 through a granulator fitted with a 1.0-mm sieve.
5. Collect in a stainless steel drum, and load into the blender.
6. Pass item 8 through a FitzMill fitted with sieve number 24230.
7. Collect in a stainless steel drum, and load into the blender.
8. Mix for 10 minutes.
9. Pass item 9 through a 500-μm sieve using a sifter.
10. Collect in a polyethylene bag.
11. Pass item 10 through a 250-μm sieve using a sifter.
12. Collect in the same polyethylene bag.
13. Mix and add 0.53 to 1.33 g powder from the step above.
14. Mix gently.
15. Add to the blender.
16. Mix for 3 minutes.
17. Unload lubricated granules in stainless steel drums.
18. Compress into 180-mg tablets, using 7-mm round concave punches.
19. Apply a sealing coat, a color coat, and finishing coat (see Appendix).

Vitamin B-Complex, Vitamin A, Vitamin C, Vitamin D, and Mineral Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
61.00	1	Ascorbic acid (coated), EC	61.00
5.50	2	Calcium pantothenate	5.50
8.00 mcg	3	Cyanocobalamin	0.008
4.00	4	Copper sulfate, $5H_2O$	4.00
1.70	5	Magnesium oxide (heavy)	1.70
10.00	6	Nicotinamide	10.00
0.575	7	Pyridoxin hydrochloride	0.575
0.16	8	Potassium iodide	0.16
2.30	9	Riboflavin	2.30
3.25	10	Thiamine mononitrate	3.25
24.00	11	Vitamin A palmitate (250000 IU/g)	24.00
4.80	12	Vitamin D3 powder (100000 IU/g)	4.80
2.20	13	Zinc sulfate, $7H_2O$	2.20
19.265	14	Lactose monohydrate	19.265
25.00	15	Cellulose (microcrystalline) (Avicel™ PH102)	25.00
3.00	16	Povidone (PVP K-90)	3.00
6.50	17	Cellulose (microcrystalline) (Avicel™ PH102)	6.50
7.00	18	Crospovidone (Kollidon® CL)	7.00
1.00	19	Colloidal silicon dioxide (Aerosil® 200)	1.00
0.75	20	Magnesium stearate	0.75
3.00	21	Microcrystalline cellulose (powder)	3.00
–	22	Alcohol (absolute)	18.46

Manufacturing Directions

1. Dissolve item 16 in item 22 using a stirrer.
2. Dissolve item 3 while stirring to obtain a clear solution.
3. Press items 10, 9, 7, 6, 2, 14, and 15 through a 500-μm stainless steel sieve in a sifter.
4. Load into mixer, and mix for 5 minutes at high speed.
5. Knead the dry powder with binding solution while mixing at high speed for 3 minutes.
6. After the addition is complete, scrape the sides and blades.
7. Mix for an additional 2 minutes using a mixer and chopper at high speed. Check the end point of granulation.
8. (The end point occurs when the granulation consists of few or no lumps.) If required, add an additional quantity of item 22, and record this extra quantity of item 22.
9. Unload the wet granules in stainless steel trays for drying.
10. Transfer the trays to an oven.
11. Keep the door partially open.
12. Switch on the oven, with air circulation, heater switched off, for 2 hours to evaporate alcohol.
13. Close the door of the oven.
14. Dry the granules at 55°C for 12 hours.
15. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
16. Check the LOD (limit: 0.8–1.2%).
17. If required, dry further at 55°C for 2 hours.
18. Check the LOD.
19. Grind the dried granules through a 1.25 mm sieve using a granulator set at medium speed.
20. Load granules into the blender.
21. Mix items 4 and 13 and 3.08 g of item 17 in a polyethylene bag.
22. Mill through a FitzMill using sieve number 1530-0030 (knives forward, medium speed).
23. Collect in stainless steel drum.
24. Add to blender.
25. Sift items 11, 12, and 1 through a 630-μm sieve.
26. Add to blender.
27. Sift items 5, 8, 18, 19, and 21 and 3.42 g of item 17 through a 500-μm sieve.
28. Add to blender.
29. Mix for 5 minutes.
30. Sift item 20 through a 250-μm sieve.
31. Mix a portion of the powder mix (~3.85 g) with sieved item 20.
32. Add to the blender.
33. Mix for 1 minute.
34. Compress into 185-mg tablets, using 7-mm, round, concave punches.
35. Coat using a subcoat, a color coat, and a finishing coat (see Appendix).

Vitamin B-Complex, Vitamin C, and Calcium Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
7.00	1	Thiamine mononitrate	7.00
5.00	2	Riboflavin	5.00
25.00	3	Nicotinamide	25.00
20.00	4	Pyridoxine hydrochloride	20.00
12.00	5	Calcium D-pantothenate	12.00
75.00	6	Calcium carbonate	75.00
164.00	7	Calcium glycerophosphate	164.00
400.00	8	Sodium bicarbonate	400.00
300.00	9	Tartaric acid (powder)	300.00
400.00	10	Sucrose (crystalline)	400.00
350.00	11	Sucrose (powder)	350.00
50.00	12	Kollidon® 30	50.00
10.00	13	Kollidon® 30	10.00
QS	14	Isopropanol	QS
550.00	15	Ascorbic acid (powder)	550.00
2.00	16	Riboflavin	2.00
5.00	17	Cyanocobalamin (gelatin coated, 0.1%)	5.00
40.00	18	PEG-6000 (powder)	40.00
50.00	19	Kollidon® CL	50.00

Manufacturing Directions

1. Granulate mixture of items 1 to 12 with solution of item 19.
2. Granulate items 13 to 18 separately, dry at 60°C with vacuum, mix with item 1, blend.
3. Compress into 2.5-g tablets, using 20-mm planar punches at medium- to high-compression force.

Vitamin B-Complex, Vitamin C, and Ferrous Sulfate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Ferrous sulfate	300.00
15.00	2	Kollidon® 30	15.00
6.00	3	Kollidon® 30	6.00
QS	4	2-Propanol	QS
45.00	5	Thiamine mononitrate	45.00
10.00	6	Riboflavin	10.00
82.00	7	Pyridoxine hydrochloride	82.00
69.00	8	Nicotinamide	69.00
470.00	9	Ascorbic acid (powder)	470.00
690.00	10	Ludipress®	690.00
50.00	11	PEG-6000 (powder)	50.00
9.00	12	Aerosil® 200	9.00

Manufacturing Directions

1. Granulate the mixture of items 1 to 2 with solution of items 5 to 12.
2. Pass through a 0.8-mm sieve.
3. Mix with items 3 and 4.
4. Compress with high compressive force 25 to 30 kN. Compress into 1750-mg tablets, using 20-mm biplanar punches.

Vitamin B-Complex, Vitamin C, and Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Niacinamide, (white powder), USP	100.00
750.00	2	Ascorbic acid; use sodium ascorbate (microcrystalline), USP	843.65
20.00	3	Calcium pantothenate, USP	30.00
10.00	4	Riboflavin, USP	10.00
5.00	5	Pyridoxine hydrochloride, USP	5.25
40.00	6	Povidone, USP	40.00
68.00	7	Anhydrous isopropyl alcohol	68.00
15.00	8	Thiamine mononitrate (powder), USP	15.75
24.79	9	Vitamin E, USP, d,l-α-tocopoheryl acid succinate	33.71
150.00 mcg	10	Folic acid (powder), USP	0.18
5.00	11	Magnesium stearate	5.00
40.00	12	Cellulose (microcrystalline), NF	40.00
4.00 mcg	13	Vitamin B12; use cyanocobalamine powder in gelatin (1000 μg/g)	4.20

Manufacturing Directions

1. Av oid unnecessary exposure to light and moisture.
2. Mill the nicotinamide and the sodium ascorbate through a 600-μm screen fitted to a FitzMill, or similar (impact forward, high speed).
3. Load into a suitable mass mixer.
4. Load calcium pantothenate, riboflavin, and pyridoxine hydrochloride into the mass mixer.
5. Dry blend for 5 minutes.
6. Dissolve Povidone in alcohol (~84 mL) in a separate container.
7. While mixing the blended powders add the Povidone solution.
8. Continue to mix until a satisfactory granule mass is obtained.
9. If required, use additional alcohol.
10. Granulate through a FitzMill, or similar, using a 5/8-in. band (15.88-mm aperture or similar) or a 4.76-mm screen with knives forward at slow speed.

11. Dry the granulation at 49°C to less than 1.5% LOD.
12. Sift the dry granulation through a 1.19-mm screen.
13. Pass remaining coarse granules through a #2 band (1.59-mm aperture or similar) using a FitzMill, or similar (knives forward, medium speed).
14. Blend together the thiamine mononitrate, vitamin E, folic acid, magnesium stearate, and a portion of the microcrystalline cellulose.
15. Mill blended powders through a 600-μm screen (impact forward, high speed).
16. Care must be taken to prevent losses.
17. Load half of the base granulation, the balance of the microcrystalline cellulose, and the powder blend into a suitable blender.
18. Blend for 5 minutes.
19. Add balance of base granulation, and blend for 15 minutes.
20. Do not mill cyanocobalamine.
21. Blend together by hand the cyanocobalamine with a portion of the blended powders.
22. Return to the blender, and blend for 15 minutes.
23. Compress using ovaloid-shaped punches.
24. Seal tablets with a subcoat, and then apply color coat and finishing coating.

Vitamin C and Calcium Carbonate Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
300.00	1	Calcium; use calcium carbonate	315.00
450.00	2	Sodium bicarbonate/tartaric acid (powder)	450.00
600.00	3	Kollidon® 30	600.00
35.00	4	Kollidon® 30	35.00
200.00	5	Isopropanol	200.00
400.00	6	Sucrose (crystalline)	400.00
500.00	7	Ascorbic acid (crystalline, with excess)	550.00
120.00	8	Kollidon® CL	120.00
60.00	9	PEG-6000 (powder)	60.00

Manufacturing Directions

1. Granulate mixture of items 1 to 3 with a solution of items 4 and 5, mix with item 6, and dry.
2. Add items 7 to 9, and press with high compressive force at a maximum atmospheric relative humidity of 30%.
3. Compress into 2500-mg tablets, using 20-mm biplanar punches.

Vitamin C and Vitamin E Lozenges

Bill of Materials			
Scale (mg/lozenge)	Item	Material Name	Quantity/1000 Lozenges (g)
100.00	1	Ascorbic acid (crystalline)	100.00
50.00	2	Vitamin E acetate (dry powder, SD 50)	100.00
400.00 g	3	Dextrose	400.00
4.00 g	4	Kollidon® 90F	4.00
25.00 g	5	Isopropanol	25.00
6.00 g	6	PEG-6000 (powder)	6.00

Manufacturing Directions

1. Granulate mixture of items 1 to 4 with isopropanol, dry, pass through a 0.8-mm sieve, mix with item 6, and press with high-compression force.
2. Compress into 600-mg tablets, using 12-mm biplanar punches.

Vitamin C Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Ascorbic acid: 222.20 mg ascorbic acid and 312.50 mg sodium ascorbate microcrystalline	500.00
850.00	2	Sorbitol (granular)	850.00
100.00	3	Lactose (120 mesh)	100.00
3.30	4	FD&C Yellow Dye No. 5 lake	3.30
82.90	5	Cellulose (microcrystalline), NF (Avicel™ PH101)	82.90
11.60	6	Silica gel	11.60
8.29	7	Flavor	8.29
0.50	8	Flavor	0.50
8.29	9	Sodium cyclamate	8.29
33.20	10	Magnesium stearate	33.20

Manufacturing Directions

1. Pass ascorbic acid, sodium ascorbate, sorbitol, lactose, FD&C Yellow Dye, microcrystalline cellulose, silica gel, flavors, and sodium cyclamate through a 420-μm screen.
2. Using a comminuting mill, pass the coarse granules through a 420-μm screen (knives forward, medium speed).
3. Transfer milled materials to a suitable blender, and blend for 5 minutes.
4. Screen the magnesium stearate by hand through an 840-μm screen, and transfer to blender.
5. Mix for 1 minute.
6. Compress using 18-mm standard concave punches.

Vitamin C Chewable Tablets

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/kg (g)
422.00	1	Ascorbic acid (powder)	422.00
283.00	2	Microcrystalline cellulose	283.00
130.00	3	Sucrose (powder)	130.00
80.00	4	Sucrose (crystalline)	80.00
24.00	5	Kollidon® VA 64	24.00
24.00	6	Cyclamate sodium	24.00
20.00	7	PEG-6000 (powder)	20.00
12.00	8	Orange flavor and strawberry flavor	12.00
2.00	9	Aerosil® 200	2.00
1.00	10	Saccharin sodium	1.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm sieve, and press into tablets with medium- to high-compression force.
2. Compress 250 mg (for 100 mg strength), 1250 mg (for 500 mg strength), or 2500 mg (for 500 mg strength).

Vitamin C Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Ascorbic acid (crystalline)	500.00
1100.00	2	Sorbitol (crystalline)	1100.00
200.00	3	Sucrose (crystalline)	200.00
200.00	4	Sucrose (powder)	200.00
300.00	5	Dextrose	30.00
100.00	6	PEG-6000 (powder)	100.00
10.00	7	Magnesium stearate	10.00
10.00	8	Aerosil® 200	10.00
1.00	9	Saccharin sodium	1.00
10.00	10	Cyclamate sodium	10.00
30.00	11	Orange flavor	30.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with medium- to high-compression force.
2. Compress into 2080-mg tablets, using 20-mm biplanar punches.

Vitamin C Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Ascorbic acid (crystalline)	100.00
450.00	2	Sodium ascorbate (crystalline)	450.00
264.00	3	Sorbitol (crystalline)	264.00
200.00	4	Sucrose (crystalline)	200.00
200.00	5	Sucrose (powder)	200.00
300.00	6	Dextrose	300.00
60.00	7	PEG-6000 (powder)	60.00
3.00	8	Magnesium stearate	3.00
4.00	9	Aerosil® 200	4.00
1.00	10	Saccharin sodium	1.00
10.00	11	Cyclamate sodium	10.00
20.00	12	Orange flavor	20.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with medium- to high-compression force.
2. Compress into 1295-mg tablets, using 16-mm biplanar punches.

Vitamin C Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
6.70	1	Anhydrous silica (colloidal) (Aerosil® 200)	6.70
40.00	2	Cellulose (microcrystalline) (Avicel™ PH101)	40.00
6.50	3	Aspartame	6.50
170.00	4	Ascorbic acid (coated), EC	170.00
10.50	5	Orange flavor (dry)	10.50
13.00	6	Carmellose sodium (sodium CMC 7 MFD)	13.00
2.80	7	Orange dye	2.80
470.00	8	Dextrates, NF	470.00
19.50	9	Magnesium stearate	19.50
13.00	10	Stearic acid (fine powder)	13.00
160.00	11	Sorbitol (powder)	160.00
388.00	12	Sodium ascorbate (granular)	388.00

Manufacturing Directions

1. Processing should be done in a controlled temperature and humidity area (limit: relative humidity, 40–50%; temperature, 20–25°C).
2. Mix items 2 and 7 in a polyethylene bag for 1 to 2 minutes.
3. Sift twice through a 250-μm sieve.
4. Collect in a polyethylene bag, and check the uniformity of dispersion.
5. If required, sift again.
6. Mix items 3, 5, and 6 in a polyethylene bag for 1 to 2 minutes.
7. Sift once through a 250-μm sieve.
8. Add to the first step, and mix for 1 to 2 minutes.
9. Sift items 8, 11, 4, and 12 once through a 1000-μm sieve, and collect in a stainless steel drum.
10. Add the sieved materials from the above steps to the stainless steel drum.
11. Mix in a drum blender for 2 to 3 minutes.
12. Mix items 10, 9, and 1 in a polyethylene bag for 1 to 2 minutes.
13. Sift twice through a 500-μm sieve.
14. Add 25.0 to 30.0 g of granules to the lubricant mixture.
15. Mix for 1 to 2 minutes.
16. Add this mixture to the granules.
17. Mix in a drum blender for 1 minute.
18. Check the moisture content (limit: moisture content NMT 3.5%).
19. Check temperature and humidity before beginning compression (limit: relative humidity, 40–50%; temperature, 20–25°C).
20. Compress into 1300-mg tablets, using 16-mm punches.
21. Fill appropriate amounts for lower strength (e.g., 100 mg tablets in 10-mm punches).

Vitamin C Chewable Tablets with Dextrose

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Ascorbic acid (crystalline); use ascorbic acid (coated, 97.5%), EC	110.00
500.00	2	Dextrose	500.00
4.00	3	Kollidon® 90F	4.00
30.00–50.00	4	Water and/or isopropanol	30.00–50.00
6.00	5	PEG-6000 (powder)	6.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 4 and 5 (in a fluidized bed), sieve, add item 6, and press with high-compression force.
2. Compress into 620-mg tablets, using 12-mm biplanar punches.
3. If no fluidized bed is available, use of water as a granulation solvent should be avoided.
4. The use of coated ascorbic acid does not increase the stability.

Vitamin C Chewable Tablets with Fructose

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
120.00	1	Ascorbic acid (powder)	120.00
500.00	2	Fructose	500.00
200.00	3	Ludipress®	200.00
100.00	4	Avicel™ PH101	100.00
15.00	5	Kollidon® VA 64	15.00
4.00	6	Aerosil® 200	4.00
35.00	7	PEG-6000 (powder)	35.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 970-mg tablets, using 12-mm biplanar punches.

Vitamin C Chewable Tablets with Sucrose

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Ascorbic acid	500.00
850.00	2	Sucrose, crystalline	850.00
575.00	3	Avicel™ PH 101	575.00
60.00	4	Kollidon® VA 64	60.00
15.00	5	Magnesium stearate	15.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with medium-compression force.
2. Compress into 2000-mg tablets, using 20-mm biplanar punches.

Vitamin C Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Vitamin C (as ascorbic acid)	1000.00
800.00	2	Tartaric acid (fine crystals)	800.00
1000.00	3	Sodium bicarbonate	1000.00
0.50	4	Riboflavin	0.50
20.00	5	Saccharin sodium	20.00
20.00	6	Sodium chloride (milled)	20.00
50.00	7	Lime flavor	50.00
1709.50	8	Sugar (fine crystals)	1709.50
QS	9	Alcohol	QS

Manufacturing Directions

1. All operations must be carried out at a relative humidity of less than 40% at 25°C.
2. Active substance granulate: If saccharin sodium is lumpy, sieve it by means of a centrifugal granulator (1 mm) or a 3-mm band sieve.
3. Suck into the mixer the entire amount of sugar, ascorbic acid, tartaric acid, and saccharin sodium (previously sieved, if required), together with 1st part sieved sodium bicarbonate (open filter, closed bypass; jacket temperature of 40°C); backflash filter twice, evacuate to ~800 mbar, and close filter.
4. Mix with mixer for approximately 10 minutes (jacket temperature 40°C) at a speed of 50 rpm.
5. Turn off the mixer, and evacuate to 10 mbar (open filter, closed bypass; jacket temperature of 40°C).
6. Separately dissolve or suspend riboflavin in alcohol.
7. Suck this granulating liquid into the evacuated vessel at a mixer speed of 30 rpm (closed filter, closed bypass; jacket temperature of 40°C).
8. With jacket heating turned off, granulate up to a product temperature of 60°C at a mixer speed of 110 rpm (time required is approximately 20–25 minutes).
9. At a jacket temperature of 56°C and a mixer rotation speed of approximately 15 rpm, dry for 2 to 5 minutes (closed filter, open bypass).
10. When dust develops in the course of further drying, close the bypass and open the filter.
11. At a mixer speed of 20 rpm and interval setting (2 minutes/15 seconds), continue the drying at a jacket temperature of approximately 58°C and vacuum of 10 mbar until a total drying time of 10 to 20 minutes is reached.
12. Sieve the active substance granulate by sucking it by means of vacuum at a jacket temperature of approximately 59°C and a mixer speed of 20 rpm through a Buehler universal mill (1.5-mm screen) directly into a suitable container.
13. Preferable relative humidity of the active substance is less than 10%.
14. Sieve milled sodium chloride and lime flavor through a round hand sieve (1 mm) with a diameter of approximately 38 cm; add to sieved sodium carbonate (2nd part) in a mixing drum, and mix (e.g., tumble mix, 19 rpm for 10 minutes).
15. Combine this dry mix (sucked by vacuum) with the active substance granulate.
16. Finally, add the remaining sieved and lump-free sodium bicarbonate (3rd part).
17. Mix the mixture that is ready for compression for 45 minutes.
18. The preferable relative humidity of the mixture is less than 20%.
19. In a suitable rotary tablet press, compress effervescent tablets with a weight of 4600 mg and a hardness of 8 kpi.

Vitamin C Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Ascorbic acid, (powder)	112.00
200.00	2	Sorbitol (instant)	200.00
1000.00	3	Anhydrous citric acid	1000.00
587.00	4	Sodium bicarbonate	587.00
65.00	5	PEG-6000 (powder)	65.00
10.00	6	Lemon flavor	10.00
25.00	7	Cyclamate sodium	25.00
1.00	8	Saccharin sodium	1.00

Manufacturing Directions

1. Dry the sodium bicarbonate for 1 hour at 100°C, mix with the other components, pass all through a 0.8-mm sieve, and press with high-compression force at a maximum atmospheric relative humidity of 30%.
2. Compress into 2050-mg tablets, using 20-mm biplanar punches.

Vitamin C Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1000.00	1	Ascorbic acid (crystalline)	1000.00
800.00	2	Sorbitol (crystalline)	800.00
150.00	3	Anhydrous citric acid	150.00
660.00	4	Sodium bicarbonate	660.00
80.00	5	PEG-6000 (powder)	80.00
QS	6	Lemon flavor	QS
QS	7	Cyclamate sodium	QS
QS	8	Saccharin sodium	QS

Manufacturing Directions

1. Dry the sodium bicarbonate for 1 hour at 100°C, mix with the other components, pass all through a 0.8-mm sieve, and press with high-compression force at a maximum atmospheric relative humidity of 30%.
2. Compress into 2690-mg tablets, using 20-mm biplanar punches.

Vitamin C Effervescent Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
500.00	1	Sodium hydrogen carbonate	500.00
430.00	2	Tartaric acid	430.00
8.00	3	Kollidon® 25	8.00
0.20	4	2-Propanol	200.00 mg
550.00	5	Ascorbic acid (crystalline)	550.00
660.00	6	Sucrose	660.00
67.00	7	PEG-6000 (powder)	67.00
67.00	8	Dextrose (powder)	67.00
10.00	9	Orange flavor	10.00
1.00	10	Saccharin sodium	1.00

Manufacturing Directions

1. Granulate mixture of items 1 and 2 with solution of items 2 and 3, pass through a 0.5-mm sieve, and dry at 60°C.
2. Dry mixture of items 5 and 6 at 60°C.
3. Mix together with the previous granules and with items 7 to 10.
4. At a maximum atmospheric relative humidity of 30%, press to effervescent tablets.
5. Compress into 2300-mg tablets, using 20-mm biplanar punches.

Vitamin C Tablets

Manufacturing Directions

1. A 5% by weight vitamin C containing tablet is produced in the following manner for a batch size of 100000 tablets (100 kg).
2. The following components are fine screened (Frewitt screening machine) to a 1.0-mm mesh size and mixed for 10 minutes in a tumbling drum mixer in a V2A high-grade steel container (200 L): Ascorbic acid 5000 g; Glucose 1H.sub.2O 89000 g Cellulose powder (tabletting aid K) 4000 g Poly(1-vinyl-2-pyrrolidone 1000 g 25000 (Kollidone 25).
3. Thereafter, 1000 g of magnesium stearate are then screened in by hand and mixed for 2 minutes in the tumbling drum mixer and compressed.

Vitamin C Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Ascorbic acid (coated)	104.00
2.40	2	Anhydrous colloidal silica (Aerosil® 200)	2.40
60.00	3	Cellulose (microcrystalline) (Avicel™ PH102)	60.00
0.13	4	FD&C Yellow Dye No.10 lake	0.13
37.00	5	Lactose (spray-dried)	37.00
3.20	6	Glyceryl behenate (glyceryl monostearate)	3.20
2.40	7	Stearic acid (fine powder)	2.40
1.00	8	Magnesium stearate	1.00

Manufacturing Directions

1. Processing should be done under controlled temperature and humidity (limit: relative humidity, 40–50%; temperature, 20–25°C).
2. Mix items 5 and 4 in a polyethylene bag for 1 to 2 minutes.
3. Sift twice through a 630-μm sieve.
4. Collect in a polyethylene bag.
5. Check the uniformity of dispersion.
6. If required, sift again.
7. Sift item 3.
8. Sift mixture from first step and item 2 through a 630-μm sieve.
9. Load into a drum blender.
10. Sift item 4 through a 630-μm sieve.
11. Load into the mix in the drum blender.
12. Mix items 6, 7, and 8 in a polyethylene bag for 1 to 2 minutes.

14. Sift through a 250-μm sieve.
15. Collect in a polyethylene bag.
16. Add 13.33 to 20.00 g of granules to the lubricant mixture.
17. Mix for 1 to 2 minutes.
18. Add this to the mix in a stainless steel drum blender.
19. Mix in a drum blender for 2 minutes.
20. Check the temperature and humidity before beginning compression (limit: relative humidity, 40–45%; temperature, 20–25°C).
21. Compress into 210-mg tablets, using 8-mm round concave punches.

Vitamin C Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Ascorbic acid (powder)	100.00
232.00	2	Ludipress®	232.00
1.00	3	Magnesium stearate	1.00

Manufacturing Directions

1. Mix all components, sieve, and press into 335-mg tablets.
2. Compression force affects disintegration time.

Vitamin C Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ascorbic acid (powder)	200.00
231.00–256.00	2	Ludipress®	231.00–256.00
25.00	3	Kollidon® VA 64	25.00
15.00	4	Kollidon® CL	15.00
1.20	5	Aerosil® 200	1.20
2.50	6	Magnesium stearate	2.50

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm screen, and press with medium-compression force (18 kN).
2. Compress into 499-mg tablets, using 12-mm biplanar punches.

Vitamin E Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Vitamin E acetate (SD 50)	200.00
493.00	2	Ludipress®	493.00
390.00	3	Sorbitol (crystalline)	390.00
100.00	4	Mannitol	100.00
400.00	5	Dicalcium phosphate (granulated with 5% Kollidon® 30)	400.00
7.00	6	Aerosil® 200	7.00
3.00	7	Magnesium stearate	3.00

Manufacturing Directions

1. Mix all components, pass through a 0.8-mm screen, and press with high-compression force.
2. Compress into 711-mg tablets, using 12-mm biplanar punches.

Vitamin E Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
150.00	1	Vitamin E acetate (dry powder, 50%)	300.00
300.00	2	Sorbitol	300.00
6.00	3	Aerosil® 200	6.00
0.20	4	Saccharin sodium	0.20
6.00	5	Magnesium stearate	6.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 620-mg tablets, using 12-mm biplanar punches.

Vitamin E Chewable Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
400.00	1	Vitamin E acetate (dry powder, SD 50)	800.00
790.00	2	Ludipress®	790.00
20.00	3	Aerosil® 200	20.00
QS	4	Flavors	QS

Manufacturing Directions

1. Pass all components through a 0.5-mm sieve, mix, and press with high-compression force.
2. Compress into 1665-mg tablets, using 20-mm biplanar punches.

Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Vitamin E acetate (dry powder, SD 50)	100.00
140.00	2	Mannitol	140.00
140.00	3	Tablettose®	140.00
15.00	4	Kollidon® VA 64	15.00
2.00	5	Magnesium stearate	2.00
10.00	6	Aerosil® 200	10.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 410-mg tablets, using 12-mm biplanar punches.

Vitamin E Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Vitamin E acetate (dry powder, SD 50)	100.00
300.00	2	Sorbitol (crystalline)	300.00
3.00	3	Magnesium stearate	3.00
3.00	4	Aerosil® 200	3.00

Manufacturing Directions

1. Pass all components through a 0.8-mm sieve, mix, and press with high-compression force.
2. Compress into 413-mg tablets, using 12-mm biplanar punches.

Voltaren Enteric-Coated Tablets (25 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
25.00	1	Diclofenac sodium	25.00
44.20	2	Lactose Spray Dried	44.20
25.00	3	Microcrystalline cellulose (Avicel PH102)	25.00
2.00	4	Povidone K30	2.00
3.00	5	Sodium starch glycolate	3.00
0.80	6	Magnesium stearate	0.80
18.60	7	Eudragit L30 D, 30% dispersion (Methacrylic acid copolymer)	18.60
0.50	8	Triethyl Citrate (Eudraflex)	0.50
1.00	9	Talc	1.00
–	10	Water, purified	15.00
2.00	11	Hydroxylpropylmethyl cellulose	2.00
0.40	12	Polyethylene glycol 6000	0.40
0.30	13	Talc	0.30
0.70	14	Titanium dioxide	0.70
0.25	15	D&C Yellow No. 10 Aluminum Lake	0.25
–	16	Water, purified	35.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass item 1, item 4 and item 5 through 0.5-mm sieve and charge in step 1.
3. Pass item 3 through 0.7-mm sieve and charge to step 1.
4. Mix step 1 for 20 minutes using tumbler.
5. Pass item 6 through 0.250-mm sieve and add to step 4.
6. Mix step 5 for 2 minutes.
7. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).
8. Charge item 10 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring.
9. Add item 8 and item 9 one by one to step 8 with stirring. Stir for 5 minutes.
10. Load core tablets from step 7 in coating pan and apply coating dispersion from step 9 to get 6.0% to 6.5% weight gain.
11. 11 Charge item 16 in a stainless steel vessel. Add item 11 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxylpropylmethyl cellulose.
12. Add item 12, Item13, item 14 and item 15 one by one to step 11 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Check that coating dispersion is clear and lump free. Pass the coating dispersion through 180-mm sieve (if required).
13. Apply coating dispersion from step 12 to step 10.

Voltaren Enteric-Coated Tablets (50 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
50.00	1	Diclofenac sodium	50.00
68.25	2	Lactose Spray Dried	68.25
45.00	3	Microcrystalline cellulose (Avicel PH102)	45.00
5.00	4	Povidone K30	5.00
5.25	5	Sodium starch glycolate	5.25
1.50	6	Magnesium stearate	1.50
32.38	7	Eudragit L30 D, 30% dispersion (Methacrylic acid copolymer)	32.38
0.875	8	Triethyl Citrate (Eudraflex)	0.875
2.00	9	Talc	2.00
–	10	Water, purified	25.00
3.50	11	Hydroxylpropylmethyl cellulose	3.50
0.70	12	Polyethylene glycol 6000	0.70
0.50	13	Talc	0.50
1.20	14	Titanium dioxide	1.20
0.20	15	FD&C Blue No. 1 Aluminum Lake	0.20
–	16	Water, purified	55.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1, 4, and 5 through 0.5-mm sieve and charge in step 1.
3. Pass item 3 through 0.7-mm sieve and charge to step 1.
4. Mix step 1 for 20 minutes using tumbler.
5. Pass item 6 through 0.250-mm sieve and add to step 4.
6. Mix step 5 for 2 minutes.
7. Compress into 175-mg tablets, using a suitable punch (8.0 mm, round).
8. Charge item 10 in a stainless steel vessel. Add item 7 slowly to the vortex while stirring.
9. Add item 8 and item 9 one by one to step 8 with stirring. Stir for 5 minutes.
10. Load core tablets from step 7 in coating pan and apply coating dispersion from step 9 to get 6.0% to 6.5% weight gain.
11. 11 Charge item 16 in a stainless steel vessel. Add item 11 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
12. Add item 12, Item13, item 14 and item 15 one by one to step 11 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Check that coating dispersion is clear and lump free. Pass the coating dispersion through 180-mm sieve (if required).
13. Apply coating dispersion from step 12 to step 10.

Voltaren Enteric-Coated Tablet (75 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
75.00	1	Diclofenac sodium	75.00
124.50	2	Lactose Monohydrate	124.50
75.00	3	Microcrystalline cellulose (Avicel PH102)	75.00
12.00	4	Povidone K30	12.00
10.50	5	Sodium starch glycolate	10.50
3.00	6	Magnesium stearate	3.00
–	7	Ethanol 95%	45.00
55.50	8	Eudragit L30 D, 30% dispersion (Methacrylic acid copolymer)	55.50
1.50	9	Triethyl Citrate (Eudraflex)	1.50
3.00	10	Talc	3.00
–	11	Water, purified	45.00
4.50	12	Hydroxylpropylmethyl cellulose	4.50
0.90	13	Polyethylene glycol 6000	0.90
0.90	14	Talc	0.90
2.00	15	Titanium dioxide	2.00
0.20	16	Red Ferric Oxide	0.20
–	17	Water, purified	60.00

Manufacturing Directions

1. Dissolve item 4 in item 7 in a stainless steel container.
2. Pass item 2, item 1 and half quantity of item 3 (37.5 g) through 0.5-mm sieve and mix well.
3. Charge step 2 in a granulator.
4. Knead step 3 with solution of step 1 for 5 to 10 minutes until a loose, moist mass is obtained.
5. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
6. Spread step over paper-lined trays, and dry at 45°C to 50°C for 8 hours (the relative humidity over the granules should be 20–35%).
7. Pass the dried granules through a 1.25-mm sieve granulator.
8. Transfer the granules to a tumbler.
9. Pass item 5 and the remaining half quantity of item 9 through 0.5-mm sieve and add to step 8 and mix for 15 minutes.
10. Pass item 6 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 300-mg tablets, using a suitable punch (10.5 mm, round).
13. Charge item 11 in a stainless steel vessel. Add item 8 slowly to the vortex while stirring.
14. Add item 9 and item 10 one by one to step 13 with stirring. Stir for 5 minutes.
15. Load core tablets from step 12 in coating pan and apply coating dispersion from step 14 to get 6.0% to 6.5% weight gain.
16. Charge item 17 in a stainless steel vessel. Add item 12 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
17. Add item 13, Item14, item 15 and item 16 one by one to step 11 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Check that coating dispersion is clear and lump free. Pass the coating dispersion through 180-mm sieve (if required).
18. Apply coating dispersion from step 17 to step 15.

VYTORIN Tablets (10 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Ezetimibe	10.00
10.00	2	Simvastatin	10.00
50.16	3	Lactose Monohydrate	50.16
25.00	4	Microcrystalline cellulose (Avicel PH102)	25.00
0.02	5	Butylated hydroxyanisole	0.02
1.50	6	Citric acid monohydrate	1.50
0.02	7	Propyl gallate	0.02
2.50	8	Croscarmellose sodium	2.50
0.80	9	Magnesium stearate	0.80
–	10	Water, purified	10.00
–	11	Ethanol 95%	5.00
2.20	12	Hydroxylpropylmethyl cellulose	2.20
–	13	Water, purified	20.00

Manufacturing Directions

1. Dissolve item 6 in item 10 in a stainless steel container.
2. Dissolve item 5 and item 7 one by one in item 11 in another stainless steel container.
3. Mix step 2 with step 1.
4. Pass items 3, 1, and 2 through 0.5-mm sieve and mix well.
5. Charge step 4 in a granulator.
6. Knead step 5 with solution of step 3 for 5 to 10 minutes until a loose, moist mass is obtained.
7. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
8. Spread step over paper-lined trays, and dry at 45°C to 50°C for 8 hours (the relative humidity over the granules should be 20–35%).
9. Pass the dried granules through a 1.25-mm sieve granulator.
10. Transfer the granules to a tumbler.
11. Pass items 4 and 8 through 0.5-mm sieve and add to step 10 and mix for 15 minutes.
12. Pass item 9 through 0.250-mm sieve and add to step 11.
13. Mix step 12 for 2 minutes.
14. Compress into 100-mg tablets, using a suitable punch (6.0 mm, round).
15. Charge item 13 in a stainless steel vessel. Add item 12 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
16. Load core tablets from step 14 in coating pan and apply coating dispersion from step 15 to get 1.5% to 1.8% weight gain.

VYTORIN Tablets (10 mg/20 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Ezetimibe	10.00
20.00	2	Simvastatin	20.00
75.24	3	Lactose monohydrate	75.24
37.50	4	Microcrystalline cellulose (Avicel PH102)	37.50
0.03	5	Butylated hydroxyanisole	0.03
2.25	6	Citric acid monohydrate	2.25
0.03	7	Propyl gallate	0.03
3.75	8	Croscarmellose sodium	3.75
1.20	9	Magnesium stearate	1.20
–	10	Water, purified	15.00
–	11	Ethanol 95%	7.50
3.3	12	Hydroxylpropylmethyl cellulose	3.3
–	13	Water, purified	30.00

Manufacturing Directions

1. Dissolve item 6 in item 10 in a stainless steel container.
2. Dissolve item 5 and item 7 one by one in item 11 in another stainless steel container.
3. Mix step 2 with step 1.
4. Pass items 3, 1, and 2 through 0.5-mm sieve and mix well.
5. Charge step 4 in a granulator.
6. Knead step 5 with solution of step 3 for 5 to 10 minutes until a loose, moist mass is obtained.
7. Granulate the moist mass using a centrifugal granulator with a 7-mm sieve.
8. Spread step over paper-lined trays, and dry at 45°C to 50°C for 8 hours (the relative humidity over the granules should be 20–35%).
9. Pass the dried granules through a 1.25-mm sieve granulator.
10. Transfer the granules to a tumbler.
11. Pass items 4 and 8 through 0.5-mm sieve and add to step 10 and mix for 15 minutes.
12. Pass item 9 through 0.250-mm sieve and add to step 11.
13. Mix step 12 for 2 minutes.
14. Compress into 150-mg tablets, using a suitable punch (7.5 mm × 6.0 mm, oval).
15. Charge item 13 in a stainless steel vessel. Add item 12 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxylpropylmethyl cellulose.
16. Load core tablets from step 14 in coating pan and apply coating dispersion from step 15 to get 1.5% to 1.8% weight gain.

Warfarin Tablets (1, 2, 2.5, 3, 4, 5, 6, 7.5, and 10 mg), Coumadin

Warfarin Sodium Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
11.470	1	Starch (maize)	11.470
0.215	2	Dye	0.215
0.119	3	Dye	0.119
3.020	4	Starch (maize)	3.020
–	5	Water, purified, ca	9.000
37.000	6	Cellulose microcrystalline	37.000
126.310	7	Lactose monohydrate	126.310
1.000	8	Warfarin sodium anhydrous[a]	1.000
0.930	9	Magnesium stearate	0.930
0.930	10	Amberlite (RP-88) ion exchange resin	0.930

[a]Factored quantity; adjust with lactose. Dyes are selected to color-code different strengths for safety.

Manufacturing Directions

Caution: Warfarin is poisonous. Wear a dust mask when handling. Send a 5-g sample to redetermine factor before granulating.

1. Granulation
   a. Roughly blend cornstarch (item 1) with dyes, and mill through a #80-mesh (117-μm aperture or similar) screen.
   b. Rough blend 200 mg of colored starch mixture from step A with cornstarch (item 4).
   c. Make a starch paste using the colored starch mixture from step 1b and approximately 18 mL purified water. *Note:* Starch paste should be smooth and thin. A thick starch paste will cause dye spots.
   d. Rough blend the remaining colored starch mixture from step 1a with the following items: cellulose microcrystalline, lactose, and warfarin sodium, and mill through a 30-mesh (600-μm aperture or similar) screen.
   e. Charge the milled material into a day mixer (or similar) and blend for 10 minutes. Mass with hot starch paste. The addition of starch paste should be finished in 2 minutes. Mass for another 15 minutes using additional purified water, if necessary. Record the amount of purified water added. (*Note:* Do not over wet or mass for too long.)
   f. Granulate through a 5/8-in. (15.88-mm aperture or similar) band.
   g. Dry overnight at 49°C to not more than a 1.5% LOD at 105°C.
      Note: Protect the granules from moisture from this step on. Make sure that the relative humidity is not greater than 40% at 24°C (54 grains).
   h. Sift and grind through a #30-mesh (600-μm aperture or similar) screen.
   i. Or, sift the dried granulation through a #20-mesh (840-μm aperture or similar) screen, and mill the coarse material through a #20-mesh (840-μm aperture or similar) screen using FitzMill (or similar), with knives forward, at medium speed.
2. Lubrication
   a. Charge the granulation into the blender.
   b. Sift magnesium stearate and Amberlite through a #30-mesh (600-μm aperture, or similar) screen into a partial drum of granulation. Mix by hand, and charge into a blender.
   c. Add the remaining granulation to a blender, and blend for 10 minutes.
   d. Discharge the blender into polyethylene-lined drums.
3. Compression: Compress using an 8-mm round flat, beveledged punch. The weight of 10 tablets is 1.85 g; thickness is 2.7 to 2.9 mm. Different dyes and different strengths of warfarin sodium can be adjusted with lactose.

YASMIN Tablet (3 mg/0.03 mg)—Active Film-Coated Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
3.00	1	Drospirenone	3.00
0.03	2	Ethinyl estradiol	0.03
74.47	3	Lactose Spray Dried	74.47
5.00	4	Cornstarch	5.00
1.80	5	Povidone K25	1.80
5.00	6	Starch 1500	5.00
0.70	7	Magnesium stearate	0.70
2.00	8	Hydroxylpropylmethyl cellulose	2.00
0.40	9	Polyethylene glycol 6000	0.40
0.30	10	Talc	0.30
0.60	11	Titanium dioxide	0.60
0.20	12	Yellow ferric oxide	0.20
–	13	Water, purified	30.00

Manufacturing Directions

1. Pass item 3 through 0.7-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 2, 4, 5, and 6 through 0.5-mm sieve and collect in a stainless steel container and mix well.
4. Add 5% (=1.9 g) powder from step 1 to step 3 and mix well.
5. Add 10% (=3.8 g) powder from step 1 to step 4 and mix well.
6. Add 15% (=5.7 g) powder from step 1 to step 5 and mix well.
7. Transfer step 6 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 7 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 90-mg tablets, using a suitable punch (5.5 mm, round).
13. Charge item 13 in a stainless steel vessel. Add item 8 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxylpropylmethyl cellulose.
14. Add items 9 to 12 one by one to step 13 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
15. Load core tablets from step 12 in coating pan and apply coating dispersion from step 14 to get 2.5% to 3.0% weight gain.

YASMIN Tablet—Inert Film-Coated Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
92.20	1	Lactose Spray Dried	92.20
5.00	2	Cornstarch	5.00
2.00	3	Povidone K25	2.00
0.80	4	Magnesium stearate	0.80
2.00	5	Hydroxylpropylmethyl cellulose	2.00
0.30	6	Talc	0.30
0.60	7	Titanium dioxide	0.60
–	8	Water, purified	30.00

Manufacturing Directions

1. Pass items 1 to 3 through 0.7-mm sieve and collect in a tumbler.
2. Mix step 1 for 5 minutes using tumbler.
3. Pass item 4 through 0.250-mm sieve and add to step 2.
4. Mix step 3 for 1 minute.
5. Compress into 100-mg tablets, using a suitable punch (4.5 mm × 4.5 mm square).
6. Charge item 8 in a stainless steel vessel. Add item 5 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxylpropylmethyl cellulose.
7. Add items 6 and 7 to step 6 with stirring. Stir for 10 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
8. Load core tablets from step 5 in coating pan and apply coating dispersion from step 7 to get 2.0% to 2.5% weight gain.

Zolmitriptan Orally Disintegrating Tablets (2.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Zolmitriptan	2.50
64.80	2	Mannitol DC Grade	64.80
10.00	3	Microcrystalline cellulose	10.00
2.50	4	Crospovidone	2.50
1.00	5	Aspartame	1.00
8.00	6	Sodium bicarbonate	8.00
8.00	7	Citric acid anhydrous	8.00
2.00	8	Orange flavor	2.00
0.70	9	Colloidal silicon dioxide (Aeosil-200)	0.70
0.50	10	Magnesium stearate	0.50

Manufacturing Directions

1. Pass items 2 and 7 through 1-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, 5, and 8 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (=5.5 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass items 3, 6, and 9 through 0.5-mm sieve and add to step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 10 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).

Zolmitriptan Orally Disintegrating Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Zolmitriptan	5.00
62.30	2	Mannitol DC grade	62.30
10.00	3	Microcrystalline cellulose	10.00
2.50	4	Crospovidone	2.50
1.00	5	Aspartame	1.00
8.00	6	Sodium bicarbonate	8.00
8.00	7	Citric acid anhydrous	8.00
2.00	8	Orange flavor	2.00
0.70	9	Colloidal silicon dioxide (Aeosil-200)	0.70
0.50	10	Magnesium stearate	0.50

Manufacturing Directions

1. Pass items 2 and 7 through 1-mm sieve and collect in a stainless steel container.
2. Charge half quantity of step 1 in a tumbler.
3. Pass items 1, 4, 5, and 8 through 0.5-mm sieve and collect in a stainless steel container.
4. Add 15% (=5.2 g) powder from step 1 to step 3 and mix well.
5. Transfer half quantity from step 4 into step 2.
6. Pass items 3, 6, and 9 through 0.5-mm sieve and add to step 2.
7. Transfer the remaining half quantity of step 4 into step 2.
8. Transfer balance quantity of step 1 into step 2.
9. Mix step 2 for 20 minutes using tumbler.
10. Pass item 10 through 0.250-mm sieve and add to step 9.
11. Mix step 10 for 2 minutes.
12. Compress into 100-mg tablets, using a suitable punch (5.0 mm × 5.5 mm, oval).

Zolmitriptan Tablets (2.5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
2.50	1	Zolmitriptan	2.50
58.70	2	Lactose Spray Dried	58.70
35.00	3	Microcrystalline cellulose (Avicel PH102)	35.00
3.00	4	Sodium starch glycolate	3.00
0.80	5	Magnesium stearate	0.80
2.20	6	Hydroxypropyl methylcellulose	2.20
0.40	7	Polyethylene glycol 4000	0.40
0.70	8	Titanium dioxide	0.70
0.20	9	Yellow Iron Oxide	0.20
–	10	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass item 1 and item 4 through 0.5-mm sieve and collect in a stainless steel container.
3. Add 5% (=3.0 g) Lactose from step 1 to step 2 and mix well.
4. Add 10% (=5.8 g) Lactose from step 1 to step 3 and mix well.
5. Transfer step 4 into step 1.
6. Pass item 3 through 0.7-mm sieve and charge to step 1.
7. Mix step 1 for 20 minutes using tumbler.
8. Pass item 5 through 0.250-mm sieve and add to step 7.
9. Mix step 8 for 2 minutes.
10. Compress into 100-mg tablets, using a suitable punch (5.5 mm, round).
11. Charge item 10 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of Hydroxypropyl methylcellulose.
12. Add items 7 to 9 one by one to step 10 with stirring. Stir for 5 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
13. Load core tablets from step 10 in coating pan and apply coating dispersion from step 12 to get 2.5% to 3.0% weight gain.

Zolmitriptan Tablets (5 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
5.00	1	Zolmitriptan	5.00
56.20	2	Lactose Spray Dried	56.20
35.00	3	Microcrystalline cellulose (Avicel PH102)	35.00
3.00	4	Sodium starch glycolate	3.00
0.80	5	Magnesium stearate	0.80
2.20	6	Hydroxypropyl methylcellulose	2.20
0.40	7	Polyethylene glycol 4000	0.40
0.70	8	Titanium dioxide	0.70
0.20	9	Red Iron Oxide	0.20
–	10	Water, purified	30.00

Manufacturing Directions

1. Pass item 2 through 0.7-mm sieve and charge in a tumbler.
2. Pass items 1 and 4 through 0.5-mm sieve and collect in a stainless steel container.
3. Add 10% (=5.6 g) Lactose from step 1 to step 2 and mix well.
4. Transfer step 3 into step 1.
5. Pass item 3 through 0.7-mm sieve and charge to step 1.
6. Mix step 1 for 20 minutes using tumbler.
7. Pass item 5 through 0.250-mm sieve and add to step 6.
8. Mix step 7 for 2 minutes.
9. Compress into 100-mg tablets, using a suitable punch (5.0 mm × 5.5 mm, oval).
10. Charge item 10 in a stainless steel vessel. Add item 6 slowly to the vortex while stirring. Stir till lumps

dissolved. Homogenize for 5 minutes. Keep for 3 to 4 hours for saturation of hydroxypropyl methylcellulose.
11. Add item 7, item 8 and item 9 one by one to step 10 with stirring. Stir for 5 minutes. Homogenize for 5 minutes. Pass the coating dispersion through 180-mm sieve (if required).
12. Load core tablets from step 9 in coating pan and apply coating dispersion from step 11.

Zolmitriptan Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
1.25	1	Zolmitriptan	1.25
0.12	2	Talc	0.12
0.15	3	Polyvinylpyrrolidone	0.15
Qs	4	Water	Qs
Qs	5	Ethanol	Qs
60.00	6	Sugar spheres	60.00
6.00	7	Eudragit S	6.00
3.00	8	Triethyl citrate	3.00
1.50	9	Talc	1.50
0.105	10	Ammonium hydroxide 1N solution	0.105
3.10	11	Hydroxypropyl methyl cellulose	3.10
0.40	12	Polyethylene glycol	0.40
0.50	13	Flavor optional	0.50
0.50	14	Color optional	0.50
Qs	15	Water	Qs
qs	16	Ethanol	qs

Manufacturing Directions

1. Prepare a dispersion containing Zolmitriptan and talc in polyvinylpyrrolidone solution prepared in water and/or ethanol or a mixture thereof.
2. Apply or spray solution (1) onto the sugar spheres using a coating pan or a fluid-bed coater until a desired amount of solution (1) is applied.
3. The coated spheres may be further seal-coated with a solution containing polyvinylpyrrolidone prepared in water and/or ethanol or a mixture thereof.
4. Prepare the coating solution by mixing water, Eudragit S100, ammonium hydroxide solution, triethyl citrate and talc to form a uniform dispersion.
5. Coat Zolmitriptan beads (from (3)) with Eudragit S coating solution using a coating pan or a fluid-bed coater until a desired coat weight is achieved.
6. Seal Coat of the Enteric-Coated Zolmitriptan Beads: Prepare a coating solution of Hydroxypropyl methylcellulose and polyethylene glycol in water or ethanol or combination thereof.
7. Coat zolmitriptan enteric-coated beads (step (5)) with the above coating solution in a coating pan or a fluid-bed coater until a desired coating weight is obtained for tablets containing 1.25 or 2.50 mg zolmitriptan.

Zolpidem Hemitartarate Tablets

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Zolpidem hemitartrate	10.00
91.00	2	Lactose monohydrate	91.00
12.00	3	Microcrystalline cellulose	12.00
2.52	4	Hydroxypropyl methyl cellulose	2.52
3.84	5	Sodium carboxymethyl cellulose	3.84
0.72	6	Magnesium stearate	0.72
–	7	Water, purified	QS

Manufacturing Directions

1. Mix items 1 to 4, and blend for 10 minutes.
2. Add item 7 to granulate, dry, and sieve granules.
3. Mix granules with items 5 and 6.
4. Compress into 120-mg tablets.

Zolpidem Tartrate Tablets (5 mg/10 mg), Ambien

Each Ambien® tablet includes the following inactive ingredients: hydroxypropyl methylcellulose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide. The 5-mg tablet also contains FD&C Red No. 40, iron oxide colorant, and polysorbate 80.

Part III

Tablet Coating Formulations

Tablet Coating Formulations

INTRODUCTION

Solid dosage forms are frequently coated for varied purposes, including the following:

- Mask taste and smell.
- Offer protection from the environment.
- Provide protection from gastric acid (enteric coating).
- Make dose easy to swallow.
- Provide identification.
- Add esthetic appeal.
- Hide surface defects.

Many types of coatings are available.

I. Sugar coating: Compressed tablets are coated with colored or uncolored sugar layer that is water-soluble and quickly dissolves after swallowing. The sugar-coat protects the enclosed drug from the environment and provides a barrier to objectionable taste or order. The sugar coat also enhances the appearance of the compressed tablet and permit imprinting manufacturing's information. Sugar coating provides a combination of insulation, taste masking, smoothing the tablet core, and coloring and modified release. The disadvantages of sugar coating are the time and expertise required in the coating process and thus increases size, weight, and shipping costs. Sugar coating process involves five separate operations:

   a. Sealing/water proofing: Prior to applying any sugar/water syrup, the tablet cores must be sealed, thoroughly dried, and free of all residual solvents. The seal coat provides a moisture barrier and hardness to the surface of the tablet in order to minimize attritional effects. Core tablets having very rapid disintegration rates conceivably could start the disintegration process during the initial phase of sugar coating. The sealants are generally water-insoluble polymers/film formers applied from an organic solvent solution. The quantities of material applied as a sealing coat will depend primarily on the tablet porosity, since highly porous tablets will tend to soak up the first application of solution, thus preventing it from spreading uniformly across the surface of every tablet in the batch. Hence, one or more further application of resin solution may be required to ensure that the tablet cores are sealed effectively. Common materials used as a sealant include shellac, zinc sulfate, cellulose acetate phthalate (CAP), polyvinylacetate phthalate, hyroxypropyl cellulose, hydroxypropyl methylcellulose, etc.

   b. Subcoating: Subcoating is the actual start of the sugar coating process and provides the rapid buildup necessary to round up the tablet edge. It also acts as the foundation for the smoothing and color coats. Generally two methods are used for subcoating. Dusting with powder and then drying follows one where the application of gum based solution and the routine repeated until the desired shape is achieved. The other method is where a suspension of dry powder in gum/sucrose solution is applied followed by drying the tablets. Thus subcoating is a sandwich of alternate layer of gum and powder. It is necessary to remove the bulk of the water after each application of coating syrup.

   c. Grossing/smoothing: The grossing/smoothing process is specifically for smoothing and filing the irregularity on the surface generated during subcoating. It also increases the tablet size to a predetermined dimension. If the subcoating is rough with high amount of irregularities, then the use of grossing syrup containing suspended solids will provide more rapid buildup and better filling qualities. Smoothing usually can be accomplished by the application of a simple syrup solution (approximately 60%–70% sugar solid). This syrup generally contains pigments, starch, gelatin, acacia, or opacifier if required. Small quantities of color suspension can be applied to impart a tint of the desired color when there are irregularities in coating.

   d. Color coating: This stage is often critical in the successful completion of a sugar coating process and involves the multiple application of syrup solution (60%–70% sugar solid) containing the requisite coloring matter. Mainly soluble dyes were used in the sugar coating to achieve the desired color, since the soluble dye will migrate to the surface during drying. But nowadays the insoluble certified lakes have virtually replaced the soluble dyes in pharmaceutical tablet coating. The most efficient process for color coating involves the use of a predispersed opacified lake suspension.

   e. Polishing: Sugar-coated tablets need to be polished to achieve a final elegance. Polishing is achieved by applying the mixture of waxes like beeswax, carnubawax, candelila wax, or hard paraffin wax to tablets in polishing pan.

II. Film Coating: Film coating is deposition of a thin film of polymer surrounding the tablet core. Conventional pan equipments may be used but nowadays more sophisticated equipments are employed to have a high degree of automation and coating time. The polymer is solubilized into solvent. Other additives like plasticizers and pigments are added. Resulting solution is sprayed onto a rotated tablet bed. The drying conditions cause removal of the solvent, giving thin deposition of coating material around each tablet core. Usually spray process is employed in preparation of film-coated tablets. Accela cota is the prototype of perforated cylindrical drum providing high drying air capacity. Fluidized bed equipment has made considerable impact where

tablets are moving in a stream of air passing through the perforated bottom of a cylindrical column. With a smaller cylindrical insert, the stream of cores is rising in the center of the device together with a spray mist applied in the middle of the bottom. For fluidized bed coating, very hard tablets (hardness > 20 N) have to be used. The fundamental requirements are independent of the actual type of equipments being used and include adequate means of atomizing the spray liquid for application to the tablet core, adequate mixing and agitation of tablet bed, and sufficient heat input in the form of drying air to provide the latent heat of evaporation of the solvent. This is particularly important with aqueous-based spraying and good exhaust facilities to remove dust and solvent laden air. The materials used in film coating include the following:

a. Film formers
   i. Hydroxypropyl methylcellulose (HPMC): It is available in different viscosity grades. It is a polymer of choice for air suspension and pan spray coating systems because of solubility characteristic in gastric fluid and organic and aqueous solvent systems. The advantages are that it does not affect tablet disintegration and drug availability; it is cheap, flexible, and highly resistant to heat, light, and moisture; it has no taste and odor; and color and other additives can be easily incorporated. The disadvantage are that when it used alone, the polymer has tendency to bridge or fill the debossed tablet surfaces. So mixture of HPMC and other polymers/plasticizers is used.
   ii. Methylhydroxy ethylcellulose (MHEC): It is available in wide variety of viscosity grades. It is not frequently used as HPMC because soluble in fewer organic solvents.
   iii. Ethylcellulose (EC): Depending on the degree of ethoxy substitution, different viscosity grades are available. It is completely insoluble in water and gastric fluids. Hence it is used in combination with water-soluble additives like HPMC and not alone. Unplasticized ethylcellulose films are brittle and require film modifiers to obtain an acceptable film formulation. Aqua coat is aqueous polymeric dispersion utilizing ethyl cellulose. These pseudolatex systems contain high solids, low-viscosity compositions that have coating properties quite different from regular ethyl cellulose solution.
   iv. Hydroxypropyl cellulose (HPC): It is soluble in water below 40°C (insoluble above 45°C), gastric fluid, and many polar organic solvents. HPC is extremely tacky as it dries from solution system. It is used for subcoat and not for color or glass coat. It gives very flexible film.
   v. Povidone: Degree of polymerization decides molecular weight of material. It is available in four viscosity grades i.e. K-15, K-30, K-60, and K-90. Average molecular weight of these grades is 10,000, 40,000, 160,000, and 360,000 respectively. K-30 is widely used as tablet binder and in tablet coating. It has excellent solubility in wide variety of organic solvents, water, gastric, and intestinal fluids. Povidone can be crosslinked with other materials to produce films with enteric properties. It is used to improve dispersion of colorants in coating solution.
   vi. Sodium carboxy methyl cellulose: It is available in medium, high, and extra high-viscosity grades. It is easily dispersed in water to form colloidal solutions but is insoluble in most organic solvents and hence not a material of choice for coating solution based on organic solvents. Films prepared by it are brittle but adhere well to tablets. Partially dried films of are tacky. So coating compositions must be modified with additives.
   vii. Polyethylene glycols (PEG): PEG with low-molecular weights (200–600) are liquid at room temperature and are used as plasticizers. High-molecular weights PEG (900–8000 series) are white, waxy solids at room temperature. Combination of PEG waxes with CAP gives films that are soluble in gastric fluids.
   viii. Acrylate polymers: It is marketed under the name of Eudragit®. Eudragit®E is cationic co-polymer. Only Eudragit®E is freely soluble in gastric fluid up to pH 5 and expandable and permeable above pH 5. This material is available as organic solution (12.5% in isopropanol/acetone), solid material, or 30% aqueous dispersion. Eudragit®RL & RS are copolymers with low content of quaternary ammonium groups. These are available only as organic solutions and solid materials. They produce films for delayed action (pH dependent).
b. Solvents: Mostly solvents are used either alone or in combination with water, ethanol, methanol, isopropanol, chloroform, acetone, methylene chloride, etc. Water is more used because there are no environmental and economic considerations. For drugs that readily hydrolyze in presence of water, nonaqueous solvents are used.
c. Plasticizers: As solvent is removed, most polymeric materials tend to pack together in three-dimensional honey comb arrangement. Both internal and external plasticizing techniques are used to modify the quality of film. Combination of plasticizer may be used to get desired effect. Concentration of plasticizer is expressed in relation to the polymer being plasticized. Recommended levels of plasticizers range from 1% to 50% by weight of the film former. Commonly used plasticizers are castor oil, PG, glycerin, lower molecular weight (200–400 series) PEG, surfactants, etc. For aqueous coating, PEG and PG are more used, while castor oil and spans are primarily used for organic-solvent–based coating solution. External plasticizer should be soluble in the solvent system used for dissolving the film former and plasticizer. The plasticizer and the film former must be at least partially soluble or miscible in each other.
d. Colorants: Colorants can be used in solution form or in suspension form. To achieve proper distribution of suspended colorants in the coating solution, requires the use of the powdered colorants (<10 microns). Most common colorants in use are certified FD & C or D & C colorants. These are synthetic dyes or lakes. Lakes are choice for sugar or film coating as they give reproducible results. Concentration of colorants in the coating solutions depends on the color

shade desired, the type of dye, and the concentration of opaquant-extenders. If very light shade is desired, concentration of less than 0.01% may be adequate; on the other hand, if a dark color is desired, a concentration of more than 2.0% may be required. The inorganic materials (e.g., iron oxide) and the natural coloring materials (e.g., anthrocyanins, carotenoids, etc) are also used to prepare coating solution. Magenta red dye is nonabsorbable in biologic system and resistant to degradation in the gastro intestinal track. Opasray® (opaque color concentrate for film coating) and Opadry® (complete film coating concentrate) are promoted as achieving less lot-to-lot color variation.

e. Opaquant-extenders: These are very fine inorganic powder used to provide more pastel colors and increase film coverage. These inorganic materials provide white coat or mask color of the tablet core. Colorants are very expensive and higher concentration is required. These inorganic materials are cheap. In presence of these inorganic materials, amount of colorants required decreases. Most commonly used materials are titanium dioxide, silicate (talc and aluminum silicates), carbonates (magnesium carbonates), oxides (magnesium oxide), and hydroxides (aluminum hydroxides).
f. Other components: Flavors, sweeteners, surfactants, antioxidants, antimicrobials, etc., may be incorporated into the coating solution.

III. Enteric Coating: The one-layer is applied as one homogenous layer, which can be whites-opaque or colored. The advantage is that is only one application needed. The two-layer system where the enteric formulation is applied first, followed by colored film. Both layers can be of enteric polymer or only the basic layer contains enteric polymer while top layer is fast disintegrating and water-soluble polymer. Polymers used for enteric coating include the following:
   a. Cellulose acetate phthalate (CAP): It is widely used in industry. Aquateric is reconstituted colloidal dispersion of latex particles. It is composed of solid or semisolid polymer spheres of CAP ranging in size from 0.05 to 3 microns. Cellulose acetate trimellitate (CAT) developed as an ammoniated aqueous formulation showed faster dissolution than a similar formulation of CAP. Disadvantages include: It dissolves above pH 6 only, delays absorption of drugs, is hygroscopic and permeable to moisture in comparison with other enteric polymer, and is susceptible to hydrolytic removal of phthalic and acetic acid changing film properties. CAP films are brittle and usually used with other hydrophobic film forming materials.
   b. Acrylate polymers: Eudragit®L & Eudragit®S are two forms of commercially available enteric acrylic resins. Both of them produce films resistant to gastric fluid. Eudragit®L & S are soluble in intestinal fluid at pH 6 & 7 respectively. Eudragit®L is available as an organic solution (Isopropanol), solid or aqueous dispersion. Eudragit®S is available only as an organic solution (Isopropanol) and solid.
   c. Hydroxy propyl methyl cellulose phthalate: HPMCP 50, 55, and 55-s (also called HP-50, HP-55, and HP-55-s) is widely used. HP-55 is recommended for general enteric preparation while HP-50 and HP-55-s for special cases. These polymers dissolve at a pH 5 to 5.5.
   d. Polyvinyl acetate phthalate: It is similar to HP-55 in stability and pH dependent solubility.
   e. Enteric coating can be combined with polysaccharides, which are enzyme degraded in colon, e.g., Cyclodextrin and galactomannan.

IV. Controlled-Release Coating: Polymers like modified acrylates, water insoluble cellulose (ethyl cellulose), etc., used for controlled-release coating.

V. Compressed Coating: This type of coating requires a specialization tablet machine. Compression coating is not widely used but it has advantages in some cases in which the tablet core cannot tolerate organic solvent or water and yet needs to be coated for taste masking or to provide delayed or enteric properties to the finished product and also to avoid incompatibility by separating incompatible ingredients.

VI. Electrostatic Coating: Electrostatic coating is an efficient method of applying coating to conductive substrates. A strong electrostatic charge is applied to the substrate. The coating material containing conductive ionic species of opposite charge is sprayed onto the charged substrate. Complete and uniform coating of corners and adaptability of this method to such relatively nonconductive substrate as pharmaceutical is limited.

VII. Dip Coating: Coating is applied to the tablet cores by dipping them into the coating liquid. The wet tablets are dried in a conventional manner in coating pan. Alternative dipping and drying steps may be repeated several times to obtain the desired coating. This process lacks the speed, versatility, and reliability of spray-coating techniques. Specialized equipment has been developed to dip-coat tablets, but no commercial pharmaceutical application has been obtained.

VIII. Vacuum Film Coating: Vacuum film coating is a new coating procedure that employs a specially designed baffled pan. The pan is hot water jacketed, and it can be sealed to achieve a vacuum system. The tablets are placed in the sealed pan, and the air in the pan is displaced by nitrogen before the desired vacuum level is obtained. The coating solution is then applied with airless spray system. The heated pan causes the evaporation, and the vapor is removed by the vacuum system. Because there is no high-velocity heated air, the energy requirement is low and coating efficiency is high. Organic solvent can be effectively used with this coating system with minimum environmental or safety concerns.

Formulations for tablet coating are often proprietary to various manufacturers as these address several formulation needs as described above. The suppliers of coating ingredients are often very open to sharing the coating technology and companies are highly encouraged to make use of them, more particularly where the coating materials have an open DMF available for regulatory filings. The following companies are a very good source of information:

Eudragit® (http://www.pharma-polymers.com/pharma-polymers/en/eudragit/).
Colorcon® (http://www.colorcon.com/products/coatings).
Methocel/Ethocel (http://www.dow.com/dowexcipients/applications/tablet_coating.htm).

The advantage of using these prepackaged formulations is consistency in color matching, as well as other considerations regarding ease of use. The most significant aspect remains the choice of colors, which often determines the method of manufacturing the coating solutions. With a limited choice of dyes and lakes available for selection, manufacturers often use a combination of several colors and dyes along with agents such as talc for opaqueness to obtain the desired color and protection.

Given below is a current listing of approved colors in various regulatory regions.

Approved Drug Colorants for Internal Use in Japan-1[a]

Name	CAS Number	Color Index Number	Precedent Limit	Compendia
Black Iron Oxide	12227-89-3	77499	1.539 mg	JPE
Caramel			1500 mg	JPE
Carbon Black	1333-86-4	77268:1	0.096 mg	JPE
Carmine	1390-65-4	75470	1.8 mg	JPE
β-Carotene	7235-40-7	40800	0.1%	JPE
Copper Chlorophyll			1.8 mg	Japan Pharmaceutical Codex
Glycyrrhiza Extract			300 mg	JP
Gold Leaf	7440-57-5		14 mg	JPE
Light Anhydrous Silicic Acid	7631-86-9		2.6 g	JP
Medicinal Carbon	16291-96-6		150 mg	JP
2-octyldodecyl Myristate	22766-83-2		100 mg	JPE
Orange Essence			15 mg	JPE
Powdered Green Tea			100 mg	JPE
Red Ferric Oxide	1309-37-1	77491	95.4 mg	JPE
Riboflavin	83-88-5		0.8 mg	JP
Riboflavin Butyrate			0.4 mg	JP
Riboflavin Sodium Phosphate			2 mg	JP
Rose Oil	8007-01-0		0.1 mg	NF
Rye Green Leaf Extract			2 mg	JPE
Sodium Copper Chlorophyllin			75 mg	Japan Pharmaceutical Codex
Sodium Hydroxide	1310-73-2		224 mg	JP
Talc	14807-96-6		3384 mg	JP
Titanium Oxide	13463-67-7	77891	384 mg	JP
Yellow Ferric Oxide	1310-14-1	77492	5.67 mg	JPE

[a]These colorants appear in the application column in the Japanese Pharmaceutical Excipients Directory 2007 (Japanese Version) as coloring agents. Precedent limits are quoted from the Japanese Pharmaceutical Excipients Directory 2007 (Japanese version). Each limit represents the maximum daily intake that a patient should consume from the use of a particular dosage form.

Approved Drug Colorants for Internal Use in Japan-2[*b]

Name	Alternate Name	Color Index Number	CAS Number	Precedent Limit
Amaranth[*d]	Red #2, Acid Red 27	16185	915-67-3	*c
Erythrosine[*d]	Red #3, Acid Red 51	45430	16423-68-0	*c
New Coccine (Ponceau4R)[*d]	Red #102, Acid Red 18	16255	2611-82-7	*c
Phloxine B	Red #104(1), Acid Red 92	45410	18472-87-2	*c
Rose Bengal	Red #105(1), Acid Red 94	45440	632-69-9	*c
Acid Red	Red #106, Acid Red 52	45100		*c
Tartrazine[*d]	Yellow #4, Acid Yellow 23	19140	1934-21-0	*c
Sunset Yellow FCF[*d]	Yellow #5	15985	2783-94-0	*c
Fast Green FCF	Green #3	42053	2353-45-9	*c
Brilliant Blue FCF[*d]	Blue #1	42090	3844-45-9	*c
Indigo Carmine[*d]	Blue #2, Acid Blue 74	73015	860-22-0	*c

[*b]Based on colors approved by the MHWs “Ministerial Ordinance to establish Tar colors which can be used in Pharmaceuticals”; No. 30; August 31, 1966. Aluminum lakes of these colors are also authorized.

[*c]Not more than 0.1% by weight of color (lake or dye) can be used in a dosage form. If one colorant was combined with other colorants, total weight of these colorants must be less than 0.1% of the final product.

[*d]These colorants make the list of the application column in the Japanese Pharmaceutical Excipients Directory 2007 (Japanese Version) as coloring agents.

Approved Drug Colorants for Use in Canada*

I. Colorants approved for internal and external drug use

Color	Alternate Name	Color Index Number	CAS Number
Acid Fuchsin D	D&C Red #33	17200	3567-66-6
Alizarin Cyanine Green F	D&C Green #5	61570	4403-90-1
Allura Red AC	FD&C Red #40	16035	25956-17-6
Amaranth	Delisted FD&C Red #2	16185	915-67-3
Anthocyanin (Derived from juice expressed from fresh edible fruits or vegetables)			
β-APO-8´ Carotenal	–	40820	1107-26-2
Brilliant Blue FCF Sodium Salt	FD&C Blue #0	42090	3844-45-8
Brilliant Blue FCF Ammonium Salt	D&C Blue #4	42090	6371-85-2
Canthaxanthin	–	40850	514-78-3
Caramel	–	–	–
Carbon Black	–	77266	1333-86-4
Carmine	–	75470	1260-17-9
Carmoisine	Azorubine	14720	3567-69-9
β-carotene	–	40800	7235-40-7
Chlorophyll	–	75810	479-61-8
Eosin YS Acid Form	D&C Red #21	45380:2	15086-94-9
Eosin YS Sodium Salt	D&C Red #22	45380	17372-87-1
Erythrosine	FD&C Red #3	45430	16423-68-0
Fast Green FCF	FD&C Green #3	42053	2353-45-9
Flaming Red	D&C Red #36	12085	2814-77-9
Helindone Pink CN	D&C Red #30	73360	2379-74-0
Indigo	D&C Blue #6	73000	482-89-3
Indigotine	FD&C Blue #2`	73015	860-22-0
Iron Oxides	Iron Oxide Red	77491	1309-37-1
	Iron Oxide Yellow	77492	51274-00-1
	Iron Oxide Black	77499	12227-89-3
Lithol Rubin B Sodium Salt	D&C Red #6	15850	5858-81-1
Lithol Rubin B Calcium Salt	D&C Red #7	15850:1	5281-04-9
Phloxine B Sodium Salt	D&C Red #28	45410	18472-87-2
Phloxine B Acid Form	D&C Red #27	45410:1	13473-26-2
Ponceau 4R	–	16255	2611-82-7
Ponceau SX	FD&C Red #4	14700	4548-53-2
Quinoline Yellow WS	D&C Yellow #10	47005	8004-92-0
Riboflavin	–	–	83-88-5
Sunset Yellow FCF	FD&C Yellow #6	15985	2783-94-0
Tartrazine	FD&C Yellow #5	19140	1934-21-0
Titanium Dioxide	–	77891	13463-67-7

II. Colorants approved for external drug use

Color	Alternate Name	Color Index Number	CAS Number
Acid Violet	Ext. D&C Violet #2	60730	–
Alizurol Purple SS	D&C Violet #2	60725	81-48-1
Annatto	–	75120	–
Bismuth Oxychloride	–	77163	–
Chromium Hydroxide Green	Pigment Green 18	77289	–
Dibromofluorescein (Solvent Red 72)	D&C Orange #5	45370:1	–
Deep Maroon	D&C Red #34	15880:1	6417-83-0
Ferric Ferrocyanide	–	77510	–
Guanine	–	75170	–
Orange II	D&C Orange #4	15510	633-96-5
Manganese Violet	–	77742	–
Mica	–	77019	–
Pyranine Concentrated	D&C Green #8	59040	6358-69-6
Quinizarin Green SS	D&C Green #6	61565	128-80-3
Toney Red	D&C Red #17	26100	85-86-9
Uranine Acid Form	D&C Yellow #7	45350:1	7/5/2321
Uranine Sodium Salt	D&C Yellow #8	45350	518-47-8
Zinc Oxide	–	77947	–

Approved Drug Colourants Listed by the European Union*

Note: Aluminum lakes prepared from colours mentioned in this list are also permitted.

Colour	E Number	Colour Index Number	Alternate Names
Allura Red AC	E129	16035	FD&C Red #40
Aluminum	E173	77000	–
Amaranth	E123	16185	Delisted FD&C Red #2
Anthocyanins	E163	–	–
Beet Root Red	E162	–	Betanin
Beta APO-8´-Carotenal	E160e	40820	–
Beta APO-8´-Carotenoic			–
Acidethyl Ester	E160f	40825	
Brilliant Black BN	E151	28440	Black PN
Brilliant Blue FCF	E133	42090	FD&C Blue #1
Brown HT	E155	20285	–
Calcium Carbonate	E170	77220	–
Canthaxanthin	E161g	40850	–
Caramel	E150a	–	–
Caramel,-Caustic Sulphite	E150b	–	–
Caramel,-Ammpnia	E150c	–	–
Caramel, Sulphite Ammonia	E150d	–	–
Carbon Vegetable Black	E153	77268:1	Carbo Medicinalis Vegetalis
Carmine	E120	75470	Carmine 40, Carminic Acid
Carmoisine	E122	14720	Azorubine
Carotene		75130	Alpha, Beta & Gamma Carotene
i. Mixed Carotenes	E160a(i)	75130	–
ii. Beta-Carotene	E160a(ii)	40800	–
Chlorophylls/Chlorophyllins		–	–
i. Chlorophylls	E140(i)	75810	–
ii. Chlorophyllins	E140(ii)	75815	–
Chlorophylls/Chlorophyllins			
Copper Complexes		75815	–
i. Copper Complexes	E141(i)		
Of Chlorophylls		–	–
ii. Copper Complexes	E141(ii)		
Of Chlorophyllins		–	–
Cochineal	E120	75470	Carminic Acid
Erythrosine	E127	45430	FD&C Red #3
Gold	E175	77480	–
Green S	E142	44090	Acid Brilliant Green BS
Indigotine	E132	73015	FD&C Blue #2, Indigo Carmine
Iron Oxides & Hydroxides	E172	77491	Iron Oxide Red
		77492	Iron Oxide Yellow
		77499	Iron Oxide Black
Lutein	E161b	–	–
Lycopene	E160d	–	–
Paprika Extract	E160c	–	Capsanthin, Capsorubin
Patent Blue V	E131	42051	Acid Blue 3
Ponceau 4R	E124	16255	Cochineal Red A
Quinoline Yellow[b]	E104	47005	China Yellow
Riboflavin		–	–
i. Riboflavin	E101(i)	–	–
ii. Riboflavin-5'-Phosphate	E101(ii)	–	–
Sunset Yellow FCF	E110	15985	FD&C Yellow #6, Orange Yellow S
Tartrazine	E102	19140	FD&C Yellow #5
Titanium Dioxide	E171	77891	–
Turmeric	E100	75300	Curcumin

This list is derived from Annex 1 of Directive 94/36/EC, colours permitted for use in foodstuffs. EMEA Guideline EMEA/CHMP/QWP/396951/2006 states that colourants mentioned in this annex are permitted for use in medicinal products.

*This is not D&C yellow #10. Although the C.I. numbers are the same, the dyes differ in composition. Quinoline yellow is primarily the disulfonated quinoline dye, whereas D&C yellow #10 is the monosulfonated color. Quinoline yellow is not accepted for use in the United States; conversely, D&C yellow #10 cannot be used in the EU.

Color Additives Exempt from Certification Permitted for Use in the United States*

Color	Color Index Number	CAS Number	21 CFR References			
			Food	Drug	Cosmetic	Medical Devices
Algae Meal (Dried)	–	–	73.275	–	–	–
Algae Meal (Haematococcus)	–	–	73.185	–	–	–
Alumina	77002	1332-73-6	–	73.1010	–	–
Aluminum Powder	77000	7429-90-5	–	73.1645	73.2645	–
Annatto Extract	75120	8015-67-6	73.30	73.1030	73.2030	–
Astaxanthin	–	–	73.35	–	–	–
Beta- Apo-8'-Carotenal	40820	1107-26-2	73.90	–	–	–
Beta Carotene	40800	7235-40-7	73.95	73.1095	73.2095	–
Beet Powder	–	57917-55-2	73.40	–	–	–
Bismuth Citrate	–	–	–	–	73.2110	–
Bismuth Oxychloride	77163	7787-59-9	–	73.1162	73.2162	–
Bronze Powder	77440	7440-50-8	–	73.1646	73.2646	–
		7740-66-6				
Calcium Carbonate	77220	471-34-1	–	73.1070	–	–
Canthaxanthin	40850	514-78-3	73.75	73.1075	–	–
Caramel	–	–	73.85	73.1085	73.2085	–
Carbazole Violet	51319	6358-30-1	–	–	–	73.3107
Carmine	75470	1390-65-4	73.100	73.1100	73.2087	–
Carrot Oil	–	–	73.300	–	–	–
Chlorophyllin Copper Complex	75810	–	–	73.1125	73.2125	73.3110
Chromium-Cobalt-Aluminum Oxide	77343	68187-11-1	–	73.1015	–	73.3110a
Chromium Hydroxide Green	77289	12182-82-0	–	73.1326	73.2326	–
Chromium Oxide Greens	77288	1308-38-9	–	73.1327	73.2327	73.3111
C.I. Vat Orange 1	59105	–	–	–	–	73.3112
Cochineal Extract	75470	1260-17-9	73.100	73.1100	–	–
Corn Endosperm Oil	–	–	73.315	–	–	–
Copper Powder	77400	7440-50-6	–	73.1647	73.2647	–
1,4-Bis [(2-hydroxyethyl) amino]-9,10-anthracenedione bis(2-propenoic) ester copolymers	–	10956-07-1	–	–	–	73.3100
1,4-Bis [(2-methylphenyl)amino]-9,10-anthracenedione	–	6737-68-4	–	–	–	73.3105
1,4-Bis[4-(2-methacryloxyethyl) phenylamino]-9,10-anthraquinone Copolymers	–	121888-69-5	–	–	–	73.3106
2-[[2,5-Diethoxy-4-[(4-methylphenyl) thiol]phenyl]azo]-1,3,5-benzenetriol	–	–	–	–	–	73.3115
16,23-Dihydrodinaptho[2,3-a:2′,3′-i] napth[2′,3′:6,7]indolo[2, 3-c]carbazole-5,10,15,17,22,24-hexone	70800	2475-33-4	–	–	–	73.3117
N,N′-(9,10-Dihydro-9,10-dioxo-1,5-anthracenediyl) bis-benzamide	61725	82-18-8	–	–	–	73.3118
7,16-Dichloro-6,15-dihydro-5,9,14,18-anthrazinetetrone	69825	130-20-1	–	–	–	73.3119
16,17-Dimethoxydinaphtho[1,2,3-cd:3′,2′,1′-lm] perylene-5,10 dione	59825	128-58-5	–	–	–	73.3120
4-[2,4-(Dimethylphenyl)azo]-2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one	–	6407-78-9	–	–	–	73.3122
Dihydroxy Acetone	–	62147-49-3	–	73.1150	73.2150	–
Disodium EDTA Copper	–	–	–	–	73.2120	–
6-Ethoxy-2-(6-ethoxy-3-oxobenzo [*b*]thien-2-(3*H*)-ylidene)benzo[*b*] thiophen-3-(2*H*)-one	73335	3263-31-8	–	–	–	73.3123
Ferric Ammonium Citrate	–	1185-57-5	–	73.1025	–	–
Ferric Ammonium Ferrocyanide	77510	25869-00-5	–	73.1298	73.2298	–
Ferric Ferrocyanide	77510	14038-43-8	–	73.1299	73.2299	–
Ferrous Gluconate	–	299-29-6	73.160	–	–	–
Ferrous Lactate	–	5905-52-2	73.165	–	–	–
Fruit Juice	–	–	73.250	–	–	–

Color Additives Exempt from Certification Permitted for Use in the United States* (*Continued*)

Color	Color Index Number	CAS Number	21 CFR References			
			Food	Drug	Cosmetic	Medical Devices
Grape Color Extract	–	–	73.169	–	–	–
Grape Skin Extract	–	–	73.170	–	–	–
Guaiazulene	–	489-84-9	–	–	73.2180	–
Guanine	75170	68-94-0 73-40-5	–	73.1329	73.2329	–
Henna	75480	83-72-7	–	–	73.2190	–
Iron Oxides, Synthetic	77491(Red) 77492(Yellow) 77499(Black)	1309-37-1 51274-00-1 12227-89-3	73.200	73.1200	73.2250	73.3125
Lead Acetate	–	6080-56-4	–	–	73.2396	–
Logwood Extract	75290	8005-33-2	–	73.1410	–	–
Manganese Violet	77742	10101-66-3	–	–	73.2775	–
Mica	77019	12001-26-2	–	73.1496	73.2496	–
Mica-Based Pearlescent Pigment	–	–	73.350	73.1350	–	73.3128
Paprika	–	–	73.340	–	–	–
Paprika Oleoresin	–	8023-77-6	73.345	–	–	–
Phaffia Yeast	–	–	73.355	–	–	–
Potassium Sodium Copper Chlorophyllin	75180	–	–	73.1125	73.2125	–
Phthalocyanine Green	74260	1328-53-6	–	–	–	73.3124
Poly(Hydroxyethyl Methacrylate)-Dye Copolymers	–	–	–	–	–	73.3121
Pyrogallol	76515	87-66-1	–	73.1375	–	–
Pyrophyllite	44004	8047-76-5	–	73.1400	73.2400	–
Riboflavin	–	83-88-5	73.450	–	–	–
Saffron	75100	42553-65-1 27876-94-4	73.500	–	–	–
Silver	77820	7440-22-4	–	–	73.2500	–
Sodium Copper Chlorophyllin	75815	28302-36-5	73.125	–	–	–
Tagetes Meal & Extract	75125	–	73.295	–	–	–
Talc	77019	14807-96-6	–	73.1550	–	–
Toasted Cotton Seed Meal	–	–	73.140	–	–	–
Titanium Dioxide	77891	13463-67-7	73.575	73.1575	73.2575	73.3126
Tomato Lycopene Extract And Concentrate			73.585	–	–	–
Turmeric	75300	458-37-7	73.600	–	–	–
Turmeric Oleoresin	75300	458-37-7	73.615	–	–	–
Ultramarine Blue	77007	57455-37-5	73.50	–	73.2725	–
Ultramarine Green	77013	–	–	–	73.2725	–
Ultramarine Pink	77007	127-96-9	–	–	73.2725	–
Ultramarine Red	77007	127-96-9	–	–	73.2725	–
Ultramarine Violet	77007	127-96-9	–	–	73.2725	–
Vegetable Juice	–	–	73.260	–	–	–
Vinyl Alcohol/Methyl Methacrylate Dye Reaction Products	–	–	–	–	–	73.3127
Zinc Oxide	77947	1314-13-2	–	73.1991	73.2991	–
Luminescent Zinc Sulfide	–	–	–	–	73.2995	–

*Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.). Additionally, there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

Provisionally Listed Color Additives Subject to U.S. Certification*

Color	Common Name	Color Index Number	CAS Number	21 CFR References		
				Food	Drug	Cosmetic
FD&C Lakes	Lakes	See Individual Color	See Individual Color	82.51	82.51	82.51
D&C Lakes	Lakes	See Individual Color	See Individual Color	–	82.1051	82.1051
Ext. D&C Lakes	Lakes	See Individual Color	See Individual Color	–	82.2051	82.2051
FD&C Blue #1 Lake	Brilliant Blue FCF	42090:2	68921-42-6	82.101	82.101	82.101
FD&C Blue #2 Lake	Indigotine	73015:1	16521-38-3	82.102	82.102	82.102
D&C Blue #4 Lake	Alphazurine FG	42090	6371-85-3	–	82.1104	82.1104
FD&C Green #3 Lake	Fast Green FCF	42053	2353-45-9	82.203	82.203	82.203
D&C Green #5 Lake	Alizarin Cyanine Green F	61575	4403-90-1	–	82.1205	82.1205
D&C Green #6 Lake	Quinizarine Green SS	61565	128-80-3	–	82.1206	82.1206
D&C Orange #4 Lake	Orange II	15510:2	633-96-5	–	82.1254	82.1254
D&C Orange #5 Lake	Dibromofluorescein	45370:2	596-03-2	–	82.1255	82.1255
D&C Orange #10 Lake	Diiodofluorescein	45425:2	38577-97-8	–	82.1260	82.1260
D&C Orange #11 Lake	Erythrosine Yellowish Na	45425:2	38577-97-8	–	82.1261	81.1261
FD&C Red #4 Lake	Ponceau SX	14700	4548-53-2	82.304	82.304	82.304
D&C Red #6 Lake	Lithol Rubin B	15850:2	17852-98-1	–	82.1306	82.1306
D&C Red #7 Lake	Lithol Rubin B Ca	15850:1	5281-04-9	–	82.1307	82.1307
D&C Red #17 Lake	Toney Lake	26100	85-86-9	–	82.1317	82.1317
D&C Red #21 Lake	Tetrabromofluorescein	45380:3	15086-94-9	–	82.1321	82.1321
D&C Red #22 Lake	Eosine	45380:3	17372-87-1	–	82.1322	82.1322
D&C Red #27 Lake	Tetrachlorotetra-Bromofluorescein	45410:2	13473-26-2	–	82.1327	82.1327
D&C Red #28 Lake	Phloxine B	45410:2	18472-87-02	–	82.1328	82.1328
D&C Red #30 Lake	Helindone Pink CN	73360	2379-74-0	–	82.1330	82.1330
D&C Red #31 Lake	Brilliant Lake Red R	15800:1	6371-76-2	–	82.1331	82.1331
D&C Red #33 Lake	Acid Fuchsine	17200	3567-66-6	–	82.1333	82.1333
D&C Red #34 Lake	Lake Bordeaux B	15880:1	6417-83-0	–	82.1334	82.1334
D&C Red #36 Lake	Flaming Red	12085	2814-77-9	–	82.1336	82.1336
D&C Violet #2 Lake	Alizurol Purple SS	60725	81-48-1	–	82.1602	82.1602
FD&C Yellow #5 Lake	Tartrazine	19140:1	12225-21-7	82.705	82.705	82.705
FD&C Yellow #6 Lake	Sunset Yellow FCF	15985:1	15790-07-5	82.706	82.706	82.706
D&C Yellow #7 Lake	Fluorescein	45350:1	2321-07-5	–	82.1707	82.1707
Ext. D&C Yellow #7 Lake	Napthol Yellow S	10316	846-70-8	–	82.2707a	82.2707a
D&C Yellow #8 Lake	Uranine	45350	518-47-8	–	82.1708	82.1708
D&C Yellow #10 Lake	Quinoline Yellow WS	47005:1	68814-04-0	–	82.1710	82.1710

*Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.). Additionally there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

List of Permanently Listed Color Additives Subject to U.S. Certification*

Color	Common Name	Color Index Number	CAS Number	21 CFR References			
				Food	Drug	Cosmetic	Medical Devices
D&C Black #2	Carbon Black	77266	1333-86-4	–	–	74.2052	–
D&C Black #3	Bone Black	77267	8021-99-6	–	–	74.2053	–
FD&C Blue #1	Brilliant Blue FCF	42090	2650-18-2	74.101	74.1101	74.2101	–
FD&C Blue #2	Indigotine	73015	860-22-0	74.102	74.1102	–	74.3102
D&C Blue #4	Alphazurine FG	42090	6371-85-3	–	74.1104	74.2104	–
D&C Blue #6	Indigo	73000	482-89-3	–	–	–	74.3106
D&C Blue #9	Indanthrene Blue	69825	130-20-1	–	74.1109	–	–
D&C Brown #1	Resorcin Brown	20170	1320-07-6	–	–	74.2151	–
FD&C Green #3	Fast Green FCF	42053	2353-45-9	74.203	74.1203	74.2203	–
D&C Green #5	Alizarin Cyanine Green F	61570	4403-90-1	–	74.1205	74.2205	–
D&C Green #6	Quinizarine Green SS	61565	128-80-3	–	74.1206	74.2206	74.3206
D&C Green #8	Pyranine Concentrated	59040	63-58-69-6	–	74.1208	74.2208	–
Orange B	–	19235	–	74.250	–	–	–
D&C Orange #4	Orange II	15510	633-96-5	–	74.1254	74.2254	–
D&C Orange #5	Dibromofluor Escein	45370:1	596-03-2	–	74.1255	74.2255	
D&C Orange #10	Diiodofluorescein	45425:1	38577-97-8	–	74.1260	74.2260	–
D&C Orange #11	Erythrosine Yellowish Na	45425	38577-97-8	–	74.1261	74.2261	
[Phthalocyaninato (2-)] Copper	Copper Phthalocyanine	74160	147-14-8	–	–	–	74.3045
FD&C Red #3	Erythrosine	45430	16423-68-0	74.303	74.1303	–	–
FD&C Red #4	Ponceau SX	14700	4548-53-2	–	74.1304	74.2304	–
D&C Red #6	Lithol Rubin B	15850	5858-81-1	–	74.1306	74.2306	–
D&C Red #7	Lithol Rubin B Ca	15850:1	4/9/5281	–	74.1307	74.2307	–
D&C Red #17	Toney Red	26100	85-86-9	–	74.1317	74.2317	74.3230
D&C Red #21	Tetrabromo Fluorescein	45380:2	15086-94-9	–	74.1321	74.2321	–
D&C Red #22	Eosine	45380	17372-87-1	–	74.1322	74.2322	–
D&C Red #27	Tetrachlorotetra-bromofluorescein	45410:1	13473-26-2	–	74.1327	74.2327	–
D&C Red #28	Phloxine B	45410	18472-87-2	–	74.1328	74.2328	–
D&C Red #30	Helindone Pink CN	73360	2379-74-0	–	74.1330	74.2330	–
D&C Red #31	Brilliant Lake Red R	15800:1	6371-76-2	–	74.1331	74.2331	–
D&C Red #33	Acid Fuchsine	17200	3567-66-6	–	74.1333	74.2333	–
D&C Red #34	Lake Bordeaux B	15880:1	6417-83-0	–	74.1334	74.2334	–
D&C Red #36	Flaming Red	12085	2814-77-9	–	74.1336	74.2336	–
D&C Red #39	Alba Red	13058	6371-55-7	–	74.1339	–	–
FD&C Red #40	Allura Red AC	16035	25956-17-6	74.340	74.1340	74.2340	–
FD&C Red #40 lake	Allura Red AC	16035:1	68583-95-9	74.340	74.1340	74.2340	–
Citrus Red #2	–	12156	6358-53-8	74.302	–	–	–
D&C Violet #2	Alizurol Purple SS	60725	81-48-1	–	74.1602	74.2602	74.3602
Ext. D&C Violet #2	Alizarin Violet	60730	4430-18-6	–	–	74.2602a	–
FD&C Yellow #5	Tartrazine	19140	1934-21-0	74.705	74.1705	74.2705	–
FD&C Yellow #6	Sunset Yellow FCF	15985	2783-94-0	74.706	74.1706	74.2706	–
D&C Yellow #7	Fluorescein	45350:1	7/5/2321	–	74.1707	74.2707	–
Ext. D&C Yellow #7	Napthol Yellow S	10316	846-70-8	–	74.1707a	74.2707a	–
D&C Yellow #8	Uranine	45350	518-47-8	–	74.1708	74.2708	–
D&C Yellow #10	Quinoline Yellow WS	47005	8004-92-0	–	74.1710	74.2710	74.3710
D&C Yellow #11	Quinoline Yellow SS	47000	8003-22-3	–	74.1711	74.2711	–

*Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.). Additionally, there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

Another choice confronting manufacturers is whether to use an aqueous coating or an organic coating system; both have their advantages and disadvantages. While organic coatings provide greater protection against moisture uptake during the coating process (important for moisture-sensitive ingredients) and are easier to apply because of the fast evaporation of solvents, problems encountered with these coatings include environmental control of organic solvents going into the atmosphere, the need to perform solvent residue tests, and the need to have explosion-proof facilities, thus aqueous coating systems are often preferred.

CELLULOSE BASED

Cellulose acetate phthalate (CAP)

Caution: Check with regulatory authorities about approved states of all dyes before using them.

HYDROXYPROPYL METHYLCELLULOSE (METHOCEL, HPMC) AQUEOUS COATINGS

Methocel-based coatings in an aqueous base are the most popular coating options; two methods of making solutions are possible.

If a lake is used, then alcohol is also included (see, for example, Holberry Red).

A. Brite Rose

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color)	20.00 g
2.00	3	PEG-8000	20.00 g
0.25	4	FD&C Red Dye No. 30 lake	2.50 g
2.00	5	Titanium dioxide (special coating grade)	20.00 g
QS	6	Deionized purified water	QS to 1 L

Manufacturing Directions

1. Charge 250 mL of water into a suitable container, and heat to 60°C to 70°C.
2. With gentle stirring, disperse the hydroxypropyl methyl cellulose onto the hot water; when the cellulose has wetted, quickly add 250 mL of cold water.
3. Stir until the dispersion is homogenous, although the solution of cellulose may not be complete.
4. Dissolve PEG-8000 in 50 mL of water, and then add to the step above.
5. Add PEG-400 to basic solution above.
6. Load a suitable size ball jar with the FD&C Red Dye No. 30 and titanium dioxide.
7. Add sufficient water to cover the pigment and balls.
8. Mill overnight or for 12 hours.
9. Other pigment reduction methods may be used to yield a particle size not greater than 1.0 μm.
10. Add milled pigments to the base solution from the step above, and bring the volume up with cold water.
11. Use within 7 days.

B. Cherry Red

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color)	20.00 g
2.00	3	PEG-8000	20.00 g
1.80	4	FD&C Red Dye No. 3 lake	18.00 g
0.10	5	FD&C Red Dye No. 2 (Amaranth)	1.00 g
2.10	6	Titanium dioxide (special coating grade)	21.00 g
QS	7	Deionized purified water, USP	QS to 1 L

C. Geranium Rose

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
0.24	4	FD&C Red Dye No. 3 lake	2.00 g
QS	5	Deionized purified water, USP	QS to 1 L

D. Gloss

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
3.33	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	33.33 g
1.66	2	PEG-400 (low color), NF	16.66 g
QS	3	Deionized purified water, USP	QS to 1 L

E. Red

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
.50	4	FD&C Red Dye No. 3 lake	25.00 g
0.50	5	Titanium dioxide	5.00 g
QS	6	Deionized purified water, USP	QS to 1 L

F. Moderate Red

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
0.50	4	FD&C Yellow Dye No. 3 aluminum lake	5.00 g
2.50	5	Ponceau Red Dye 4R lake	25.00 g
1.00	6	Titanium dioxide (special coating grade), USP	10.00 g
QS	7	Deionized purified water, USP	QS to 1 L

G. Clear

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color)[a]	20.00 g
2.00	5	PEG-8000 (optional)	20.00 g
QS	6	Deionized purified water	QS to 1 L

[a]Increase amount to 6.00 if item 5 is not used.

Manufacturing Directions

1. Charge approximately 500 mL of water into a suitable vessel.
2. Heat water to 65°C to 70°C.
3. Add the PEG-8000 to the hot water and dissolve (if used).
4. While maintaining gentle agitation, sprinkle the hydroxypropyl methyl cellulose onto the surface of the hot water solution.
5. Position stirring head to avoid excessive entrainment of air.
6. When the cellulose has been dispersed, add the PEG-400.
7. Continue to stir until dispersion is homogeneous, although solution of cellulose may not be complete.
8. Stop stirring, and allow solution to stand until entrained air is removed.
9. Dissolve sorbic acid in alcohol, and ensure that the solution is complete.
10. When the solution from the step above is clear, add 250 mL of cold water, mix well, and add sorbic acid solution.
11. Mix, then bring up to volume with cold water.
12. Store coating solution in well-filled, well-sealed containers.
13. Use within 3 months.

H. Green

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color)	20.00 g
2.00	5	PEG-8000	20.00 g
1.00	6	Titanium dioxide (coating grade)	10.00 g
0.01	7	Dye Yellow E104 aluminum lake	0.10 g
0.0032	8	FD&C Blue Dye No. 1 lake (11 – 13%)	0.032 g
QS	9	Deionized purified water	QS to 1 L

I. Holberry Red

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color)	20.00 g
2.00	5	PEG-8000	20.00 g
1.00	6	Titanium dioxide (coating grade)	10.00 g
1.50	7	FD&C Red Dye No. 40 lake (29%)	15.00 g
0.50	8	FD&C Blue Dye No. 3 lake	5.00 g
QS	9	Deionized purified water	QS to 1 L

J. Sun Orange

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methyl cellulose 2910 (15 cps)	60.00 g
0.17	2	Sorbic acid, NF	1.70 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color), NF	20.00 g
2.00	5	PEG-8000	20.00 g
2.38	6	Titanium dioxide (coating grade), USP	23.80 g
2.47	7	FD&C Yellow Dye No. 5	24.70 g
0.16	8	FD&C Yellow Dye No. 6	1.60 g
QS	9	Deionized purified water, USP	QS to 1 L

K. Opadry Yellow

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
10.00	1	Hydroxypropyl methyl cellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.20	4	Titanium dioxide	1.20
0.30	5	FD&C Blue Dye No. 1 lake	0.30
0.50	6	FD&C Blue Dye No. 2 (dispersed)	0.50
0.75	7	Opadry-OY-S 29019 (clear)	0.75
QS	8	Purified water	225.00

Manufacturing Directions

1. The formula for this coating solution is prepared to obtain a weight gain of 10 mg per caplet (around 600 mg in weight).
2. Disperse item 1 in 175 g of purified water (70°C–80°C) while stirring.
3. Hold overnight for complete dispersion.
4. Disperse items 2 and 3 in 25 g of purified water (25°C–30°C).
5. Hold overnight for complete hydration.
6. Add mixture from previous step.
7. Homogenize using a homogenizer (gap setting = 1.5 mm).
8. Homogenize items 4, 5, and 6 in 50 g of hypromellose dispersion from the step above twice, using a homogenizer (gap setting = 1.5 mm).
9. Pass the dispersion twice through a 90-μm sieve.
10. (*Note*: This is a critical step; follow instructions closely to prevent foreign particles and spots.) Preparation of polishing solution: Disperse item 7 in 25 g of purified water with slow stirring.
11. Make a vortex by slow stirring and add the powder in such a way as to avoid foam formation.

L. Opadry Yellow

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Hydroxypropyl methyl cellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.34	4	Titanium dioxide	1.34
0.046	5	Sunset Yellow E110, FCF	0.046
1.34	6	FD&C Yellow Dye No. 10 lake	1.34
0.75	7	Opadry-OY-S 29019 (clear)	0.75
QS	8	Purified water	225.00

M. Opadry Red

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
10.00	1	Hydroxypropyl methyl cellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.34	4	Titanium dioxide	1.34
0.15	5	Iron oxide red	0.15
0.75	6	Opadry-OY-S (clear)	0.75
QS	7	Purified water	225.00

N. Opadry Green

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets(g)
10.00	1	Hydroxypropyl methyl cellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
2.125	4	Titanium dioxide	2.125
0.053	5	FD&C Blue Dye No. 1 lake	0.053
0.15	6	FD&C Yellow Dye No. 10 lake	0.15
0.75	7	Opadry-OY-S (clear)	0.75
QS	8	Purified water	225.00

Manufacturing Directions

1. Disperse item 1 in 175 g of purified water (70°C–80°C) while stirring.
2. Keep overnight for complete dispersion.
3. Disperse items 2 and 3 in 25 g of purified water (25°C–30°C).
4. Keep overnight for complete hydration.
5. Add together and homogenize using homogenizer (gap setting = 1.5 mm).
6. Homogenize items 4, 5, and 6 in 50 g of hypromellose dispersion twice, using homogenizer (gap setting = 1.5 mm).
7. Pass the dispersion twice through a 90-μm sieve.
8. (*Note*: This is a critical step; follow instructions closely to prevent foreign particles and spots.) Disperse item 7 in 25 g of purified water while stirring slowly.
9. Make a vortex by slow stirring and add the powder in such a way as to avoid foam formation.
10. Follow the parameters for coating in Accela Cota:

Caplet load	620 g
Pan speed	4 rpm
Drying air temperature	70°C–75°C
Exhaust temperature	50°C–55°C
Fluid pressure	15 – 20 psi
Valve on spray gun	One revolution open
Atomizing pressure	55 psi
Nozzle orifice	1 mm
Nozzle distance to bed	250–280 mm
Difference of air pressure	–1.0 to –1.5 cm
Spray rate	200–225 g/min
Coating time	3.0–3.5 hours

11. Stir the dispersion at slow speed (6–10 rpm) continuously.
12. Spray the polishing solution under the same conditions as above, adjusting the spray rate to 180 g/min.
13. Check the caplet surface every 5 minutes for sticking.
14. If sticking tends to appear, stop the coating immediately.
15. When the spraying is over, roll the tablets in a pan for 10 minutes with cold air blowing onto the caplets.
16. Unload the film-coated caplets into stainless steel containers lined with polyethylene bags.
17. Appearance is a light green, film-coated caplet that is smooth, with no sticking or chipping on the caplet surface.
18. Weight gain per caplet is NLT 10 mg/tablet.

O. White Coating

Bill of Materials			
Scale(mg/tablet)	Item	Material Name	Quantity/1000 Tablets(g)
22.75	1	Hypromellose	22.75
4.54	2	Polyethylene glycol	4.54
12.50	3	Talc (fine powder)	12.50
10.00	4	Titanium dioxide	10.00
1.30	5	FD&C Yellow No. 10 lake	1.30
–	6	Purified water	~24.00
–	7	Ethanol (95%)	~21.00

HYDROXYPROPYL METHYLCELLULOSE OPAQUE ORGANIC COATING

A. Brite Green

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L(g)
1.00	1	Titanium dioxide	10.00
50.00 v/v	2	Alcohol (200 proof), SD 3A	~397.00
1.69	3	PEG-400 (low color), NF	16.90
0.02	4	FD&C Yellow Dye No. 5	0.20
0.0068	5	FD&C Blue Dye No. 1	0.068
4.00	6	Hydroxypropyl methyl cellulose 2910 (15 cps)	40.00
QS	7	Methylene chloride	~625.00

Manufacturing Directions

1. Charge titanium dioxide and QS with alcohol into a Ball mill.
2. Mill the material for 16 hours.
3. Charge 465 mL alcohol into a suitable mixing tank.
4. Start agitation.
5. Slowly add PEG-400 to mixing tank.
6. Mix for 5 minutes.
7. Add FD&C Yellow Dye to the mixing tank with continued agitation.
8. Rinse bottle with alcohol tapped from mixing tank.
9. Return rinse to mixing tank.
10. Add FD&C Blue Dye to the mixing tank, and rinse.
11. Mix for 2 hours.
12. Tap approximately 10 mL of solution from mixing tank after 1/2, 1, and 1.5 hours of mixing.
13. Put solution back into mixing tank. (*Note*: Tapping solution ensures that dye is not tapped into lower valve and/or pipeline.) Rinse the Ball mill with two rinses of 11.6 mL alcohol.
14. Reseal the Ball mill, and allow it to run for 2 to 5 minutes between rinses.
15. Empty content of the Ball mill and rinses into mixing tank.
16. Slow sprinkle hydroxypropyl methyl cellulose into mixing tank with constant agitation.
17. Agitate for an additional 15 minutes. (*Note*: Prevent the development of lumps by slowly sprinkling hydroxypropyl methyl cellulose into the alcohol.) After mixing 10 minutes, tap approximately 10 mL from the mixing tank and put back into tank to recirculate.
18. Add sufficient methylene chloride (~474 mL) to bring up to volume.
19. Continue agitation for 2 hours.
20. After 1/2, 1, and 1.5 hours, tap approximately 10 mL of solution from mixing tank and put back into mixing tank to recirculate.
21. (*Note*: No residue should be present in the solution when tapped at 1.5 hours; if some is present, then continue agitation and tap every 15 minutes until no residue is observed.) (*Caution*: Avoid contact with methylene chloride and vapors; they may have toxic effects when swallowed or inhaled.) (*Note*: Nitrogen pressure may be used to assist bottle filling.) Strain mixing tank contents through two-ply cheesecloth, or similar, into suitable approved containers (one half the total number of bottles). (*Note*: Lumps may obstruct spray nozzle.)

B. Red Mahogany

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L(g)
0.40	1	Titanium dioxide	4.00
45.00 v/v	2	Alcohol (200 proof), SD 3A	~375.30
0.40	3	Vanillin (crystals)	4.00
1.00	4	Propylene glycol	10.00
1.50	5	FD&C Red Dye No. 40 lake (29%)	15.00
1.00	6	Dye Brown lake blend	10.00
4.00	7	Hydroxypropyl methyl cellulose 2910 (15 cps)	40.00
QS	8	Methylene chloride	~530.40

C. Sun Orange

Bill of Materials			
Scale(%)	Item	Material Name	Quantity/L(g)
3.00 (w/v)	1	Titanium dioxide	30.00
50.00 (v/v)	2	Alcohol (200 proof), SD 3A	~397.00
2.11 (w/v)	3	Propylene glycol	21.10
3.11 (w/v)	4	FD&C Yellow Dye No. 5	31.10
0.20 (w/v)	5	FD&C Yellow Dye No. 6	2.00
4.00 (w/v)	6	Hydroxypropyl methyl cellulose 2910 (15 cps)	40.00
QS	7	Methylene chloride	~625.00

D. Dark Red

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L(g)
1.00	1	Titanium dioxide	10.00
20.00 v/v	2	Alcohol (200 proof), SD 3A	~200.00 mL
2.00	3	PEG-400 (low color)	20.00
0.02	4	Ponceau 4R dye (red)	20.00
0.0068	5	FD&C Blue Dye No. 1	0.068
2.95	6	Hydroxypropyl methyl cellulose 2910 (15 cps)	29.50
QS	7	Methylene chloride	QS to 1 L

E. Deep Yellow

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
50.00	2	Alcohol (200 proof), SD 3A	~397.00 g
2.00	3	PEG-400 (low color)	20.00 g
2.00	4	FD&C Yellow Dye No. 5 lake	20.00 g
2.95	5	Hydroxypropyl methyl cellulose 2910 (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

F. Pale Yellow

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
1.50	1	Titanium dioxide	15.00 g
50.00	2	Alcohol (200 proof), SD 3A	~397.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
0.50	4	FD&C Yellow Dye No. 10 aluminum lake (14–17%)	5.00 g
2.95	5	Hydroxypropyl methyl cellulose 2910 (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

G. Scarlet Red

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
20.00	2	Alcohol (200 proof), SD 3A	~200.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
2.00	4	FD&C Yellow Dye No. 7 lake	20.00 g
1.00	5	FD&C Yellow Dye No. 5 lake	10.00 g
2.95	6	Hydroxypropyl methyl cellulose 2910 (15 cps)	29.50 g
QS	7	Methylene chloride	QS to 1 L

HYDROXYPROPYL METHYL CELLULOSE/HYDROXYPROPYL CELLULOSE (KLUCEL®) COATING

A. White

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
0.50	2	Hydroxypropyl cellulose, NC	5.00 g
45.00	3	Alcohol (200 proof), SD 3A	~450.00 g
2.00	4	Propylene glycol	20.00 g
4.50	5	Hydroxypropyl methyl cellulose 2910 (15 cps)	45.00 g
QS	6	Methylene chloride	QS to 1 L

Manufacturing Directions

1. Place titanium dioxide and sufficient methylene chloride into suitably sized ball jars to cover the balls.
2. Mill for not less than 16 hours.
3. While mixing alcohol, add and disperse hydroxypropyl methylcellulose, hydroxypropyl cellulose, and propylene glycol, followed by 250 mL of methylene chloride.
4. Continue mixing until the dissolution is complete.
5. While mixing the solution from the second step, empty into it the contents of the ball jar, rinse the balls and jar with methylene chloride, add the rinsing to the batch, and mix.
6. Bring the batch up to volume with methylene chloride, and mix well until homogeneous.
7. Strain the batch through muslin into suitable, approved bottles.
8. Seal and store.

HYDROXYPROPYL METHYL CELLULOSE/ETHYL CELLULOSE COATING

A. Reddish Orange Opaque

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
1.16	1	Titanium dioxide	11.60 g
45.00	2	Alcohol (dehydrated; 200 proof)	~450.00 g
0.20	3	Vanillin (crystals), NF	2.00 g
0.50	4	Albumen powder (white hen egg)	5.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
1.30	4	FD&C Red Dye No. 3	13.00 g
0.05	5	FD&C Red Dye No. 2 (Amaranth), USP	0.50 g
0.20	6	FD&C Yellow Dye No. 6	2.00 g
2.95	5	Hydroxypropyl methyl cellulose 2910, USP (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

Manufacturing Directions

1. Load vanillin, albumen, titanium dioxide, FD&C Red Dye No. 3, FD&C Red Dye No. 2, and FD&C Yellow Dye No. 6 into a suitable size ball jar.
2. Add sufficient methylene chloride to cover the pigments and balls.
3. Mill for 24 hours.
4. Measure 400 mL of alcohol into a suitable stainless steel container.
5. Sprinkle the hydroxypropyl methylcellulose/ethylcellulose onto the surface of the alcohol while stirring vigorously.
6. When the hydroxypropyl methyl cellulose/ethylcellulose has been wetted, quickly add 300 mL methylene chloride while stirring vigorously.
7. Add the PEG-400 to the solution from above, and rinse the container with the remaining alcohol; add the rinsings to the bulk.
8. Empty the contents of the ball jar from the first step into the coating solution from previous step, while stirring vigorously.
9. Rinse the ball jar with methylene chloride; add the rinsings to the bulk.
10. Bring up to volume with methylene chloride.

B. Subcoating Solution

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
45.00	1	Alcohol (190 proof), USP	450.00 mL
0.50	2	Hydroxypropyl cellulose, NF	5.00 g
4.50	3	Hydroxypropyl methyl cellulose 2910, USP (15 cps)	45.00 g
QS	4	Methylene chloride	QS to 1 L

HYDROXY METHYL CELLULOSE/HYDROXY CELLULOSE COATING

A. Blue

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methyl cellulose	10.00 g
1.00	2	Hydroxy ethyl cellulose (15 cps)	10.00 g
0.312	3	Titanium dioxide	3.21 g
1.00	4	FD&C Blue Dye No. 1 lake (12%)	10.00 g
0.375	5	Castor oil (odorless)	3.75 g
0.375	6	Sorbitan monooleate	3.75 g
50.00	7	Alcohol (200 proof), SD 3A	500.00 mL
QS	8	Methylene chloride	QS to 1 L

Manufacturing Directions

1. Premix hydroxypropyl methyl cellulose and hydroxypropyl cellulose, and add to 440 mL alcohol with rapid agitation.
2. Mix for not less than 1 hour.
3. Charge FD&C Blue Dye and titanium dioxide into a ball mill.
4. Cover the balls and materials with 60 mL of alcohol, and mill for 16 hours.
5. Add contents to mixing tank, and add the castor oil and sorbitan monooleate.
6. Rinse the ball mill with methylene chloride, and add the rinsings to the mixing tank.
7. Bring up to a volume of 1 L with methylene chloride, and mix for at least 1 hour.

B. Clear (50:50)

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methyl cellulose	10.00 g
1.00	2	Hydroxy ethyl cellulose, USP (15 cps)	10.00 g
0.375	3	Castor oil (odorless)	3.75 g
50.00	4	Alcohol (200 proof), SD 3A	500.00 mL
QS	5	Methylene chloride	QS to 1 L

HYDROXY METHYL CELLULOSE/ETHYL CELLULOSE COATING

A. Clear

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methyl cellulose	10.00
1.00	2	Hydroxy ethyl cellulose, USP (15 cps)	10.00
0.375	3	Castor oil (odorless), USP	3.75
50.00	4	Alcohol (200 proof), SD 3A	500.00 mL
QS	5	Methylene chloride	QS to 1 L

Manufacturing Directions

1. Charge alcohol into mixing tank.
2. Turn on mixer to mixing speed; maintain mixing speed throughout preparation of coating solution.
3. Charge hydroxypropyl methyl cellulose and ethyl cellulose into the mixing tank.
4. Let mix for 1 hour.
5. Add methylene chloride (~500 mL) to bring the final volume up to 1 L.
6. Mix for 1 hour.
7. Solution need not be agitated at all times.
8. Keep tank tightly closed at all times.
9. Rubber stopper on bottles must be protected from methylene chloride with a polyethylene layer.

POLYVINYLPYRROLIDONE (PVP) COATINGS

A. Subcoating

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
20.00	1	Povidone USP K-29–32[a]	200.00 g
80.00	2	Alcohol (200 proof), SD 3A	800 mL

[a]May be substituted with Kollidon® VA 64 (polyvinylpyrrolidone/vinylacetate copolymer; 10%), and item 2 can be replaced with isopropyl alcohol.

Manufacturing Directions

1. Spray the solution onto the warm tablet cores (30°C–40°C) for a few minutes before continuing with the main aqueous coating procedure.
2. The amount of 0.4 mg/cm^2 tablet surface is sufficient for good subcoating protection.
3. No plasticizer is needed in this formulation due to the plasticity of Kollidon VA 64.

B. Kollidon® VA 64 (Polyvinylpyrrolidone/Vinylacetate Copolymer, BASF)

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg
5.00	1	Kollidon® VA 64	50.00 g
4.00	2	Lutrol E 6000	40.00 g
0.50	3	Glycerin, USP	5.00 g
1.50	4	Iron oxide or lake	15.00 g
3.00	5	Titanium dioxide	30.00 g
5.00	6	Talc	50.00 g
QS	7	Purified water	QS to 1 L

Manufacturing Directions

Pass the suspension through a disk mill prior to use and spray under the following conditions.

Sugar-Coating Pan

Spray gun	Walther WAXV with 1-mm nozzle
Spraying time	3 seconds
Pause	0.5 seconds
Dry air	6 seconds
Pause	3 seconds

Accela Cota (Continuous Spraying)

Spray gun	Walther WAXV with 0.8-mm nozzle
Temperature at inlet	45°C
Temperature at outlet	38°C
Spraying pressure	2 bar
Spraying time	~50 minutes

If the film is too sticky, a certain part of the Kollidon should be substituted by HPMC or sucrose.

Kollidon® VA 64 and Polyvinyl Alcohol

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg
5.0	1	Kollidon® VA 64	50.00 g
4.00	2	Lutrol E 6000	40.00 g
6.00	3	Polyvinyl alcohol	76.00 g
68.00	4	Purified water	680.00 g
0.50	5	Glycerin, USP	5.00 g
1.50	6	Iron oxide or lake	18.00 g
3.00	7	Titanium dioxide	37.00 g
5.00	8	Talc	50.00 g
QS	9	Purified water	168.00 g

Manufacturing Directions

1. Dissolve items 1 to 3 in item 4, add polyvinyl alcohol, and stir for 45 minutes, avoiding the formation of too many air bubbles.
2. Suspend the pigments and talc in 168 mL of water, and pass this mixture through a colloid mill.
3. To obtain the final coating suspension, mix this solution with the first solution.
4. Suggested conditions for coating using Accela-Cota are as follows.

Tablet core loading	5.0 kg
Amount of coating suspension	1.26 kg
Inlet air temperature	59°C
Outlet air temperature	46°C
Nozzle	1.0 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying rate	15 g/min
Spraying time (continuously)	83 minutes
Final drying	5 minutes
Quantity of film former applied	$\sim$3 mg/cm^2

D. Kollidon® 30 and Shellac

Bill of Materials			
Scale (%, w/w)	Item	Material Name	Quantity/kg(g)
2.00	1	Kollidon® 25 or 30	20.00
17.70	2	Shellac	177.00
18.50	3	Titanium dioxide	185.00
6.50	4	Talc	65.00
1.50	5	Cetyl alcohol	15.00
3.00	6	Sorbitan trioleate	30.00
5.00	7	Color lake	50.00
QS	8	Isopropanol or alcohol	458.00

Manufacturing Directions

1. Dissolve shellac and sorbitane trioleate in the warm solvent and then Kollidon and cetyl alcohol.
2. Add titanium dioxide, talc, and lake, and then mix in the colloid mill.
3. Application of the coating suspension: About 50 g of suspension is applied to 1 kg of tablet cores in a conventional coating pan or in an Accela-Cota pan (1–2 mg film formers/cm^2).

E. Kollidon® VA 64 and Hydroxypropyl Methyl Cellulose

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg
4.00	1	Kollidon® VA 64	53.00 g
1.00	2	Lutrol E 6000	12.00 g
6.00	3	Hydroxypropyl methyl cellulose	79.00 g
1.50	4	Iron oxide or lake	18.00 g
3.00	5	Titanium dioxide	37.00 g
4.00	6	Talc	50.00 g
QS	7	Purified water	QS to 1 kg

Manufacturing Directions

1. Dissolve Lutrol and Kollidon in a portion of the water, add hydroxypropyl methyl cellulose, and stir for 45 minutes, avoiding the formation of too many air bubbles.
2. Suspend the pigments and talc in a portion of the water, and pass this mixture through a colloid mill.
3. Mix the two portions.
4. Conditions for coating using Acela-Cota are as follows.

Tablet core loading	5.0 kg
Core size	9-mm biconvex
Amount of coating suspension applied	1.2 kg
Inlet air temperature	60°C
Outlet air temperature	40°C
Nozzle	1.0 mm
Rotation speed of the pan	12 rpm
Spraying pressure	2.0 bar
Spraying rate	50 g/min
Spraying time (continuously)	34 minutes
Final drying	2 minutes
Drying after spraying	5 minutes at 60°C
Quantity of film-former applied	3.14 mg/cm^2

F. Povidone, Ethyl Cellulose, and Talc

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
7.50	1	Povidone (PVP K-29-32), USP	75.00 g
4.25	2	Ethyl cellulose, NF	42.50 g
0.50	3	PEG-400, NF	5.00 g
5.00	4	Talc	50.00 g
45.00	5	Alcohol (200 proof), SD 3A	450.00 mL
QS	6	Methylene chloride, NF	QS to 1 L

Manufacturing Directions

1. Dissolve Povidone in alcohol and then add PEG-400.
2. Add ethyl cellulose to this solution.
3. Mix until evenly dispersed, then bring up to volume with methylene chloride with constant stirring.
4. Add talc to this solution, and stir to ensure distribution.
5. Solution should be freshly prepared and used within 10 days of manufacture.
6. Thoroughly disperse talc before use.
7. If batch is more than 200 L, do not add talc.
8. If coating solution is manufactured without talc, then solution should be used within 4 weeks.

CELLULOSE ACETATE PHTHALATE AND CARBOWAX COATINGS

A. Brite Green

Bill of Materials			
Scale(%, w/v)	Item	Material Name	Quantity/L
6.00	1	Cellulose acetate phthalate (carbowax)	60.00 g
1.86	2	Propylene glycol	18.65 g
0.66	3	Sorbitan monooleate (Span 80)	6.00 g
0.12	4	Castor oil (odorless)	1.25 g
0.85	5	FD&C Blue Dye No.1	0.85 g
3.11	6	FD&C Yellow Dye No. 5 lake	31.10 g
5.33	7	Titanium dioxide	53.30 g
21.58	8	Methylene chloride	215.00 g
QS	9	Acetone	QS to 1 L

Manufacturing Directions

1. Place methylene chloride in a suitably sized mixing tank.
2. While stirring, add propylene glycol, Span 80, and castor oil.
3. To this mixture add cellulose acetate phthalate, and allow to soak for overnight.
4. Load dyes and titanium dioxide into a suitable ball jar.
5. Add sufficient acetone to cover the raw materials and balls.
6. Ball mill overnight.
7. Melt carbowax with a portion of the acetone using gentle heat.
8. Add the melted carbowax to the mixture from the second step.
9. Empty contents of ball jar mill to this mixture.
10. Rinse the ball jar with acetone, and add rinsings.
11. Add acetone to volume and mix well.
12. If necessary, strain solution through gauge before storage or use.

B. Cherry Red

In the formulation given above, use, FD&C Red Dye No.3 (6.800 g), FD&C Red Dye No. 2 (Amaranth, USP; 1.00 g), and FD&C Yellow Dye (5.40 g).

C. Clear

Delete dyes.

D. Orange

Use FD&C Yellow Dye No. 6 (4.00 g) and FD&C Yellow Dye No. 5 (12.00 g).

SUGAR COATINGS

A. Basic

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg
4.00	1	Kollidon® VA 64	40.00 g
16.00	2	Sucrose	160.00 g
2.40	3	Titanium dioxide	24.00 g
1.20	4	Color lake	12.00 g
3.20	5	Lutrol E 4000	32.00 g
4.00	6	Talc	40.00 g
QS	7	Purified water	QS to 1 kg

Manufacturing Directions

1. Dissolve sucrose, Kollidon, and Lutrol in the water, and suspend the other components.
2. Pass through a colloid mill.
3. Use the following conditions for use in Accela-Cota.

Tablet core loading	5.00 kg
Amount of coating suspension	1.20 kg
Inlet air temperature	45°C
Outlet air temperature	35°C
Nozzle	0.80 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying time (continuously)	50 minutes
Quantity of film-former applied	4.00 mg/cm^2

B. Automatic

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity, g/kg
4.00	1	Kollidon® 30	40.00
38.00	2	Sucrose	380.00
4.50	3	Titanium dioxide	45.00
QS	4	Color lake	QS
4.50	5	Calcium carbonate	45.00
14.50	6	Talc	145.00
QS	7	Purified water	QS to 1 kg

Manufacturing Directions

1. Dissolve sucrose in hot water, then mix with glycerol.
2. Dissolve Kollidon and suspend the other components.
3. Coating procedure: Coat 4 kg of tablet cores with a weight of 420 mg each by spraying with 2.5 kg of the above suspension in a conventional coating pan under the following conditions:

Spray phase	5 seconds
Interval	10 minutes
Drying phase (warm air)	10 minutes
Total coating time	16 hours

C. Manual, White

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg(g)
0.33	1	Kollidon® 30	3.36
0.29	2	Carmellose sodium	2.92
0.21	3	Aerosil® 200	2.14
QS	4	Color lake (white)	QS
1.62	5	Talc	16.20
0.10	6	Polysorbate or Cremophor RH40	1.00
1.40	7	Titanium dioxide	14.00
62.70	8	Sucrose	627.00
33.40	9	Purified water	334.00

Manufacturing Directions

1. Dissolve Kollidon, polysorbate or Cremophor, and sucrose in water, and suspend the other components in this solution.
2. Mix in a colloid mill.
3. Start with formulation without the color and then apply the color coat.
4. The polishing can be done by means of a solution of beeswax or PEG-6000.

ENTERIC COATINGS

A. Kollicoat® and Kollidon® Enteric Film Coating

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg
0.50	1	Titanium dioxide	5.00 g
2.00	2	Talc	20.00 g
0.50	3	Iron oxide	5.00 g
0.50	4	Kollidon® 25 or Kollidon® 30	5.00 g
50.00	5	Kollicoat® MAE 30 DP (methacrylic acid/ethyl acrylate copolymer, 1:1)	500.00 g
1.50	6	Triethyl citrate	15.00 g
QS	7	Purified water	QS to 1 kg

Manufacturing Directions/Conditions

Tablet core loading	5 kg
Core size	9-mm biconvex
Quantity of suspension applied	1890 g
Quantity of solids/cm^2	9 mg
Quantity of film-forming agent/cm^2	6 mg
Speed of the coating pan	12 rpm
Spray nozzle	0.8 mm
Spraying pressure	2.0 bar
Type of spraying	Continuous
Inlet air temperature	50°C
Outlet air temperature	~30°C
Spraying time	~60 minutes
Spraying rate	~30 g/min

EUDRAGIT® ENTERIC AQUEOUS

A. Brick Red

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg (g)
46.667	1	Distilled purified water	466.667
1.519	2	Talc (powder)	15.198
0.798	3	Titanium dioxide (special coating grade)	7.983
1.55	4	Iron oxide, red	15.50
0.426	5	Polysorbate 80	4.262
0.015	6	Dimethyl polysiloxane emulsion (30%)	0.155
47.60	7	Eudragit®; use Eudragit® L 30D-55	476.00
1.426	8	Triethyl citrate (Eudraflex®)	14.259

Manufacturing Directions

1. Weigh the quantity of water needed.
2. Put approximately 21.5% of the total quantity of water in a suitable mixing container.
3. Add talc powder, and stir vigorously until well suspended (approximately 20 minutes).
4. Add the following to this suspension, and mix thoroughly: titanium dioxide, iron oxide, Tween 80, and dimethyl polysiloxane emulsion (30%).
5. (*Note*: The pigments may requirehomogenizing with colloid, corrundum disc mill, or ball mill.) Put the Eudragit in a suitable mixing vessel, and add the following with continuous mixing: homogenized pigment mixture, Eudraflex (i.e., triethyl citrate), and remaining quantity of water. *Note*: When PEG-8000 is used as a plasticizer, it should be incorporated as a 10% aqueous solution.

B. Yellow

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg(g)
46.66	1	Distilled purified water	466.66
1.25	2	Talc (powder)	12.57
0.77	3	Titanium dioxide (special coating grade)	7.79
1.83	4	FD&C Yellow Dye No. 10 aluminum lake (14 to 17%)	18.36
0.42	5	Polysorbate 80	4.27
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.12
47.6	7	Eudragit®; use methacrylic acid copolymer, NF (Eudragit® L 30D-55)	476.00
1.42	8	Triethyl citrate (Eudraflex®)	14.21

C. Brown

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg(g)
46.66	1	Distilled purified water	466.66
0.47	2	Titanium dioxide (special grade coating), USP	4.76
0.85	3	Iron oxide, black	8.53
2.26	4	Iron oxide, red	22.61
0.25	5	Iron oxide, yellow	2.57
0.42	6	Polysorbate 80	4.26
0.01	7	Dimethyl polysiloxane emulsion	0.09
47.63	8	Eudragit®; use Eudragit® L 30D-55	476.33
1.42	9	Triethyl citrate (Eudraflex®)	14.28

D. Dark Orange

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg(g)
46.66	1	Distilled purified water	466.66
2.51	2	Talc (powder)	25.18
0.39	3	Titanium dioxide (special coating grade)	3.92
0.93	4	FD&C Yellow Dye No. 6 aluminum lake	9.32
0.42	5	Polysorbate 80	4.29
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.13
47.63	7	Eudragit®; use Eudragit® L 30D-55	476.33
1.42	8	Triethyl citrate (Eudraflex®)	14.28

E. Orange

Bill of Materials			
Scale(%, w/w)	Item	Material Name	Quantity/kg(g)
46.66	1	Distilled purified water	466.66
2.60	2	Talc (powder)	26.00
0.78	3	Titanium dioxide (special coating grade)	7.84
0.46	4	FD&C Yellow Dye No. 6 aluminum lake	4.66
0.42	5	Polysorbate 80	4.27
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.11
47.61	7	Eudragit®; use Eudragit® L 30D-55	476.16
1.42	8	Triethyl citrate (Eudraflex®)	14.29

F. Dispersed Orange

Bill of Materials			
Scale(mg/tablet)	Item	Material Name	Quantity/1000 Tablets(g)
0.92	1	Opagloss NA 7150	0.92
7.07	2	Methacrylic acid copolymer (Eudragit® L 100–55)	7.07
0.09	3	Sodium hydroxide pellets (caustic soda)	0.09
0.73	4	PEG-6000	0.73
2.50	5	Talc (fine powder)	2.50
0.10	6	Simethicone emulsion 30% (simethicone antifoam M30)	0.10
0.27	7	Povidone (PVP K-25)	0.27
50.00	8	Sucrose	50.00
0.54	9	Povidone (PVP K-25)	0.54
0.36	10	Titanium dioxide	0.36
0.36	11	FD&C Yellow Dye No. 10 lake	0.36
0.04	12	Dispersed orange[a]	0.04
1.07	13	Sucrose	1.07
0.38	14	Polishing emulsion	0.38
–	15	Purified water	65.41

[a]Dispersed orange: This material is the aluminum lake of Sunset Yellow FCF (E110).

HYDROXYPROPYL METHYL CELLULOSE PHTHALATE ENTERIC COATING

A. Clear Enteric

Bill of Materials			
Scale(%)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified Water	100.00 mL
4.00 (w/v)	3	Hydroxypropyl methyl cellulose	40.00 g
0.30 (w/v)	4	Vanillin (crystals)	3.00 g
0.40 (w/v)	5	Acetylated monoglycerides	4.00 g
QS	6	Alcohol (200 proof), SD 3A	QS to 1 L

Manufacturing Directions

1. Charge acetone, purified water, and 470 mL of alcohol into a suitable mixing tank.
2. Add hydroxypropyl methylcellulose phthalate, vanillin crystals (if used), and the distilled acetylated monoglycerides.
3. Mix until a clear solution is obtained.
4. Bring up to 1 L with alcohol, and record volume used.
5. Mix for 1 hour.

B. Orchid Pink Opaque

Bill of Materials			
Scale (%)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified water	100.00 mL
8.00 (w/v)	3	Hydroxypropyl methylcellulose phthalate	80.00 g
0.80 (w/v)	4	Diacetylated monoglycerides	8.00 g
0.06 (w/v)	5	Dye Red D&C No. 30 Lake	0.60 g
0.006 (w/v)	6	FD&C Blue Dye No. 2 aluminum lake (14%)	0.06 g
0.70 (w/v)	7	Titanium dioxide	7.00 g
QS	8	Alcohol (200 proof), SD 3A	1

C. Light Apricot Orange

Bill of Materials			
Scale (%, w/v)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified water	100.00 mL
8.00	3	Hydroxypropyl methyl cellulose phthalate	80.00 g
0.80	4	Diacetylated monoglycerides	8.00 g
0.10	5	FD&C Yellow Dye No. 10 aluminum lake (14–17%)	1.00 g
0.06	6	FD&C Red Dye No. 3 aluminum lake (14%)	0.60 g
0.70	7	Titanium dioxide	7.00 g
QS	8	Alcohol (200 proof), SD 3A	To 1 kg

Part IV

Composition of Proprietary Products Approved in the US

Composition of Proprietary Products Approved in the US

- ABILIFY® (aripiprazole) tablets are available in 5-, 10-, 15-, 20-, and 30-mg strengths. Inactive ingredients include cornstarch, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and microcrystalline cellulose. Colorants include ferric oxide (yellow or red) and FD&C Blue No. 2 Aluminum Lake.
- ACCOLATE (Zafirlukast) is supplied as 10- and 20-mg tablets for oral administration. Inactive ingredients: Film-coated tablets containing croscarmellose sodium, lactose, magnesium stearate, microcrystalline cellulose, povidone, hypromellose, and titanium dioxide.
- ACEON® (perindopril erbumine) tablets are available in 2-, 4-, and 8-mg strengths for oral administration. In addition to perindopril erbumine, each tablet contains the following inactive ingredients: colloidal silica (hydrophobic), lactose, magnesium stearate, and microcrystalline cellulose. The 4- and 8-mg tablets also contain iron oxide.
- ACIPHEX® delayed-release tablets is rabeprazole sodium and is available for oral administration as delayed-release, enteric-coated tablets containing 20 mg of rabeprazole sodium. Inactive ingredients are carnauba wax, crospovidone, diacetylated monoglycerides, ethylcellulose, hydroxypropyl cellulose, hypromellose phthalate, magnesium stearate, mannitol, sodium hydroxide, sodium stearyl fumarate, talc, titanium dioxide, and yellow ferric oxide as a coloring agent.
- Actiq (oral transmucosal fentanyl citrate) is formulated as a white to off-white solid drug matrix on a handle that is radiopaque and is fracture resistant (ABS plastic) under normal conditions when used as directed. Actiq is designed to be dissolved slowly in the mouth in a manner to facilitate transmucosal absorption. The handle allows the Actiq unit to be removed from the mouth if signs of excessive opioid effects appear during administration. Active ingredient: Fentanyl citrate, USP is a highly lipophilic compound (octanol–water partition coefficient at pH 7.4 is 816:1) that is freely soluble in organic solvents and sparingly soluble in water (1:40). The pK_a's of the tertiary nitrogen are 7.3 and 8.4. Actiq is available in six strengths equivalent to 200, 400, 600, 800, 1200, or 1600 mcg fentanyl base that is identified by the text on the solid drug matrix, the dosage unit handle tag, the blister package, and the shelf carton. Inactive ingredients: Hydrated dextrates, citric acid, dibasic sodium phosphate, artificial berry flavor, magnesium stearate, modified food starch, and confectioner's sugar.
- ACTONEL (risedronate sodium tablets) tablet for oral administration contains the equivalent of 5, 30, or 35 mg of anhydrous risedronate sodium in the form of the hemi-pentahydrate with small amounts of monohydrate. Inactive ingredients: Crospovidone, ferric oxide red (35-mg tablets only), ferric oxide yellow (5 and 35-mg tablets only), hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, silicon dioxide, and titanium dioxide.
- ACTONEL with CALCIUM is a co-package product containing ACTONEL (risedronate sodium tablets, 35 mg) for once weekly dosing and calcium carbonate tablets, USP (1250 mg, equivalent to 500 mg of elemental calcium) for daily dosing for the remaining 6 days of the week. Each package contains a 28-day course of therapy. Each ACTONEL tablet in the ACTONEL with CALCIUM co-package contains the equivalent of 35 mg of anhydrous risedronate sodium in the form of the hemi-pentahydrate with small amounts of monohydrate. Inactive ingredients—ACTONEL: Crospovidone, ferric oxide red, ferric oxide yellow, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, silicon dioxide, and titanium dioxide. CALCIUM: Pregelatinized starch, sodium starch glycolate, FD&C Blue #2, magnesium stearate, polyethylene glycol 3350, hypromellose, Opaspray Light Blue, and polysorbate 80.
- ACTOPLUS MET™ (pioglitazone hydrochloride and metformin hydrochloride) tablets containing 15 mg of pioglitazone hydrochloride (as the base) with 500 mg of metformin hydrochloride (15 mg/500 mg) or 15 mg of pioglitazone hydrochloride (as the base) with 850 mg of metformin hydrochloride (15 mg/850 mg) formulated with the following excipients: povidone USP, microcrystalline cellulose NF, croscarmellose sodium NF, magnesium stearate NF, hypromellose 2910 USP, polyethylene glycol 8000 NF, titanium dioxide USP, and talc USP.
- ACTOPLUS MET™ (pioglitazone hydrochloride and metformin hydrochloride) tablets contain two oral antihyperglycemic drugs. ACTOPLUS MET is available as a tablet for oral administration containing 15 mg of pioglitazone hydrochloride (as the base) with 500 mg of metformin hydrochloride (15 mg/500 mg) or 15 mg of pioglitazone hydrochloride (as the base) with 850 mg of metformin hydrochloride (15 mg/850 mg) formulated with the following excipients: povidone USP, microcrystalline cellulose NF, croscarmellose sodium NF, magnesium stearate NF, hypromellose 2910 USP, polyethylene glycol 8000 NF, titanium dioxide USP, and talc USP.
- ACTOS (pioglitazone hydrochloride) is available as a tablet for oral administration containing 15, 30, or 45 mg of pioglitazone (as the base) formulated with the following excipients: lactose monohydrate NF, hydroxypropyl cellulose NF, carboxymethylcellulose calcium NF, and magnesium stearate NF.
- ACTOS (pioglitazone hydrochloride) is available as a tablet for oral administration containing 15, 30, or 45 mg of pioglitazone (as the base) formulated with the following excipients: lactose monohydrate NF, hydroxypropyl cellulose NF, carboxymethylcellulose calcium NF, and magnesium stearate NF.

- ADIPEX-P tablets contain the inactive ingredients cornstarch, lactose (anhydrous), magnesium stearate, microcrystalline cellulose, pregelatinized starch, sucrose, and FD&C Blue #1.
- ALDOCLOR (methyldopa-chlorothiazide) combines two antihypertensives: methyldopa and chlorothiazide is supplied as tablets for oral use, each containing 250 mg of methyldopa and 250 mg of chlorothiazide. Each tablet contains the following inactive ingredients: calcium disodium edetate, cellulose, citric acid, D&C Yellow 10 aluminum lake, ethylcellulose, FD&C Yellow 6 aluminum lake, gelatin, glycerin, guar gum, hydroxypropyl methylcellulose, magnesium stearate, starch, talc, titanium dioxide, and FD&C Blue 2 aluminum lake.
- ALDORIL Methyldopa is supplied as tablets in four strengths for oral use: ALDORIL 15 contains 250 mg of methyldopa and 15 mg of hydrochlorothiazide. ALDORIL 25 contains 250 mg of methyldopa and 25 mg of hydrochlorothiazide. ALDORIL D30 contains 500 mg of methyldopa and 30 mg of hydrochlorothiazide. ALDORIL D50 contains 500 mg of methyldopa and 50 mg of hydrochlorothiazide. Each tablet contains the following inactive ingredients: calcium disodium edetate, calcium phosphate, cellulose, citric acid, colloidal silicon dioxide, ethylcellulose, guar gum, hydroxypropyl methylcellulose, magnesium stearate, propylene glycol, talc, and titanium dioxide. ALDORIL 15 and ALDORIL D30 also contain iron oxide.
- ALKERAN (melphalan) is a film-coated tablet containing 2 mg of melphalan and the inactive ingredients colloidal silicon dioxide, crospovidone, hypromellose, macrogol/PEG 400, magnesium stearate, microcrystalline cellulose, and titanium dioxide.
- ALTOPREV™ lovastatin extended-release tablets are designed for once-a-day oral administration and deliver 10, mg, 40, or 60 mg of lovastatin. In addition to the active ingredient lovastatin, each tablet contains the following inactive ingredients: acetyltributyl citrate, butylated hydroxyanisole, candelilla wax, cellulose acetate, confectioner's sugar (contains cornstarch), FD&C yellow # 6, glyceryl monostearate, hypromellose, hypromellose phthalate, lactose, methacrylic acid copolymer, type B, polyethylene glycols (PEG 400, PEG 8000), polyethylene oxides, polysorbate 80, propylene glycol, silicon dioxide, sodium chloride, sodium lauryl sulfate, synthetic black iron oxide, red iron oxide, talc, titanium dioxide, and triacetin.
- AMPRAL® (acamprosate calcium) tablet contains acamprosate calcium 333 mg, equivalent to 300 mg of acamprosate. Inactive ingredients in CAMPRAL tablets include crospovidone, microcrystalline cellulose, magnesium silicate, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate, talc, propylene glycol, and Eudragit® L30D or equivalent. Sulfites are used in the synthesis of the drug substance and traces of residual sulfites may be present in the drug product.
- ANADROL® (oxymetholone) tablets for oral administration contain 50 mg of the steroid oxymetholone. Inactive ingredients: lactose, magnesium stearate, povidone, and starch.
- Appearex® is a biotin preparation. Each Appearex® tablet contains as its active ingredient 2.5 mg of biotin, a dose clinically proven to improve nail strength and quality. Inactive ingredients include lactose monohydrate, cornstarch, povidone (K25), and magnesium stearate.
- ARICEPT® (donepezil hydrochloride) is a film-coated tablet containing 5 or 10 mg of donepezil hydrochloride. Inactive ingredients are lactose monohydrate, cornstarch, microcrystalline cellulose, hydroxypropyl cellulose, and magnesium stearate. The film coating contains talc, polyethylene glycol, hypromellose, and titanium dioxide. Additionally, the 10-mg tablet contains yellow iron oxide (synthetic) as a coloring agent. ARICEPT® ODT tablets are available for oral administration. Each ARICEPT® ODT tablet contains 5 or 10 mg of donepezil hydrochloride. Inactive ingredients are carrageenan, mannitol, colloidal silicon dioxide, and polyvinyl alcohol. Additionally, the 10-mg tablet contains ferric oxide (yellow) as a coloring agent.
- ARIMIDEX® (anastrozole) tablets for oral administration contain 1 mg of anastrozole, a nonsteroidal aromatase inhibitor. Each tablet contains as inactive ingredients: lactose, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol, povidone, sodium starch glycolate, and titanium dioxide.
- AROMASIN® tablets for oral administration contain 25 mg of exemestane. Each AROMASIN tablet contains the following inactive ingredients: mannitol, crospovidone, polysorbate 80, hypromellose, colloidal silicon dioxide, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, simethicone, polyethylene glycol 6000, sucrose, magnesium carbonate, titanium dioxide, methylparaben, and polyvinyl alcohol.
- ARTHROTEC (diclofenac sodium/misoprostol) oral tablets are white to off-white, round, biconvex, and approximately 11 mm in diameter. Each tablet consists of an enteric-coated core containing 50 mg (ARTHROTEC 50) or 75 mg (ARTHROTEC 75) diclofenac sodium surrounded by an outer mantle containing 200 mcg misoprostol. Inactive ingredients in ARTHROTEC: colloidal silicon dioxide, crospovidone, hydrogenated castor oil, hypromellose, lactose, magnesium stearate, methacrylic acid copolymer, microcrystalline cellulose, povidone (polyvidone) K-30, sodium hydroxide, starch (corn), talc, and triethyl citrate.
- Asacol delayed-release tablet for oral administration contains 400 mg of mesalamine, an anti-inflammatory drug. The Asacol delayed-release tablets are coated with acrylic based resin, Eudragit S (methacrylic acid copolymer B, NF), which dissolves at pH 7 or greater, releasing mesalamine in the terminal ileum and beyond for topical anti-inflammatory action in the colon. Inactive ingredients: Each tablet contains colloidal silicon dioxide, dibutyl phthalate, edible black ink, iron oxide red, iron oxide yellow, lactose, magnesium stearate, methacrylic acid copolymer B (Eudragit S), polyethylene glycol, povidone, sodium starch glycolate, and talc.
- ATACAND (candesartan cilexetil) is available for oral use as tablets containing either 4, 8, 16, or 32 mg of candesartan cilexetil and the following inactive ingredients: hydroxypropyl cellulose, polyethylene glycol, lactose, cornstarch, carboxymethylcellulose calcium, and magnesium stearate. Ferric oxide (reddish brown) is added to the 8-, 16-, and 32- mg tablets as a colorant.
- ATACAND HCT (candesartan cilexetil-hydrochlorothiazide). ATACAND HCT 16-12.5 contains 16 mg of candesartan cilexetil and 12.5 mg of hydrochlorothiazide. ATACAND HCT 32-12.5 contains 32 mg of candesartan cilexetil and 12.5 mg of hydrochlorothiazide. The inactive ingredients of the tablets are calcium carboxymethylcellulose, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, cornstarch, polyethylene glycol 8000, and ferric oxide (yellow). Ferric oxide (reddish brown) is also added to the 16-12.5 mg tablet as colorant.

- Aygestin (norethindrone acetate tablets, USP)—5-mg oral tablets contain the following inactive ingredients: lactose, magnesium stearate, and microcrystalline cellulose.
- Beelith. Each tablet contains magnesium oxide 600 mg and pyridoxine hydrochloride (vitamin B6) 25 mg equivalent to vitamin B6 20 mg. Each tablet yields 362 mg of magnesium and supplies 90% of the Adult U.S. Recommended Daily Allowance (RDA) for magnesium and 1000% of the Adult RDA for vitamin B6. Inactive ingredients FD&C Yellow No. 6, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide. May also contain D&C Yellow No. 10, FD&C Yellow No. 5 (Tartrazine), hydroxypropyl cellulose, polydextrose, stearic acid, and/or triacetin.
- Bethanol chloride. Each tablet for oral administration contains 5, 10, 25, or 50 mg of bethanechol chloride, USP. Tablets also contain the following inactive ingredients: anhydrous lactose, colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, and (25 and 50 mg) D&C Yellow #10 and FD&C Yellow #6.
- BIAXIN Clarithromycin tablet (clarithromycin tablets, USP) contains 250 or 500 mg of clarithromycin and the following inactive ingredients: 250-mg tablets—hypromellose, hydroxypropyl cellulose, croscarmellose sodium, D&C Yellow No. 10, FD&C Blue No. 1, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, propylene glycol, silicon dioxide, sorbic acid, sorbitan monooleate, stearic acid, talc, titanium dioxide, and vanillin. 500-mg tablets—hypromellose, hydroxypropyl cellulose, colloidal silicon dioxide, croscarmellose sodium, D&C Yellow No. 10, magnesium stearate, microcrystalline cellulose, povidone, propylene glycol, sorbic acid, sorbitan monooleate, titanium dioxide, and vanillin. Each yellow oval film-coated BIAXIN XL tablet (clarithromycin extended-release tablets) contains 500 mg of clarithromycin and the following inactive ingredients: cellulosic polymers, D&C Yellow No. 10, lactose monohydrate, magnesium stearate, propylene glycol, sorbic acid, sorbitan monooleate, talc, titanium dioxide, and vanillin.
- BIAXIN® Filmtab® (clarithromycin tablets, USP) oval film-coated immediate-release tablet contains 500 mg of clarithromycin and the following inactive ingredients: hypromellose, hydroxypropyl cellulose, colloidal silicon dioxide, croscarmellose sodium, D&C Yellow No. 10, magnesium stearate, microcrystalline cellulose, povidone, propylene glycol, sorbic acid, sorbitan monooleate, titanium dioxide, and vanillin.
- BiDil is a fixed-dose combination of isosorbide dinitrate and hydralazine hydrochloride. Each BiDil tablet for oral administration contains 20 mg of isosorbide dinitrate and 37.5 mg of hydralazine hydrochloride. The inactive ingredients in BiDil tablets include anhydrous lactose, microcrystalline cellulose, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate, hypromellose, FD&C Yellow No. 6 aluminum lake, polyethylene glycol, titanium dioxide, polysorbate 80.
- BLOCADREN (Timolol Maleate) is supplied as tablets in three strengths containing 5, 10, or 20 mg timolol maleate for oral administration. Inactive ingredients are cellulose, FD&C Blue 2, magnesium stearate, and starch.
- Buphenyl® (sodium phenylbutyrate) tablets for oral administration contain sodium phenylbutyrate. Each tablet of Buphenyl contains 500 mg of sodium phenylbutyrate and the inactive ingredients microcrystalline cellulose, magnesium stearate, and colloidal silicon dioxide.
- CADUET® contains amlodipine besylate. CADUET tablets are formulated for oral administration in several combination strengths from 2.5/10 to 10/80 mg. Each tablet also contains calcium carbonate, croscarmellose sodium, microcrystalline cellulose, pregelatinized starch, polysorbate 80, hydroxypropyl cellulose, purified water, colloidal silicon dioxide (anhydrous), magnesium stearate, Opadry® II White 85F28751 (polyvinyl alcohol, titanium dioxide, PEG 3000 and talc), or Opadry® II Blue 85F10919 (polyvinyl alcohol, titanium dioxide, PEG 3000, talc and FD&C blue #2). Combinations of atorvastatin with 2.5 and 5 mg amlodipine are film coated white, and combinations of atorvastatin with 10 mg amlodipine are film coated blue.
- Calcium polycarbophil 625 mg (equivalent to 500-mg polycarbophil). Inactive ingredients: calcium carbonate, caramel, crospovidone, hypromellose, light mineral oil, magnesium stearate, microcrystalline cellulose, povidone, silicon dioxide, and sodium lauryl sulfate
- CANESTIN synthetic conjugated estrogens tablets contain a blend of nine synthetic estrogenic substances. The estrogenic substances are sodium estrone sulfate, sodium equilin sulfate, sodium 17(α)-dihydroequilenin sulfate, sodium 17(α)-estradiol sulfate, sodium 17(β)-dihydroequilenin sulfate, sodium 17(α)-dihydroequilenin sulfate, sodium 17(β)-dihydroequilenin sulfate, sodium equilenin sulfate, and sodium 17(β)-estradiol sulfate. Tablets for oral administration are available in 0.3-, 0.45-, 0.625-, 0.9-, and 1.25-mg strengths of synthetic conjugated estrogens. Tablets also contain the following inactive ingredients: ethylcellulose, hypromellose, lactose monohydrate, magnesium stearate, polyethylene glycol, polysorbate 80, pregelatinized starch, titanium dioxide, and triethyl citrate; 0.3-mg tablets also contain FD&C Blue No. 2 aluminum lake and D&C Yellow No. 10 aluminum lake; 0.45-mg tablets also contain FD&C Yellow No. 6/Sunset Yellow FCF lake; 0.625-mg tablets also contain FD&C Red No. 40 aluminum lake; 0.9-mg tablets do not contain additional color additives; 1.25-mg tablets also contain FD&C Blue No. 2 aluminum lake.
- Captopril tablet for oral administration contains 12.5, 25, 50, or 100 mg of captopril and the following inactive ingredients: anhydrous lactose, colloidal silicon dioxide, crospovidone, microcrystalline cellulose and stearic acid.
- CARDURA® XL (doxazosin mesylate extended-release tablets) contains doxazosin mesylate. CARDURA XL is an extended-release tablet for oral use and is designed to deliver 4 or 8 mg of doxazosin as the free base. Each 4- and 8-mg tablet contains 5.1 and 10.2 mg doxazosin mesylate (includes a 5% overage) to provide 4 and 8 mg doxazosin as a free base, respectively. The inactive ingredients for CARDURA XL: polyethylene oxide, sodium chloride, hypromellose, red ferric oxide, titanium dioxide, magnesium stearate, cellulose acetate, Macrogol®, pharmaceutical glaze, and black iron oxide. CARDURA XL is similar in appearance to a conventional tablet. It consists, however, of an osmotically active drug core surrounded by a semipermeable membrane. The core itself is divided into two layers: an "active" layer containing the drug and a "push" layer containing pharmacologically inert (but osmotically active) components. The membrane surrounding the tablet is permeable to water but not to drug or osmotic excipients. As water from the gastrointestinal tract enters the tablet, pressure increases in the osmotic layer and "pushes" against the drug layer, resulting in the release of drug through a small, laser-drilled orifice in the

membrane on the drug side of the tablet. CARDURA XL utilizes GITS (Gastrointestinal Therapeutic System), which is designed to provide a controlled rate of delivery of doxazosin into the gastrointestinal lumen, which is independent of pH or gastrointestinal (GI) motility. The function of CARDURA XL depends upon the existence of an osmotic gradient between the contents of the bilayer core and fluid in the GI tract. Drug delivery is essentially constant as long as the osmotic gradient remains constant, and then gradually falls to zero. The biologically inert components of the tablet remain intact during GI transit and are eliminated in the feces as an insoluble shell.

- CASODEX® (bicalutamide) tablets for oral administration contain 50 mg of bicalutamide. The inactive ingredients of CASODEX tablets are lactose, magnesium stearate, methylhydroxypropyl cellulose, polyethylene glycol, polyvidone, sodium starch glycolate, and titanium dioxide.
- CEFTIN tablets film-coated and contain the equivalent of 250 or 500 mg of cefuroxime as cefuroxime axetil. CEFTIN tablets contain the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, hydrogenated vegetable oil, hypromellose, methylparaben, microcrystalline cellulose, propylene glycol, propylparaben, sodium benzoate, sodium lauryl sulfate, and titanium dioxide.
- CELEBREX (celecoxib) oral capsules contain either 100, 200, or 400 mg of celecoxib. The inactive ingredients in CELEBREX capsules: croscarmellose sodium, edible inks, gelatin, lactose monohydrate, magnesium stearate, povidone, sodium lauryl sulfate, and titanium dioxide.
- Celexa® (citalopram HBr) 10-mg tablets are film-coated, oval shaped containing citalopram HBr in strengths equivalent to 10-mg citalopram base. Celexa 20-mg and 40-mg tablets are film-coated, oval, scored tablets containing citalopram HBr in strengths equivalent to 20 or 40 mg of citalopram base. The tablets also contain the following inactive ingredients: copolyvidone, cornstarch, croscarmellose sodium, glycerin, lactose monohydrate, magnesium stearate, hypromellose, microcrystalline cellulose, polyethylene glycol, and titanium dioxide. Iron oxides are used as coloring agents in the beige (10 mg) and pink (20 mg) tablets.
- CHANTIX™ tablets contain the active ingredient, varenicline (as the tartrate salt). CHANTIX is supplied for oral administration in two strengths: a 0.5-mg capsular biconvex, white to off-white, film-coated tablet and a 1-mg capsular biconvex, light blue film-coated tablet. Each 0.5-mg CHANTIX tablet contains 0.85 mg of varenicline tartrate equivalent to 0.5 mg of varenicline free base; each 1-mg CHANTIX tablet contains 1.71 mg of varenicline tartrate equivalent to 1 mg of varenicline free base. The following inactive ingredients are included in the tablets: microcrystalline cellulose, anhydrous dibasic calcium phosphate, croscarmellose sodium, colloidal silicon dioxide, magnesium stearate, Opadry® White (for 0.5 mg), Opadry® Blue (for 1 mg), and Opadry® Clear.
- Chlorpheniramine-Ibuprofen-Pseudoephedrine tablet. Active ingredients (in each caplet): chlorpheniramine maleate (2 mg), ibuprofen (200 mg), pseudoephedrine HCl (30 mg). Inactive ingredients: carnauba wax, croscarmellose sodium, FD&C red no. 40 aluminum lake, FD&C yellow no. 6 aluminum lake, glyceryl behenate, hypromellose, iron oxide black, microcrystalline cellulose, polydextrose, polyethylene glycol, pregelatinized starch, propylene glycol, silicon dioxide, starch, and titanium dioxide. Active ingredients (in each caplet): chlorpheniramine maleate (2 mg), Ibuprofen (200 mg), Pseudoephedrine HCl (30 mg). Inactive ingredients: carnauba wax, croscarmellose sodium, FD&C Red No. 40 aluminum lake, FD&C Yellow No. 6 aluminum lake, glyceryl behenate, hypromellose, iron oxide black, microcrystalline cellulose, polydextrose, polyethylene glycol, pregelatinized starch, propylene glycol, silicon dioxide, starch, and titanium dioxide.
- CIALIS® (tadalafil) is available as film-coated, almond-shaped tablets for oral administration. Each tablet contains 5, 10, or 20 mg of tadalafil and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, hypromellose, iron oxide, lactose monohydrate, magnesium stearate, microcrystalline cellulose, sodium lauryl sulfate, talc, titanium dioxide, and triacetin.
- CIPRO XR (ciprofloxacin extended-release tablets) contains ciprofloxacin, a synthetic broad-spectrum antimicrobial agent for oral administration. CIPRO XR tablets are coated, bilayer tablets consisting of an immediate-release layer and an erosion-matrix type controlled-release layer. The tablets contain a combination of two types of ciprofloxacin drug substance, ciprofloxacin hydrochloride and ciprofloxacin betaine (base). The drug substance is a faintly yellowish to light yellow crystalline substance. CIPRO XR is available in 500- and 1000-mg (ciprofloxacin equivalent) tablet strengths. CIPRO XR tablets are nearly white to slightly yellowish, film-coated, oblong-shaped tablets. Each CIPRO XR 500-mg tablet contains 500 mg of ciprofloxacin as ciprofloxacin HCl (287.5 mg, calculated as ciprofloxacin on the dried basis) and ciprofloxacin (212.6 mg, calculated on the dried basis). Each CIPRO XR 1000-mg tablet contains 1000 mg of ciprofloxacin as ciprofloxacin HCl (574.9 mg, calculated as ciprofloxacin on the dried basis) and ciprofloxacin (425.2 mg, calculated on the dried basis). The inactive ingredients are crospovidone, hypromellose, magnesium stearate, polyethylene glycol, silica colloidal anhydrous, succinic acid, and titanium dioxide.
- Citracal Prenatal Rx is a scored, white, modified oval shaped multivitamin/multimineral tablet. Each tablet contains: vitamin A (vitamin A palmitate), 2700 IU; vitamin C (ascorbic acid), 120 mg; calcium (calcium citrate), 125 mg; iron (carbonyl iron, ferrous gluconate), 27 mg; vitamin D3 (cholecalciferol), 400 IU; vitamin E (dl-tocopheryl acetate), 30 IU; thiamin (vitamin B1), 3 mg; riboflavin (vitamin B2), 3.4 mg; niacinamide (vitamin B3), 20 mg; pyridoxine HCl (vitamin B6), 20 mg; folic acid 1 mg; iodine (potassium iodide), 150 mcg; zinc (zinc oxide), 25 mg; copper (cupric oxide), 2 mg; docusate sodium, 50 mg; calcium (as Ultradense® calcium citrate), 200 mg; polyethylene glycol; croscarmellose sodium; polyvinyl alcohol-part hydrolyzed; color added;, magnesium silicate; and magnesium stearate.
- CLARINEX (desloratadine) tablets are light blue, round, film-coated tablets containing 5 mg of desloratadine, an antihistamine, to be administered orally. It also contains the following excipients: dibasic calcium phosphate dihydrate USP, microcrystalline cellulose NF, cornstarch NF, talc USP, carnauba wax NF, white wax NF, coating material consisting of lactose monohydrate, hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and FD&C Blue #2 Aluminum Lake.
- CLARINEX RediTabs® brand of desloratadine orally disintegrating tablets. Each RediTabs tablet contains either 5 or 2.5 mg of desloratadine. It also contains the following inactive ingredients: mannitol USP, microcrystalline

cellulose NF, pregelatinized starch, NF, sodium starch glycolate, USP, magnesium stearate NF, butylated methacrylate copolymer, crospovidone, NF, aspartame NF, citric acid USP, sodium bicarbonate USP, colloidal silicon dioxide, NF, ferric oxide red NF, and tutti-frutti flavoring.

- CLARINEX-D® 24-hour extended-release tablets are light blue oval shaped tablets containing 5 mg of desloratadine in the tablet coating for immediate-release and 240 mg of pseudoephedrine sulfate, USP in the tablet core for extended-release. The inactive ingredients contained in CLARINEX-D® 24-hour extended-release tablets are hypromellose USP, ethylcellulose NF, dibasic calcium phosphate dihydrate USP, magnesium stearate NF, povidone USP, silicone dioxide NF, talc USP, polyacrylate dispersion, polyethylene glycol NF, simethicone USP, Blue Lake Blend 50726 (FD&C Blue No. 2 Lake, titanium dioxide USP and edetate disodium USP), and ink (Opacode® S-1-17746 or Opacode® S-1-4159).
- CLINORIL (Sulindac) is available in 150- and 200-mg tablets for oral administration. Each tablet contains the following inactive ingredients: cellulose, magnesium stearate, starch. Sulindac is a nonsteroidal, anti-inflammatory indene derivative.
- CLORPRES® is a combination of clonidine hydrochloride and chlorthalidone. CLORPRES® is available as tablets for oral administration in three dosage strengths: 0.1 mg/15 mg, 0.2 mg/15 mg, and 0.3 mg/15 mg of clonidine hydrochloride/chlorthalidone, respectively. The inactive ingredients are ammonium chloride, colloidal silicon dioxide, croscarmellose sodium (Type A), magnesium stearate, microcrystalline cellulose, sodium lauryl sulfate, D&C yellow #10.
- Clozapine tablets, for oral administration, are available containing 25 and 100 mg of clozapine. In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, crospovidone, lactose (monohydrate), magnesium stearate, microcrystalline cellulose, and sodium lauryl sulfate. In addition, the 25-mg tablet contains FD&C red #40 lake and the 100-mg tablet contains FD&C blue #2 lake.
- COMBIVIR tablets are combination tablets containing lamivudine and zidovudine. Lamivudine (EPIVIR®, 3TC®) and zidovudine (RETROVIR®, azidothymidine, AZT, or ZDV) are synthetic nucleoside analogues with activity against human immunodeficiency virus (HIV). COMBIVIR tablets are for oral administration. Each film-coated tablet contains 150 mg of lamivudine, 300 mg of zidovudine, and the inactive ingredients colloidal silicon dioxide, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, and titanium dioxide. Lamivudine is a white to off-white crystalline solid with a solubility of approximately 70 mg/mL in water at 20°C. Zidovudine is a white to beige, odorless, crystalline solid with a solubility of 20.1 mg/mL in water at 25°C.
- Combunox™ tablet contains oxycodone HCl, USP 5 mg, and ibuprofen, USP 400 mg. Combunox tablets include sodium starch glycolate, microcrystalline cellulose, colloidal silicon dioxide, stearic acid, calcium stearate, carboxymethylcellulose, povidone, and Opadry® II White, Y-22 7719 coloring agent. Opadry® II White, Y-22 7719 coloring agent consists of titanium dioxide, polydextrose, hypromellose, triacetin, and polyethylene glycol 8000.
- Comtan® (entacapone) is available as tablets containing 200-mg entacapone. The inactive ingredients of the Comtan tablet are microcrystalline cellulose, mannitol, croscarmellose sodium, hydrogenated vegetable oil, hydroxypropyl methylcellulose, polysorbate 80, glycerol 85%, sucrose, magnesium stearate, yellow iron oxide, red oxide, and titanium dioxide.
- CONCERTA® is available in four tablet strengths. Each extended-release tablet for once-a-day oral administration contains 18, 27, 36, or 54 mg of methylphenidate HCl USP and is designed to have a 12-hour duration of effect. CONCERTA® also contains the following inert ingredients: butylated hydroxytoluene, carnauba wax, cellulose acetate, hypromellose, lactose, phosphoric acid, poloxamer, polyethylene glycol, polyethylene oxides, povidone, propylene glycol, sodium chloride, stearic acid, succinic acid, synthetic iron oxides, titanium dioxide, and triacetin. CONCERTA® uses osmotic pressure to deliver methylphenidate HCl at a controlled rate. The system, which resembles a conventional tablet in appearance, comprises an osmotically active trilayer core surrounded by a semipermeable membrane with an immediate-release drug overcoat. The trilayer core is composed of two drug layers containing the drug and excipients, and a push layer containing osmotically active components. There is a precision-laser drilled orifice on the drug-layer end of the tablet. In an aqueous environment, such as the gastrointestinal tract, the drug overcoat dissolves within 1 hour, providing an initial dose of methylphenidate. Water permeates through the membrane into the tablet core. As the osmotically active polymer excipients expand, methylphenidate is released through the orifice. The membrane controls the rate at which water enters the tablet core, which in turn controls drug delivery. Furthermore, the drug release rate from the system increases with time over a period of 6 to 7 hours due to the drug concentration gradient incorporated into the two drug layers of CONCERTA®. The biologically inert components of the tablet remain intact during gastrointestinal transit and are eliminated in the stool as a tablet shell along with insoluble core components.
- COREG (Carvedilol) is a white, oval, film-coated tablet containing 3.125, 6.25, 12.5, or 25 mg of carvedilol. The 6.25-, 12.5-, and 25-mg tablets are TILTAB® tablets. Inactive ingredients consist of colloidal silicon dioxide, crospovidone, hypromellose, lactose, magnesium stearate, polyethylene glycol, polysorbate 80, povidone, sucrose, and titanium dioxide.
- Covera-HS (verapamil hydrochloride) for oral administration as pale yellow, round, film-coated tablets containing 240 mg of verapamil hydrochloride and as lavender, round, film-coated tablets containing 180 mg of verapamil hydrochloride. Inactive ingredients are black ferric oxide, BHT, cellulose acetate, hydroxyethyl cellulose, hydroxypropyl cellulose, hypromellose, magnesium stearate, polyethylene glycol, polyethylene oxide, polysorbate 80, povidone, sodium chloride, titanium dioxide, and coloring agents: 240-mg FD&C Blue No. 2 Lake and D&C Yellow No. 10 Lake; 180-mg FD&C Blue No. 2 Lake and D&C Red No. 30 Lake. System components and performance: The Covera-HS formulation has been designed to initiate the release of verapamil 4 to 5 hours after ingestion. This delay is introduced by a layer between the active drug core and outer semipermeable membrane. As water from the gastrointestinal tract enters the tablet, this delay coating is solubilized and released. As tablet hydration continues, the osmotic layer expands and pushes against the drug layer, releasing drug through precision laser-drilled orifices in the outer membrane at a constant rate. This

controlled rate of drug delivery in the gastrointestinal lumen is independent of posture, pH, gastrointestinal motility, and fed or fasting conditions. The biologically inert components of the delivery system remain intact during GI transit and are eliminated in the feces as an insoluble shell.

- COZAAR (losartan potassium) is available as tablets for oral administration containing either 25, 50, or 100 mg of losartan potassium and the following inactive ingredients: microcrystalline cellulose, lactose hydrous, pregelatinized starch, magnesium stearate, hydroxypropyl cellulose, hypromellose, titanium dioxide, D&C yellow No. 10 aluminum lake and FD&C blue No. 2 aluminum lake. COZAAR 25-, 50-, and 100-mg tablets contain potassium in the following amounts: 2.12 mg (0.054 mEq), 4.24 mg (0.108 mEq), and 8.48 mg (0.216 mEq), respectively. COZAAR 25 mg, COZAAR 50 mg, and COZAAR 100 mg may also contain carnauba wax.
- CRESTOR® (rosuvastatin calcium) tablets for oral administration contain 5, 10, 20, or 40 mg of rosuvastatin and the following inactive ingredients: microcrystalline cellulose NF, lactose monohydrate NF, tribasic calcium phosphate NF, crospovidone NF, magnesium stearate NF, hypromellose NF, triacetin NF, titanium dioxide USP, yellow ferric oxide, and red ferric oxide NF.
- DARANIDE (Dichlorphenamide) is supplied as tablets, for oral administration, each containing 50 mg of dichlorphenamide. Inactive ingredients are D&C Yellow 10, lactose, magnesium stearate, and starch.
- DARAPRIM (pyrimethamine) tablet contains 25 mg of pyrimethamine and the inactive ingredients corn and potato starch, lactose, and magnesium stearate.
- Darvocet (Propoxyphene Napsylate). Each tablet of Darvocet A500™ contains 100 mg of propoxyphene napsylate and 500 mg of acetaminophen. Each tablet also contains anhydrous lactose, colloidal silicon dioxide, crospovidone, magnesium stearate (powder), microcrystalline cellulose, povidone, pregelatinized cornstarch, and stearic acid (powder). Film coating is composed of carnauba wax, hypromellose 2910 6cP, polyethylene glycol, purified water, sodium citrate, titanium dioxide, FD&C Red No. 40 Aluminum Lake, and FD&C Yellow No. 6 Aluminum Lake.
- DECADRON (dexamethasone tablets, USP) tablets, for oral administration, are supplied in two potencies, 0.5 and 0.75 mg. Inactive ingredients are calcium phosphate, lactose, magnesium stearate, and starch. Tablets DECADRON 0.5 mg also contain D&C Yellow 10 and FD&C Yellow 6. Tablets DECADRON 0.75 mg also contain FD&C Blue 1.
- DEPAKOTE (Divalproex sodium) is a stable coordination compound composed of sodium valproate and valproic acid in a 1:1 molar relationship and formed during the partial neutralization of valproic acid with 0.5 equivalent of sodium hydroxide. Divalproex sodium occurs as a white powder with a characteristic odor. DEPAKOTE tablets are for oral administration. DEPAKOTE tablets are supplied in three dosage strengths containing divalproex sodium equivalent to 125, 250, or 500 mg of valproic acid. Inactive ingredients DEPAKOTE tablets: cellulosic polymers, diacetylated monoglycerides, povidone, pregelatinized starch (contains cornstarch), silica gel, talc, titanium dioxide, and vanillin. In addition, 125-mg tablets contain FD&C Blue No. 1 and FD&C Red No. 40, 250-mg tablets contain FD&C Yellow No. 6 and iron oxide, and 500-mg tablets contain D&C Red No. 30, FD&C Blue No. 2, and iron oxide. DEPAKOTE ER 250- and 500-mg tablets are for oral administration. DEPAKOTE ER tablets contain divalproex sodium in a once-a-day extended-release formulation equivalent to 250 and 500 mg of valproic acid. Inactive ingredients for DEPAKOTE ER 250- and 500-mg tablets: FD&C Blue No. 1, hypromellose, lactose, microcrystalline cellulose, polyethylene glycol, potassium sorbate, propylene glycol, silicon dioxide, titanium dioxide, and triacetin. In addition, 500-mg tablets contain iron oxide and polydextrose.
- DESOXYN (methamphetamine hydrochloride tablets, USP), contain 5 mg of methamphetamine hydrochloride for oral administration. Inactive ingredients: cornstarch, lactose, sodium paraminobenzoate, stearic acid, and talc.
- DETROL tablets contain tolterodine tartrate. DETROL tablets for oral administration contain 1 or 2 mg of tolterodine tartrate. The inactive ingredients are colloidal anhydrous silica, calcium hydrogen phosphate dihydrate, cellulose microcrystalline, hypromellose, magnesium stearate, sodium starch glycolate (pH 3.0–5.0), stearic acid, and titanium dioxide.
- DEXEDRINE (dextroamphetamine sulfate) is the dextro isomer of the compound dl-amphetamine sulfate. Each triangular, orange, scored tablet is debossed SKF and E19 and contains dextroamphetamine sulfate, 5 mg. Inactive ingredients consist of calcium sulfate, FD&C Yellow No. 5 (tartrazine), FD&C Yellow No. 6, gelatin, lactose, mineral oil, starch, stearic acid, sucrose, talc, and trace amounts of other inactive ingredients.
- Didronel tablets contain either 200 or 400 mg of etidronate disodium. Inactive ingredients: Each tablet contains magnesium stearate, microcrystalline cellulose, and starch.
- DIGITEK (digoxin) is one of the cardiac (or digitalis) glycosides. Each tablet contains the labeled amount of digoxin USP and the following inactive ingredients: cornstarch, croscarmellose sodium, microcrystalline cellulose, pregelatinized starch, lactose monohydrate and anhydrous lactose, silicon dioxide and stearic acid. In addition, the 125-mcg (0.125-mg) tablet contains D&C Yellow No. 10 Aluminum Lake.
- DILAUDID TABLET contains hydromorphone hydrochloride. In addition, the tablets include lactose anhydrous, and magnesium stearate. DILAUDID 8-mg tablet may contain traces of sodium metabisulfite. Color coded tablets (for oral administration) containing 2-mg hydromorphone hydrochloride (orange tablet) and D&C red #30 Lake dye, D&C yellow #10 Lake dye, lactose, and magnesium stearate, 4-mg hydromorphone hydrochloride (yellow tablet) and D&C yellow #10 Lake dye, lactose, and magnesium stearate.
- Diovan HCT® (valsartan and hydrochlorothiazide, USP) tablets are formulated for oral administration to contain valsartan and hydrochlorothiazide, USP 80/12.5 mg, 160/12.5 mg, and 160/25 mg. The inactive ingredients of the tablets are colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, iron oxides, magnesium stearate, microcrystalline cellulose, polyethylene glycol, talc, and titanium dioxide.
- Diovan® (valsartan) is available as tablets for oral administration, containing 40, 80, 160, or 320 mg of valsartan. The inactive ingredients of the tablets are colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, iron oxides (yellow, black and/or red), magnesium stearate, microcrystalline cellulose, polyethylene glycol 8000, and titanium dioxide.
- Disulfiram tablet for oral administration contains 250 or 500 mg of disulfiram, USP. Tablets also contain colloidal

silicon dioxide, anhydrous lactose, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, and stearic acid.

- DOLOBID. Diflunisal tablets DOLOBID contain the following inactive ingredients: cellulose, FD&C Yellow 6, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, starch, talc, and titanium dioxide.
- DOSTINEX tablets contain 0.5 mg of cabergoline. Inactive ingredients consist of leucine, USP, and lactose, NF.
- Each MOTRIN® IB tablet and caplet contains ibuprofen 200 mg. Tablets and caplets: carnauba wax, cornstarch, FD&C Yellow #6, hypromellose, iron oxide, polydextrose, polyethylene glycol, silicon dioxide, stearic acid, and titanium dioxide.
- EES (Erythromycin ethylsuccinate) is an ester of erythromycin suitable for oral administration. E.E.S. 400® Filmtab® tablets: Each tablet contains erythromycin ethylsuccinate equivalent to 400 mg of erythromycin. Inactive ingredients: Cellulosic polymers, confectioner's sugar (contains cornstarch), cornstarch, D&C Red No. 30, D&C Yellow No. 10, FD&C Red No. 40, magnesium stearate, polacrilin potassium, polyethylene glycol, propylene glycol, sodium citrate, sorbic acid, and titanium dioxide.
- Effexor (venlafaxine hydrochloride) tablets contain venlafaxine hydrochloride equivalent to 25, 37.5, 50, 75, or 100 mg of venlafaxine. Inactive ingredients consist of cellulose, iron oxides, lactose, magnesium stearate, and sodium starch glycolate.
- ENABLEX® (darifenacin) is an extended-release tablet that contains 7.5 or 15 mg of darifenacin as its hydrobromide salt. ENABLEX is a once-a-day extended-release tablet and contains the following inactive ingredients: dibasic calcium phosphate anhydrous, hydroxypropyl methylcellulose (hypromellose), lactose monohydrate, magnesium stearate, titanium dioxide, and triacetin. The 15-mg tablet also contains FD&C Yellow No. 6 Aluminum Lake.
- Encora™ is a prescription vitamin and mineral nutritional supplement with essential fatty acids consisting of two capsules and two tablets on each blister card designated for AM and PM oral administration as follows. AM tablet is an oval-shaped, light pink film-coated tablet containing the following ingredients: calcium (calcium carbonate), 400 mg; vitamin D3 (cholecalciferol), 200 IU; vitamin C (as Ester-C® †), 25 mg; folic acid, USP, 2 mg; and vitamin B6 (pyridoxine hydrochloride, USP), 25 mg. PM tablet is an oval-shaped, purple film-coated tablet containing the following ingredients: calcium (calcium carbonate), 600 mg; vitamin D3 (cholecalciferol), 600 IU; vitamin C (as Ester-C®), 25 mg; folic acid, USP, 0.5 mg; and vitamin B6 (pyridoxine hydrochloride, USP), 12.5 mg. AM and PM capsule is a pink soft gelatin capsule containing the following ingredients: essential fatty acids (omega-3), 650 mg; DHA and EPA, 550 mg; α-linolenic acid (ALA), 100 mg; linoleic acid (LA), 10 mg; and vitamin E (dl-tocopheryl acetate), 50 IU. Ester-C® is a patented pharmaceutical grade material consisting of calcium ascorbate and calcium theonate. Eicosapentaenoic acid (EPA) to docosahexaenoic acid (DHA) ratio is approximately 2.7:1. Inactive ingredients (tablets): acacia, butylated hydroxyanisole, butylated hydroxytoluene, colloidal silicon dioxide, cornstarch, croscarmellose sodium, D&C Red No. 27 aluminum lake, hydrolyzed gelatin, lecithin, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, sodium lauryl sulfate, stearic acid, sucrose, talc, titanium dioxide, and vegetable oil. The AM tablet also contains FD&C Blue No. 2 aluminum lake. The PM tablet also contains FD&C Blue No. 1 aluminum lake. Inactive ingredients (capsule): D&C Red No. 33, ethyl vanillin, FD&C Red No. 40, gelatin, glycerin, soybean oil, and titanium dioxide.
- ENJUVIA (synthetic conjugated estrogens, B) tablets contain a blend of ten synthetic estrogenic substances. The estrogenic substances are sodium estrone sulfate, sodium equilin sulfate, sodium 17α-dihydroequilenin sulfate, sodium 17α-estradiol sulfate, sodium 17β-dihydroequilenin sulfate, sodium 17α-dihydroequilenin sulfate, sodium 17β-dihydroequilenin sulfate, sodium equilenin sulfate, sodium 17β-estradiol sulfate, and sodium Δ8, 9-dehydroestrone sulfate. ENJUVIA tablets for oral administration are available in 0.3-, 0.45-, 0.625-, and 1.25-mg strengths of synthetic conjugated estrogens, B. These tablets contain the following inactive ingredients: ascorbyl palmitate, butylated hydroxyanisole, colloidal silicon dioxide, edetate disodium dehydrate, plasticized ethylcellulose, hypromellose, lactose monohydrate, magnesium stearate, purified water, iron oxide red, titanium dioxide, polyethylene glycol, polysorbate 80, triacetate, and triacetin/glycerol. In addition, the 0.45-mg tablets contain iron oxide black and iron oxide yellow, and the 1.25-mg tablets contain iron oxide yellow.
- EPHEDRINE-GUAIFENESI. Active ingredients (in each tablet): Ephedrine HCl, USP, 12.5 mg; Guaifenesin, USP, 200 mg. Inactive ingredients: crospovidone, D&C yellow no. 10 aluminum lake, FD&C yellow no. 6 aluminum lake, magnesium stearate, microcrystalline cellulose, povidone, and silicon dioxide (colloidal).
- EPIVIR (also known as 3TC) is a lamivudine, a white to off-white crystalline solid with a solubility of approximately 70 mg/mL in water at 20°C. EPIVIR tablets are for oral administration. Each 150-mg film-coated tablet contains 150 mg of lamivudine and the inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, and titanium dioxide. Each 300-mg film-coated tablet contains 300 mg of lamivudine and the inactive ingredients black iron oxide, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, and titanium dioxide.
- EPIVIR-HBV is lamivudine, a white to off-white crystalline solid with a solubility of approximately 70 mg/mL in water at 20°C. EPIVIR-HBV tablets are for oral administration. Each tablet contains 100 mg of lamivudine and the inactive ingredients hypromellose, macrogol 400, magnesium stearate, microcrystalline cellulose, polysorbate 80, red iron oxide, sodium starch glycolate, titanium dioxide, and yellow iron oxide.
- EPZICOM tablets contain the following two synthetic nucleoside analogues: abacavir sulfate (ZIAGEN®, also a component of TRIZIVIR®) and lamivudine (also known as EPIVIR® or 3TC). EPZICOM tablets are for oral administration. Each orange, film-coated tablet contains the active ingredients 600 mg of abacavir as abacavir sulfate and 300 mg of lamivudine and the inactive ingredients magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The tablets are coated with a film (Opadry® orange YS 1–13065-A) that is made of FD&C Yellow No. 6, hypromellose, polyethylene glycol 400, polysorbate 80, and titanium dioxide. Abacavir sulfate is a white to off-white solid with a solubility of approximately 77 mg/mL in distilled water at 25°C. In vivo, abacavir

sulfate dissociates to its free base, abacavir. All dosages for abacavir sulfate are expressed in terms of abacavir. Lamivudine is a white to off-white crystalline solid with a solubility of approximately 70 mg/mL in water at 20°C.

- EryPed chewable tablets contain erythromycin ethylsuccinate equivalent to 200 mg of erythromycin and is scored for division into half-dose (100 mg) portions. Inactive ingredients: EryPed chewable tablets: Citric acid, confectioner's sugar (contains cornstarch), magnesium aluminum silicate, magnesium stearate, sodium carboxymethylcellulose, sodium citrate, and artificial flavor.
- ERY-TAB (erythromycin delayed-release tablets) are available in three dosage strengths, each white oval tablet containing either 250, 333, or 500 mg of erythromycin as the free base. ERY-TAB tablets comply with USP Drug Release Test 1. Inactive ingredients : Ammonium hydroxide, colloidal silicon dioxide, croscarmellose sodium, crospovidone, diacetylated monoglycerides, hydroxypropyl cellulose, hypromellose, hypromellose phthalate, magnesium stearate, microcrystalline cellulose, povidone, propylene glycol, sodium citrate, sorbitan monooleate, talc, and titanium dioxide.
- ERYTHROCIN STEARATE Filmtab tablets (erythromycin stearate tablets, USP) containing the stearate salt of erythromycin in a unique film coating. Inactive ingredients: 250-mg tablet—Cellulosic polymers, cornstarch, D&C Red No. 7, polacrilin potassium, polyethylene glycol, povidone, propylene glycol, sodium carboxymethylcellulose, sodium citrate, sorbic acid, sorbitan monooleate, and titanium dioxide. 500-mg tablet—Cellulosic polymers, cornstarch, FD&C Red No. 3, magnesium hydroxide, polacrilin potassium, povidone, propylene glycol, sorbitan monooleate, titanium dioxide, and vanillin.
- Erythromycin Base Filmtab (erythromycin tablets, USP) are available in two strengths containing either 250 or 500 mg of erythromycin base. Inactive ingredients: Colloidal silicon dioxide, croscarmellose sodium, crospovidone, D&C Red No. 30 Aluminum Lake, hydroxypropyl cellulose, hypromellose, hydroxypropyl methylcellulose phthalate, magnesium stearate, microcrystalline cellulose, povidone, polyethylene glycol, propylene glycol, sodium citrate, sodium hydroxide, sorbic acid, sorbitan monooleate, talc, and titanium dioxide.
- ESKALITH contains lithium carbonate, a white, light alkaline powder. ESKALITH CR controlled-release tablets: Each round, yellow, biconvex tablet, debossed with SKF and J10 on one side and scored on the other side, contains lithium carbonate, 450 mg. Inactive ingredients consist of alginic acid, gelatin, iron oxide, magnesium stearate, and sodium starch glycolate. ESKALITH CR tablets 450 mg are designed to release a portion of the dose initially and the remainder gradually; the release pattern of the controlled-release tablets reduces the variability in lithium blood levels seen with the immediate-release dosage forms.
- ESTRATEST® tablets: Each dark green, capsule shaped, sugar-coated oral tablet contains: 1.25 mg of Esterified Estrogens, USP, and 2.5 mg of Methyltestosterone, USP. ESTRATEST® H.S. (half-strength) tablets: Each light green, capsule shaped, sugar-coated oral tablet contains 0.625 mg of Esterified Estrogens, USP, and 1.25 mg of Methyltestosterone, USP. Esterified Estrogens, USP is a mixture of the sodium salts of the sulfate esters of the estrogenic substances, principally estrone, that are of the type excreted by pregnant mares. Esterified Estrogens contain not less than 75.0% and not more than 85.0% of sodium estrone sulfate, and not less than 6.0% and not more than 15.0% of sodium equilin sulfate, in such proportion that the total of these two components is not less than 90.0%. ESTRATEST and ESTRATEST H.S. tablets contain the following inactive ingredients: acacia, acetylated monoglycerides, calcium carbonate, carboxymethylcellulose sodium, carnauba wax NF, citric acid, colloidal silicon dioxide, gelatin, iron oxide, lactose, magnesium stearate, methylparaben, microcrystalline cellulose, pharmaceutical glaze, povidone, propylene glycol, propylparaben, shellac glaze, sodium benzoate, sodium bicarbonate, sorbic acid, starch, sucrose, talc, titanium dioxide, and tribasic calcium phosphate. ESTRATEST tablets also contain: FD&C Blue No. 1 Lake, FD&C Yellow No. 6 Lake, and D&C Yellow No. 10 Lake. ESTRATEST H.S. tablets also contain: D&C Yellow No. 10 Lake, FD&C Blue No. 1 Lake, FD&C Blue No. 2 Lake, FD&C Yellow No. 6 Lake, and FD&C Red No. 40 Lake.
- EVISTA® (raloxifene hydrochloride) tablet contains 60 mg of raloxifene HCl, which is the molar equivalent of 55.71 mg of free base. Inactive ingredients include anhydrous lactose, carnauba wax, crospovidone, FD&C Blue No. 2 aluminum lake, hypromellose, lactose monohydrate, magnesium stearate, modified pharmaceutical glaze, polyethylene glycol, polysorbate 80, povidone, propylene glycol, and titanium dioxide.
- FACTIVE (gemifloxacin mesylate). Each white to off-white, oval, film-coated FACTIVE tablet has breaklines and GE 320 debossed on both faces and contains gemifloxacin mesylate equivalent to 320 mg gemifloxacin. The inactive ingredients are crospovidone, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, and titanium dioxide.
- Famvir® (famciclovir) contains famciclovir. Tablets for oral administration: Each white, film-coated tablet contains famciclovir. The 125-mg and 250-mg tablets are round and the 500-mg tablets are oval. Inactive ingredients consist of hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, magnesium stearate, polyethylene glycols, sodium starch glycolate, and titanium dioxide.
- FazaClo® (clozapine, USP) is available as scored, yellow, orally disintegrating tablets of 25 and 100 mg for oral administration without water. Each orally disintegrating tablet contains clozapine equivalent to 25 or 100 mg. Active ingredient: Each 25-mg orally disintegrating tablet contains 3.1 mg aspartame, thus, 1.74 mg phenylalanine. Each 100-mg orally disintegrating tablet contains 12.4 mg aspartame, thus, 6.96 mg phenylalanine.
- Femara® (letrozole tablets) for oral administration contains 2.5 mg of letrozole. Femara® (letrozole tablets) is available as 2.5-mg tablets for oral administration. Inactive ingredients: Colloidal silicon dioxide, ferric oxide, hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, talc, and titanium dioxide.
- Ferrets tablets are for use as a dietary iron supplement. Each tablet contains: Iron (from 325 mg ferrous fumarate) 106 mg. Other ingredients: Microcrystalline cellulose, sodium starch glycolate, magnesium stearate, Opadry II clear, and Opadry II Red 40L15175.
- FLEXERIL 5 mg (Cyclobenzaprine HCl) is supplied as a 5-mg tablet for oral administration. FLEXERIL 10 mg (Cyclobenzaprine HCl) is supplied as a 10-mg tablet for oral administration. FLEXERIL 5 mg (Cyclobenzaprine HCl) tablets contain the following inactive ingredients: hydroxypropyl cellulose, hypromellose, lactose,

magnesium stearate, starch, titanium dioxide, Yellow D&C #10 Aluminum Lake HT, and Yellow FD&C #6 Aluminum Lake. FLEXERIL 10 mg (Cyclobenzaprine HCl) tablets contain the following inactive ingredients: hydroxypropyl cellulose, hypromellose, iron oxide, lactose, magnesium stearate, starch, and titanium dioxide.

- Flumadine® (rimantadine hydrochloride) film-coated tablet contains 100 mg of rimantadine hydrochloride plus hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, FD&C Yellow No. 6 Lake, and FD&C Yellow No. 6. The film coat contains hydroxypropyl methylcellulose and polyethylene glycol.
- Focalin™ (dexmethylphenidate hydrochloride) is the *d*-threoenantiomer of racemic methylphenidate hydrochloride, which is a 50/50 mixture of the *d*-threo and *l*-threoenantiomers. Focalin is a central nervous system (CNS) stimulant, available in three tablet strengths. Each tablet contains dexmethylphenidate hydrochloride 2.5, 5, or 10 mg for oral administration. Focalin also contains the following inert ingredients: pregelatinized starch, lactose monohydrate, sodium starch glycolate, microcrystalline cellulose, magnesium stearate, and FD&C Blue No. 1 #5516 aluminum lake (2.5-mg tablets), D&C Yellow Lake #10 (5-mg tablets); the 10-mg tablet contains no dye.
- FORTAMET™ (metformin hydrochloride) extended-release tablets are designed for once-a-day oral administration and deliver 500 or 1000 mg of metformin hydrochloride. In addition to the active ingredient metformin hydrochloride, each tablet contains the following inactive ingredients: candelilla wax, cellulose acetate, hypromellose, magnesium stearate, polyethylene glycols (PEG 400, PEG 8000), polysorbate 80, povidone, sodium lauryl sulfate, synthetic black iron oxides, titanium dioxide, and triacetin.
- FOSAMAX (alendronate sodium) tablets for oral administration contain 6.53, 13.05, 45.68, 52.21 or 91.37 mg of alendronate monosodium salt trihydrate, which is the molar equivalent of 5, 10, 35, 40 and 70 mg, respectively, of free acid, and the following inactive ingredients: microcrystalline cellulose, anhydrous lactose, croscarmellose sodium, and magnesium stearate. Tablets FOSAMAX 10 mg also contain carnauba wax.
- FOSAMAX PLUS D contains alendronate sodium, contains 91.37 mg of alendronate monosodium salt trihydrate, the molar equivalent of 70 mg of free acid, and 70 mcg of cholecalciferol equivalent to 2800 International Units (IU) vitamin D. Each tablet contains the following inactive ingredients: microcrystalline cellulose, lactose anhydrous, medium chain triglycerides, gelatin, croscarmellose sodium, sucrose, colloidal silicon dioxide, magnesium stearate, butylated hydroxytoluene, modified food starch, and sodium aluminum silicate.
- FOSRENOL® contains lanthanum carbonate (2:3) hydrate. Each FOSRENOL®, white to off-white, chewable tablet contains lanthanum carbonate hydrate equivalent to 250, 500, 750, or 1000 mg of elemental lanthanum and the following inactive ingredients: dextrates (hydrated) NF, colloidal silicon dioxide NF, and magnesium stearate NF.
- FROVA (frovatriptan succinate) tablet for oral administration contains 3.91 mg of frovatriptan succinate, equivalent to 2.5 mg of frovatriptan base. Each tablet also contains the inactive ingredients lactose NF, microcrystalline cellulose NF, colloidal silicon dioxide NF, sodium starch glycolate NF, magnesium stearate NF, hydroxypropyl methylcellulose USP, polyethylene glycol 3000 USP, triacetin USP, and titanium dioxide USP.
- Furosemide tablet for oral administration contains 20, 40, or 80 mg of furosemide and the following inactive ingredients: colloidal silicon dioxide, lactose monohydrate, microcrystalline cellulose, pregelatinized starch and stearic acid. Furosemide tablets, USP 20, 40, and 80 mg meet USP Dissolution Test 1.
- GABITRIL (tiagabine HCl) tablets contain the following inactive ingredients: Ascorbic acid, colloidal silicon dioxide, crospovidone, hydrogenated vegetable oil wax, hydroxypropyl cellulose, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, pregelatinized starch, stearic acid, and titanium dioxide. In addition, individual tablets contain the following ingredients: 2-mg tablets—FD&C Yellow No. 6. 4-mg tablets—D&C Yellow No. 10. 12-mg tablets—D&C Yellow No. 10 and FD&C Blue No. 1. 16-mg tablets—FD&C Blue No. 2.
- Gleevec® (imatinib mesylate) film-coated tablets contain imatinib mesylate equivalent to 100 or 400 mg of imatinib free base. Inactive ingredients: colloidal silicon dioxide (NF), crospovidone (NF), hydroxypropyl methylcellulose (USP), magnesium stearate (NF), and microcrystalline cellulose (NF). Tablet coating: ferric oxide, red (NF); ferric oxide, yellow (NF); hydroxypropyl methylcellulose (USP); polyethylene glycol (NF); and talc (USP).
- Gris-PEG® tablets contain ultramicrosize crystals of griseofulvin. Active ingredient: griseofulvin ultramicrosize 125 mg. Inactive ingredients: colloidal silicon dioxide, lactose, magnesium stearate, methylcellulose, methylparaben, polyethylene glycol 400 and 8000, polyvinylpyrrolidone, and titanium dioxide. Or, active ingredient: griseofulvin ultramicrosize 250 mg. Inactive ingredients: colloidal silicon dioxide, magnesium stearate, methylcellulose, methylparaben, polyethylene glycol 400 and 8000, povidone, sodium lauryl sulfate, and titanium dioxide.
- Guanidine (amino-methanamidine) tablet contains 125 mg of guanidine hydrochloride with no color additive in the base. It also contains the following inactive ingredients: colloidal silicon dioxide, magnesium stearate, mannitol, and microcrystalline cellulose.
- HYDROCORTONE (Hydrocortisone) tablets contain 10 mg of hydrocortisone in each tablet. Inactive ingredients are lactose, magnesium stearate, and starch.
- HYZAAR 50-12.5 (losartan potassium-hydrochlorothiazide), HYZAAR 100-12.5 (losartan potassium-hydrochlorothiazide), and HYZAAR 100-25 (losartan potassium-hydrochlorothiazide) are available for oral administration in two tablet combinations of losartan and hydrochlorothiazide. HYZAAR 50-12.5 contains 50 mg of losartan potassium and 12.5 mg of hydrochlorothiazide. HYZAAR 100-12.5 contains 100 mg of losartan potassium and 12.5 mg of hydrochlorothiazide. HYZAAR 100-25 contains 100 mg of losartan potassium and 25 mg of hydrochlorothiazide. Inactive ingredients are microcrystalline cellulose, lactose hydrous, pregelatinized starch, magnesium stearate, hydroxypropyl cellulose, hypromellose, and titanium dioxide. HYZAAR 50-12.5 and HYZAAR 100-25 also contain D&C yellow No. 10 aluminum lake. HYZAAR 50-12.5, HYZAAR 100-12.5, and HYZAAR 100-25 may also contain carnauba wax. HYZAAR 50-12.5 contains 4.24 mg (0.108 mEq) of potassium, HYZAAR 100-12.5 contains 8.48 mg (0.216 mEq) of potassium, and HYZAAR 100-25 contains 8.48 mg (0.216 mEq) of potassium.

- IBUPROFEN. Active ingredient: Each tablet, caplet, gel caplet, or liquigel capsule contains ibuprofen (200 mg). Inactive ingredients: Tablets and caplets—acetylated monoglyceride, beeswax and/or carnauba wax, croscarmellose sodium, iron oxides, lecithin, methylparaben, microcrystalline cellulose, pharmaceutical glaze, povidone, propylparaben, silicon dioxide, simethicone, sodium benzoate, sodium lauryl sulfate, starch, stearic acid, sucrose, and titanium dioxide. Gel Caplets—croscarmellose sodium, FD&C red no. 40, FD&C yellow no. 6, gelatin, glycerin, hypromellose, iron oxides, medium chain triglycerides, pharmaceutical ink, propyl gallate, silicon dioxide, sodium lauryl sulfate, starch, stearic acid, titanium dioxide, and triacetin.
- Ibuprofen 50 mg. Inactive ingredients: (Grape flavor) artificial flavor, aspartame, cellulose acetate phthalate, D&C Red No. 30 Lake, FD&C Blue No. 2 Lake, gelatin, magnasweet, magnesium stearate, mannitol, microcrystalline cellulose, silicon dioxide, and sodium starch glycolate. Active ingredient (in each tablet): ibuprofen 100 mg. Inactive ingredients: acetylated monoglycerides, carnauba wax, colloidal silicon dioxide, croscarmellose sodium, iron oxides, methylparaben, microcrystalline cellulose, povidone, pregelatinized starch, propylene glycol, propylparaben, shellac, sodium benzoate, starch, stearic acid, sucrose, and titanium dioxide. Active ingredient: Each brown, oval capsule contains solubilized ibuprofen, a pain reliever, equal to 200 mg of ibuprofen (present as the free acid and potassium salt). Inactive ingredients: D&C Yellow No. 10, FD&C Green No. 3, FD&C Red No. 40, gelatin, light mineral oil, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan, and sorbitol. Active ingredients (in each caplet): Ibuprofen (200 mg) and pseudoephedrine HCl (30 mg). Inactive ingredients: carnauba or equivalent wax, croscarmellose sodium, iron oxide, methylparaben, microcrystalline cellulose, propylparaben, silicon dioxide, sodium benzoate, sodium lauryl sulfate, starch, stearic acid, sucrose, and titanium dioxide. Active ingredients (in each tablet or caplet): Ibuprofen (200 mg) and pseudoephedrine HCl (30 mg). Inactive Ingredients (tablets and caplets): carnauba or equivalent wax, croscarmellose sodium, iron oxides, methylparaben, microcrystalline cellulose, propylparaben, silicon dioxide, sodium benzoate, sodium lauryl sulfate, starch, stearic acid, sucrose, and titanium dioxide.
- Ibuprofen 50 mg. Inactive ingredients: (White grape flavor) artificial flavor, carboxymethylcellulose sodium, citric acid, edetate disodium, glycerin, microcrystalline cellulose, polysorbate 80, propylene glycol, purified water, sodium benzoate, sorbitol solution, sucrose, and xanthan gum. Inactive ingredients: (grape flavor) artificial flavor, carboxymethyl cellulose sodium, citric acid, edetate disodium, FD&C blue no. 1, FD&C red no. 40, glycerin, microcrystalline cellulose, polysorbate 80, purified water, sodium benzoate, sorbitol solution, sucrose, and xanthan gum
- IMDUR (Isosorbide mononitrate (ISMN) tablets contain 30, 60, or 120 mg of isosorbide mononitrate in an extended-release formulation. The inactive ingredients are aluminum silicate, colloidal silicon dioxide, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxide, magnesium stearate, paraffin wax, polyethylene glycol, titanium dioxide, and trace amounts of ethanol.
- IMITREX tablets sumatriptan (as the succinate) contains 35, 70, or 140 mg of sumatriptan succinate equivalent to 25, 50, or 100 mg of sumatriptan, respectively. Each tablet also contains the inactive ingredients croscarmellose sodium, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, and sodium bicarbonate. Each 100-mg tablet also contains hypromellose, iron oxide, titanium dioxide, and triacetin.
- Indapamide tablet for oral administration contains 1.25 or 2.5 mg of indapamide and the following inactive ingredients: anhydrous lactose, colloidal silicon dioxide, hypromellose, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, pregelatinized starch, sodium lauryl sulfate, and titanium dioxide. Additionally, the 1.25 mg product contains glyceryl triacetate and D&C Red No. 30 Aluminum Lake and the 2.5 mg product contains triacetin.
- Inderal (propranolol hydrochloride) LA capsules contain the following inactive ingredients: cellulose, ethylcellulose, gelatin capsules, hypromellose, and titanium dioxide. In addition, Inderal LA 60-, 80-, and 120-mg capsules contain D&C Red No. 28 and FD&C Blue No. 1; Inderal LA 160-mg capsules contain FD&C Blue No. 1.
- INTELECTOL® tablet contains vinpocetine 5 mg. Other ingredients: Lactose, hydroxypropyl cellulose, magnesium stearate, and talc.
- INVERSINE® (Mecamylamine HCl) is supplied as tablets for oral use, each containing 2.5-mg mecamylamine HCl. Inactive ingredients are acacia, calcium phosphate, D&C Yellow 10, FD&C Yellow 6, lactose, magnesium stearate, starch, and talc.
- IRESSA® (gefitinib tablets) contain 250 mg of gefitinib and are available as brown film-coated tablets for daily oral administration. It is a white-colored powder. Gefitinib is a free base. The molecule has pK a s of 5.4 and 7.2 and therefore ionizes progressively in solution as the pH falls. Inactive ingredients of IRESSA tablets (core): Lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone, sodium lauryl sulfate, and magnesium stearate. Inactive ingredients of IRESSA tablets (coating): Hypromellose, polyethylene glycol 300, titanium dioxide, red ferric oxide, and yellow ferric oxide.
- KALETRA (lopinavir/ritonavir) film-coated tablets are available for oral administration in a strength of 200 mg of lopinavir and 50 mg of ritonavir with the following inactive ingredients: copovidone, sorbitan monolaurate, colloidal silicon dioxide, and sodium stearyl fumarate. The following are the ingredients in the film coating: hypromellose, titanium dioxide, polyethylene glycol 400, hydroxypropyl cellulose, talc, colloidal silicon dioxide, polyethylene 3350, yellow ferric oxide E172, and polysorbate 80.
- K-DUR® 20 product is an immediately dispersing extended-release oral dosage form of potassium chloride containing 1500 mg of microencapsulated potassium chloride, USP equivalent to 20 mEq of potassium in a tablet. The K-DUR® 10 product is an immediately dispersing extended-release oral dosage form of potassium chloride containing 750 mg of microencapsulated potassium chloride, USP equivalent to 10 mEq of potassium in a tablet. K-DUR is a tablet formulation (not enteric coated or wax matrix) containing individually microencapsulated potassium chloride crystals which disperse upon tablet disintegration. In simulated gastric fluid at 37°C and in the absence of outside agitation, K-DUR begins disintegrating into microencapsulated crystals within seconds and completely disintegrates within 1 minute. The microencapsulated crystals are formulated to provide an extended release of potassium chloride. Inactive ingredients:

crospovidone, ethylcellulose, hydroxypropyl cellulose, magnesium stearate, and microcrystalline cellulose.

- Keppra® (levetiracetam) tablets and as a clear, colorless, grape-flavored liquid (100 mg/mL) for oral administration. Inactive ingredients: colloidal silicon dioxide, cornstarch, hydroxypropyl methylcellulose, magnesium stearate, polyethylene glycol 4000, povidone, talc, titanium dioxide, and coloring agents. The individual tablets contain the following coloring agents: 250-mg tablets—FD&C Blue No. 2; 500-mg tablets—yellow iron oxide; 750-mg tablets—FD&C Blue No. 2, FD&C Yellow No. 6 and red iron oxide.
- KETEK® tablets contain telithromycin. KETEK tablets are light-orange, oval, film-coated tablets, each containing 400-mg telithromycin, plus the following inactive ingredients: cornstarch, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, red ferric oxide, talc, titanium dioxide, and yellow ferric oxide.
- K-PHOS® ORIGINAL (sodium free) tablet contains potassium acid phosphate 500 mg. Each tablet yields approximately 114 mg of phosphorus and 144 mg of potassium or 3.7 mEq. Inactive ingredients: Magnesium stearate, microcrystalline cellulose, starch, and syloid. Each tablet of K-PHOS® NEUTRAL contains 852 mg of dibasic sodium phosphate anhydrous, 155 mg of monobasic potassium phosphate, and 130 mg of monobasic sodium phosphate monohydrate. Each tablet yields approximately 250 mg of phosphorus, 298 mg of sodium (13.0 mEq), and 45 mg of potassium (1.1 mEq). Inactive ingredients: Magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate, and sugar.
- K-TAB (potassium chloride extended-release tablets) 750 mg of potassium chloride, USP, equivalent to 10 mEq of potassium in a film-coated (not enteric-coated), wax matrix tablet. This formulation is intended to slow the release of potassium so that the likelihood of a high localized concentration of potassium chloride within the gastrointestinal tract is reduced. The expended inert, porous, wax/polymer matrix is not absorbed and may be excreted intact in the stool. Inactive ingredients: Castor oil, cellulosic polymers, colloidal silicon dioxide, D&C Yellow No. 10, magnesium stearate, paraffin, polyvinyl acetate, titanium dioxide, vanillin, and vitamin E.
- LAMICTAL (lamotrigine), tablets are supplied for oral administration as 25-mg (white), 100-mg (peach), 150-mg (cream), and 200- mg (blue) tablets. Each tablet contains the labeled amount of lamotrigine and the following inactive ingredients: lactose; magnesium stearate; microcrystalline cellulose; povidone; sodium starch glycolate; FD&C Yellow No. 6 Lake (100-mg tablet only); ferric oxide, yellow (150-mg tablet only); and FD&C Blue No. 2 Lake (200-mg tablet only). LAMICTAL chewable dispersible tablets are supplied for oral administration. The tablets contain 2 mg (white), 5 mg (white), or 25 mg (white) of lamotrigine and the following inactive ingredients: blackcurrant flavor, calcium carbonate, low-substituted hydroxypropyl cellulose, magnesium aluminum silicate, magnesium stearate, povidone, saccharin sodium, and sodium starch glycolate.
- LAMISIL® (terbinafine hydrochloride tablets) terbinafine hydrochloride (equivalent to 250 mg base). Inactive ingredients: colloidal silicon dioxide, NF; hydroxypropyl methylcellulose, USP; magnesium stearate, NF; microcrystalline cellulose, NF; sodium starch glycolate, NF.
- LANOXIN (digoxin) is supplied as 125-mcg (0.125-mg) or 250-mcg (0.25-mg) tablets for oral administration. Each tablet contains the labeled amount of digoxin USP and the following inactive ingredients: corn and potato starches, lactose, and magnesium stearate. In addition, the dyes used in the 125-mcg (0.125-mg) tablets are D&C Yellow No. 10 and FD&C Yellow No. 6.
- LEUKERAN (chlorambucil) is available in tablet form for oral administration. Each film-coated tablet contains 2 mg chlorambucil and the inactive ingredients colloidal silicon dioxide, hypromellose, lactose (anhydrous), macrogol/PEG 400, microcrystalline cellulose, red iron oxide, stearic acid, titanium dioxide, and yellow iron oxide.
- LEVITRA® is formulated as orange, round, film-coated tablets containing 2.5, 5, 10, and 20 mg of vardenafil, respectively. In addition to the active ingredient, vardenafil HCl, each tablet contains microcrystalline cellulose, crospovidone, colloidal silicon dioxide, magnesium stearate, hypromellose, polyethylene glycol, titanium dioxide, yellow ferric oxide, and red ferric oxide.
- Levonorgestrel. Twenty-one pink active tablets each containing 0.10 mg of levonorgestrel. The inactive ingredients present are cellulose, hypromellose, iron oxide, lactose, magnesium stearate, polacrilin potassium, polyethylene glycol, titanium dioxide, and wax E. Seven light-green inert tablets, each containing cellulose, FD&C blue no. 1, hypromellose, iron oxide, lactose, magnesium stearate, polacrilin potassium, polyethylene glycol, titanium dioxide, and wax E.
- LEVOTHROID® (levothyroxine sodium tablets, USP) contains synthetic crystalline L-3, 3′, 5, 5′-tetraiodothyronine sodium salt [levothyroxine (T 4) sodium]. Inactive ingredients: Microcrystalline cellulose, calcium phosphate dibasic, povidone and magnesium stearate. The following are the coloring additives per tablet strength: 25 FD&C Yellow No. 6 Aluminum Lake; 50 None; 75 FD&C Blue No. 2 Aluminum Lake, FD&C Red No. 40 Aluminum Lake; 88 FD&C Yellow No. 6 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake; 100 FD&C Yellow No. 6 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake; 112 D&C Red No. 27 Aluminum Lake, D&C Red No. 30 Aluminum Lake; 125 FD&C Blue No. 1 Aluminum Lake, FD&C Red No. 40 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake; 137 FD&C Blue No. 1 Aluminum Lake; 150 FD&C Blue No. 2 Aluminum Lake; 175 FD&C Blue No. 1 Aluminum Lake, D&C Red No. 30 Aluminum Lake, D&C Red No. 27 Aluminum Lake; 200 FD&C Red No. 40 Aluminum Lake; 300 FD&C Yellow No. 6 Aluminum Lake, FD&C Blue No.1 Aluminum Lake, D&C Yellow No. 10 Aluminum Lake.
- Lexapro® (escitalopram oxalate) tablets are film-coated, round tablets containing escitalopram oxalate in strengths equivalent to 5, 10, and 20 mg escitalopram base. The 10- and 20-mg tablets are scored. The tablets also contain the following inactive ingredients: talc, croscarmellose sodium, microcrystalline cellulose/colloidal silicon dioxide, and magnesium stearate. The film coating contains hypromellose, titanium dioxide, and polyethylene glycol.
- LEXIVA (fosamprenavir calcium) tablets are available for oral administration in a strength of 700 mg of fosamprenavir as fosamprenavir calcium (equivalent to approximately 600 mg of amprenavir). Each 700-mg tablet contains the inactive ingredients colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and povidone K30. The tablet film-coating

contains the inactive ingredients hypromellose, iron oxide red, titanium dioxide, and triacetin.

- Librium is available as capsules containing 5, 10, or 25 mg chlordiazepoxide HCl. Each capsule also contains cornstarch, lactose and talc. Gelatin capsule shells may contain methyl and propyl parabens and potassium sorbate, with the following dye systems: 5-mg capsules—FD&C Yellow No. 6 plus D&C Yellow No. 10 and either FD&C Blue No. 1 or FD&C Green No. 3. 10-mg capsules—D&C Yellow No. 10 and either FD&C Blue No. 1 plus FD&C Red No. 3 or FD&C Green No.3 plus FD&C Red No. 40. 25-mg capsules—D&C Yellow No. 10 and either FD&C Green No. 3 or FD&C Blue No. 1
- LIPITOR® (atorvastatin calcium) tablets for oral administration contain 10, 20, 40, or 80 mg atorvastatin and the following inactive ingredients: calcium carbonate, USP; candelilla wax, FCC; croscarmellose sodium, NF; hydroxypropyl cellulose, NF; lactose monohydrate, NF; magnesium stearate, NF; microcrystalline cellulose, NF; Opadry White YS-1–7040 (hypromellose, polyethylene glycol, talc, titanium dioxide); polysorbate 80, NF; simethicone emulsion.
- LOFIBRA® (fenofibrate tablets) is a lipid regulating agent available as tablets for oral administration. Each tablet contains 54 or 160 mg of fenofibrate. Each 54 mg LOFIBRA® tablet contains the following inactive ingredients: colloidal silicone dioxide, croscarmellose sodium, crospovidone, iron oxide yellow, lactose monohydrate, lecithin, microcrystalline cellulose, polyvinyl alcohol, povidone, sodium lauryl sulfate, sodium starch glycolate, sodium stearyl fumarate, talc, titanium dioxide, xanthan gum, and D&C yellow #10 lake. Each 160 mg LOFIBRA® tablet contains the following inactive ingredients: colloidal silicone dioxide, croscarmellose sodium, crospovidone, lactose monohydrate, lecithin, microcrystalline cellulose, polyvinyl alcohol, povidone, sodium lauryl sulfate, sodium starch glycolate, sodium stearyl fumarate, talc, titanium dioxide, and xanthan gum.
- LORATIDINE. Active ingredient (in each tablet): Loratadine 10 mg. Inactive ingredients (Loratadine orally disintegrating tablets): artificial & natural flavor, aspartame, citric acid, colloidal silicon dioxide, corn syrup solids, crospovidone, magnesium stearate, mannitol, microcrystalline cellulose, modified food starch, and sodium bicarbonate. Inactive ingredients (Loratadine swallow tablets): lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate
- LORATIDINE-PSEUDOEPHEDRINE. Active ingredients (in each tablet): Loratadine (5 mg) and pseudoephedrine sulfate (120 mg). Inactive ingredients: croscarmellose sodium, dibasic calcium phosphate, hypromellose, lactose monohydrate, magnesium stearate, pharmaceutical ink, povidone, and titanium dioxide.
- Lortab. Hydrocodone bitartrate and acetaminophen is supplied in tablet form for oral administration. Each Lortab 2.5/500 tablet contains hydrocodone bitartrate (2.5 mg) and acetaminophen (500 mg). In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, stearic acid and sugar spheres, which are composed of starch derived from corn, sucrose, and FD&C Red #3. Each Lortab 5/500 tablet contains hydrocodone bitartrate (5 mg) and acetaminophen (500 mg). In addition, each tablet contains the following inactive ingredients: cornstarch, FD&C Blue # 1 Lake, gelatin, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, sodium starch glycolate, and sugar spheres. Each Lortab 7.5/500 tablet contains hydrocodone bitartrate (7.5 mg) and acetaminophen (500 mg). In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, stearic acid, and sugar spheres, which are composed of starch derived from corn, sucrose, FD&C Blue #1 and D&C Yellow #10. Each Lortab 10/500 tablet contains hydrocodone bitartrate (10 mg) and acetaminophen (500 mg). In addition, each tablet contains the following inactive ingredients: D&C Red No. 27 Aluminum Lake, D&C Red No. 30 Aluminum Lake, colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, starch (corn), and stearic acid.
- Lotensin HCT is a combination of benazepril hydrochloride and hydrochlorothiazide USP. The tablets are formulated for oral administration with a combination of 5, 10, or 20 mg of benazepril hydrochloride and 6.25, 12.5, or 25 mg of hydrochlorothiazide USP. The inactive ingredients of the tablets are cellulose compounds, crospovidone, hydrogenated castor oil, iron oxides (10/12.5-mg, 20/12.5-mg, and 20/25-mg tablets), lactose, polyethylene glycol, talc, and titanium dioxide.
- Lotensin is supplied as tablets containing 5, 10, 20, and 40 mg of benazepril hydrochloride for oral administration. The inactive ingredients are colloidal silicon dioxide, crospovidone, hydrogenated castor oil (5-, 10-, and 20-mg tablets), hypromellose, iron oxides, lactose, magnesium stearate (40-mg tablets), microcrystalline cellulose, polysorbate 80, propylene glycol (5- and 40-mg tablets), starch, talc, and titanium dioxide.
- LOTRONEX tablets is alosetron hydrochloride (HCl) and is a white to beige solid that has a solubility of 61 mg/mL in water, 42 mg/mL in 0.1M hydrochloric acid, 0.3 mg/mL in pH 6 phosphate buffer, and <0.1 mg/mL in pH 8 phosphate buffer. LOTRONEX tablets are supplied for oral administration as 0.5-mg (white) and 1-mg (blue) tablets. The 0.5-mg tablet contains 0.562 mg alosetron HCl equivalent to 0.5 mg alosetron and the 1-mg tablet contains 1.124 mg alosetron HCl equivalent to 1 mg of alosetron. Each tablet also contains the inactive ingredients: lactose (anhydrous), magnesium stearate, microcrystalline cellulose, and pregelatinized starch. The white film-coat for the 0.5-mg tablet contains hypromellose, titanium dioxide, and triacetin. The blue film-coat for the 1-mg tablet contains hypromellose, titanium dioxide, triacetin, and indigo carmine.
- MALARONE (atovaquone and proguanil hydrochloride) is a fixed-dose combination of the antimalarial agents atovaquone and proguanil hydrochloride. MALARONE tablets and MALARONE pediatric tablets are for oral administration. Each MALARONE tablet contains 250 mg of atovaquone and 100 mg of proguanil hydrochloride and each MALARONE pediatric tablet contains 62.5 mg of atovaquone and 25 mg of proguanil hydrochloride. The inactive ingredients in both tablets are low-substituted hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, poloxamer 188, povidone K30, and sodium starch glycolate. The tablet coating contains hypromellose, polyethylene glycol 400, polyethylene glycol 8000, red iron oxide, and titanium dioxide.
- MAVIK (Trandolapril) tablets contain 1, 2, or 4 mg of trandolapril for oral administration. Each tablet also contains cornstarch, croscarmellose sodium, hypromellose, iron oxide, lactose, povidone, and sodium stearyl fumarate.

- MAXALT contains rizatriptan benzoate. MAXALT tablets and MAXALT-MLT orally disintegrating tablets are available for oral administration in strengths of 5 and 10 mg (corresponding to 7.265 or 14.53 mg of the benzoate salt, respectively). Each compressed tablet contains the following inactive ingredients: lactose monohydrate, microcrystalline cellulose, pregelatinized starch, ferric oxide (red), and magnesium stearate. Each lyophilized orally disintegrating tablet contains the following inactive ingredients: gelatin, mannitol, glycine, aspartame, and peppermint flavor.
- MAXZIDE® (triamterene and hydrochlorothiazide) combines triamterene with hydrochlorothiazide. Each MAXZIDE® tablet contains: Triamterene, USP 75 mg; Hydrochlorothiazide, USP 50 mg. Each MAXZIDE®-25 MG tablet contains: Triamterene, USP 37.5 mg; hydrochlorothiazide, USP 25 mg. MAXZIDE® and MAXZIDE®-25 MG tablets for oral administration contain the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, powdered cellulose, sodium lauryl sulfate, and D&C Yellow #10. MAXZIDE®-25 MG tablets also contain FD&C Blue #1.
- MEBARAL (mephobarbital) is available as tablets for oral administration. Inactive ingredients: Lactose, starch, stearic acid, and talc.
- Melatonin. Each tablet contains Melatonin 3 mg, methylcobalamin (vitamin B12), 1 mg; folic acid, 0.4 mg.
- MEPHYTON Phytonadione tablets containing 5 mg of phytonadione are yellow, compressed tablets, scored on one side. Inactive ingredients are acacia, calcium phosphate, colloidal silicon dioxide, lactose, magnesium stearate, starch, and talc.
- MEVACOR® (Lovastatin), tablets are supplied as 10-, 20-, and 40-mg tablets for oral administration. In addition to the active ingredient lovastatin, each tablet contains the following inactive ingredients: cellulose, lactose, magnesium stearate, and starch. Butylated hydroxyanisole (BHA) is added as a preservative. Tablets MEVACOR 10 mg also contain red ferric oxide and yellow ferric oxide. Tablets MEVACOR 20 mg also contain FD&C Blue 2. Tablets MEVACOR 40 mg also contain D&C Yellow 10 aluminum lake and FD&C Blue 2 aluminum lake.
- MIDAMOR (Amiloride HCl) is available for oral use as tablets containing 5 mg of anhydrous amiloride HCl. Each tablet contains the following inactive ingredients: calcium phosphate, D&C Yellow 10, iron oxide, lactose, magnesium stearate, and starch.
- Minocycline hydrochloride tablets for oral administration contain minocycline HCl equivalent to 50, 75, or 100 mg of minocycline. In addition, 50-, 75-, and 100-mg tablets contain the following inactive ingredients: Colloidal silicon dioxide, lactose anhydrous, magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate. The 50-mg tablets also contain Opadry White which contains titanium dioxide, hydroxypropyl methylcellulose, polyethylene glycol, and polysorbate 80. The 75- and 100-mg tablets contain Opadry Gray which contains titanium dioxide, hydroxypropyl methylcellulose, polyethylene glycol, and iron oxide black.
- MIRADON tablets contain a synthetic anticoagulant, anisindione, an indanedione derivative. Each tablet contains 50 mg anisindione. They also contain: cornstarch, FD&C Red No. 3, gelatin, lactose, and hydrogenated cotton-seed oil.
- MS CONTIN® Controlled-release tablets 15, 30, 60, 100, and 200 mg of morphine sulfate and further contain the following inactive ingredients: cetostearyl alcohol, hydroxyethyl cellulose, hypromellose, magnesium stearate, polyethylene glycol, talc, and titanium dioxide. MS CONTIN® controlled-release tablets 15 mg also contains FD&C Blue No. 2, lactose and polysorbate 80. MS CONTIN® controlled-release tablets 30 mg also contains D&C Red No. 7, FD&C Blue No. 1, lactose and polysorbate 80. MS CONTIN® controlled-release tablets 60 mg also contains D&C Red No. 30, D&C Yellow No. 10, hydroxypropyl cellulose, and lactose. MS CONTIN® controlled-release tablets 100 mg also contains black iron oxide. MS CONTIN® controlled-release tablets 200 mg also contains D&C Yellow No. 10, FD&C Blue No. 1, and hydroxypropyl cellulose.
- Myfortic® (mycophenolic acid) delayed-release tablets are an enteric formulation of mycophenolate sodium that delivers the active moiety mycophenolic acid (MPA). Myfortic is available for oral use as delayed-release tablets containing either 180 or 360 mg of mycophenolic acid. Inactive ingredients include colloidal silicon dioxide, crospovidone, lactose anhydrous, magnesium stearate, povidone (K-30), and starch. The enteric coating of the tablet consists of hypromellose phthalate, titanium dioxide, iron oxide yellow, and indigotine (180 mg) or iron oxide red (360 mg).
- MYLERAN (busulfan) film-coated tablet contains 2 mg busulfan and the inactive ingredients hypromellose, lactose (anhydrous), magnesium stearate, pregelatinized starch, triacetin, and titanium dioxide.
- Nadolol tablet for oral administration contains 20, 40, or 80 mg of nadolol and the following inactive ingredients: croscarmellose sodium, lactose (anhydrous), magnesium stearate, microcrystalline cellulose, sodium lauryl sulfate, and D&C Yellow #10 Aluminum Lake.
- Namenda® (memantine hydrochloride) capsule-shaped, film-coated tablets containing 5 and 10 mg of memantine hydrochloride. The tablets also contain the following inactive ingredients: microcrystalline cellulose/colloidal silicon dioxide, talc, croscarmellose sodium, and magnesium stearate. In addition the following inactive ingredients are also present as components of the film coat: hypromellose, titanium dioxide, polyethylene glycol 400, FD&C yellow #6 and FD&C blue #2 (5-mg tablets), and hypromellose, titanium dioxide, macrogol/polyethylene glycol 400 and iron oxide black (10-mg tablets).
- Neurontin® (gabapentin) tablets are elliptical film-coated tablets containing 600 and 800 mg of gabapentin. The inactive ingredients for the tablets are poloxamer 407, copolyvidonum, cornstarch, magnesium stearate, hydroxypropyl cellulose, talc, candelilla wax, and purified water.
- NEXAVAR film-coated tablet contains sorafenib tosylate (274 mg) equivalent to 200 mg of sorafenib and the following inactive ingredients: croscarmellose sodium, microcrystalline cellulose, hypromellose, sodium lauryl sulphate, magnesium stearate, polyethylene glycol, titanium dioxide, and ferric oxide red.
- Nicomide® tablets for oral administration are peach-colored, oval-shaped tablets imprinted "Sirius" in blue ink on one side. Each oral tablet provides nicotinamide, USP, 750 mg; zinc oxide, USP, 25 mg; cupric oxide, USP 1.5 mg; folic acid, USP 500 mcg. Nicomide® has been designed to provide biphasic delivery of each of the active ingredients in order to minimize the potential for competitive antagonism in absorption of its ingredients. The biphasic

delivery system facilitates the immediate release of 750 mg nicotinamide, 1.5 mg cupric oxide, and 500 mcg folic acid as well as the sustained release of 25 mg zinc oxide. The biphasic delivery system also minimizes the potential for drug interaction induced deficiency states and impaired absorptions of other therapeutic agents. Inactive ingredients: Carnauba wax powder, ethyl cellulose, FD&C Blue # 1, FD&C Yellow # 6 Aluminum Lake, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, propylene glycol, shellac, stearic acid, and titanium dioxide.

- NIRAVAM™ (alprazolam orally disintegrating tablets) contains either 0.25, 0.5, 1, or 2 mg of alprazolam and the following inactive ingredients: colloidal silicon dioxide, cornstarch, crospovidone, magnesium stearate, mannitol, methacrylic acid copolymer, microcrystalline cellulose, natural and artificial orange flavor, sucralose, and sucrose. In addition, the 0.25- and 0.5-mg tablets contain yellow iron oxide.
- Nystatin Vaginal tablets, USP, are available as oval-shaped compressed tablets for intravaginal administration, each containing 100,000 units Nystatin, USP. Inactive ingredients include cornstarch, ethylcellulose, anhydrous lactose, microcrystalline cellulose, polyethylene glycol, and stearic acid.
- OptiNate™ is a prescription prenatal/postnatal multivitamin/mineral capsule and tablet combination with essential fatty acids. Each tablet contains elemental iron (carbonyl iron), 90 mg; biotin, 30 mcg; pantothenic acid (calcium pantothenate, USP), 6 mg; calcium (calcium carbonate, USP), 200 mg; copper (cupric oxide), 2 mg; zinc (zinc oxide, USP), 15 mg; folate, 1 mg (*l*-methylfolate as Metafolin® 600 mcg) (folic acid, USP 400 mcg); vitamin D3 (cholecalciferol), 400 IU; vitamin E (dl-tocopheryl acetate), 10 IU; vitamin C (ascorbic acid, USP), 120 mg; vitamin B1 (thiamine mononitrate), 3 mg; vitamin B2 (riboflavin, USP), 3.4 mg; vitamin B6 (pyridoxine HCl), 20 mg; vitamin B12 (cyanocobalamin), 12 mcg; niacinamide, USP, 20 mg; magnesium (magnesium oxide, USP), 30 mg; docusate sodium, USP, 50 mg. Each L-Vcaps™ capsule contains docosahexaenoic acid (DHA) 250 mg. DHA is contained in the oil derived from microalgae. Other ingredients (OptiNate™ Omega-3L-Vcaps™): Hypromellose, iron oxide, beeswax, ascorbyl palmitate, mixed tocopherols, and other ingredients. Other ingredients (OptiNate™ tablets): Calcium phosphate dibasic, carnauba wax, crospovidone, dextrin, dl-tocopherol, gelatin, hypromellose, lactose, magnesium stearate, mono- and diglycerides, polacrilin, pregelatinized starch, propylene glycol, silicon dioxide, sodium benzoate, partially hydrogenated soybean oil, starch, stearic acid, sucrose, titanium dioxide, and other ingredients.
- ORAP® (pimozide) tablet contains either 1 or 2 mg of pimozide and the following inactive ingredients: calcium stearate, microcrystalline cellulose, lactose anhydrous, and cornstarch.
- OxyContin® (oxycodone hydrochloride controlled-release) tablets contain the following inactive ingredients: ammonio methacrylate copolymer, hypromellose, lactose, magnesium stearate, polyethylene glycol 400, povidone, sodium hydroxide, sorbic acid, stearyl alcohol, talc, titanium dioxide, and triacetin. The 10-mg tablets also contain hydroxypropyl cellulose. The 20-mg tablets also contain polysorbate 80 and red iron oxide. The 40-mg tablets also contain polysorbate 80 and yellow iron oxide. The 80-mg tablets also contain FD&C blue No. 2, hydroxypropyl cellulose, and yellow iron oxide. The 160-mg tablets also contain FD&C blue No. 2 and polysorbate 80.
- Pacerone® (Amiodarone HCl) tablets are available in four strengths, containing 100, 200, 300, and 400 mg amiodarone hydrochloride, for oral administration. The 100-mg tablets are white tablets with the following inactive ingredients: anhydrous lactose, colloidal silicone dioxide, cornstarch, magnesium stearate, and povidone. The 200-mg tablets are pink, scored tablets with the following inactive ingredients: lactose monohydrate, magnesium stearate, povidone, pregelatinized cornstarch, sodium starch glycolate, stearic acid, FD&C Red 40, and FD&C Yellow 6. The 300-mg tablets are peach, scored tablets with the following inactive ingredients: colloidal silicone dioxide, cornstarch, anhydrous lactose, magnesium stearate, povidone, and FD&C Yellow 6 Lake. The 400-mg tablets are light yellow, scored tablets with the following inactive ingredients: colloidal silicon dioxide, cornstarch, lactose monohydrate, magnesium stearate, povidone, and D&C Yellow 10 Aluminum Lake.
- Pacerone® (Amiodarone HCl) tablets are available in four strengths, containing 100, 200, 300, and 400 mg of amiodarone hydrochloride, for oral administration. The 100-mg tablets are white tablets with the following inactive ingredients: anhydrous lactose, colloidal silicone dioxide, cornstarch, magnesium stearate and povidone. The 200-mg tablets are pink, scored tablets with the following inactive ingredients: lactose monohydrate, magnesium stearate, povidone, pregelatinized cornstarch, sodium starch glycolate, stearic acid, FD&C Red 40, and FD&C Yellow 6. The 300-mg tablets are peach, scored tablets with the following inactive ingredients: colloidal silicone dioxide, cornstarch, anhydrous lactose, magnesium stearate, povidone, and FD&C Yellow 6 Lake. The 400-mg tablets are light yellow, scored tablets with the following inactive ingredients: colloidal silicon dioxide, cornstarch, lactose monohydrate, magnesium stearate, povidone, and D&C Yellow 10 Aluminum Lake.
- PARCOPA™ (carbidopa-levodopa orally disintegrating tablets) is a combination of carbidopa and levodopa. PARCOPA™ 25/100 contains 25 mg of carbidopa and 100 mg of levodopa. PARCOPA™ 10/100 contains 10 mg of carbidopa and 100 mg of levodopa. PARCOPA™ 25/250 contains 25 mg of carbidopa and 250 mg of levodopa. Inactive ingredients are aspartame, citric acid, crospovidone, magnesium stearate, mannitol, microcrystalline cellulose, natural and artificial mint flavor, and sodium bicarbonate. PARCOPA™ 10/100 and 25/250 also contain FD&C blue #2 HT aluminum lake. PARCOPA™ 25/100 also contains yellow 10 iron oxide.
- PARNATE, tranylcypromine sulfate rose-red, film-coated tablet contains tranylcypromine sulfate equivalent to 10 mg of tranylcypromine. Inactive ingredients consist of cellulose, citric acid, croscarmellose sodium, D&C Red No. 7, FD&C Blue No. 2, FD&C Red No. 40, FD&C Yellow No. 6, gelatin, iron oxide, lactose, magnesium stearate, talc, titanium dioxide, and trace amounts of other inactive ingredients.
- PAXIL CR (paroxetine hydrochloride) enteric, film-coated, controlled-release tablet contains paroxetine hydrochloride equivalent to paroxetine as follows: 12.5 mg (yellow), 25 mg (pink), and 37.5 mg (blue). One layer of the tablet consists of a degradable barrier layer and the other contains the active material in a hydrophilic matrix. Inactive ingredients consist of hypromellose, polyvinylpyrrolidone, lactose monohydrate, magnesium stearate, colloidal

silicon dioxide, glyceryl behenate, methacrylic acid copolymer type C, sodium lauryl sulfate, polysorbate 80, talc, triethyl citrate, and one or more of the following colorants: Yellow ferric oxide, red ferric oxide, D&C Red No. 30, D&C Yellow No. 6, D&C Yellow No. 10, FD&C Blue No. 2. Each film-coated tablet contains paroxetine hydrochloride equivalent to paroxetine as follows: 10 mg, yellow (scored); 20 mg, pink (scored); 30 mg, blue; 40 mg, green. Inactive ingredients consist of dibasic calcium phosphate dihydrate, hypromellose, magnesium stearate, polyethylene glycols, polysorbate 80, sodium starch glycolate, titanium dioxide, and one or more of the following: D&C Red No. 30, D&C Yellow No. 10, FD&C Blue No. 2, and FD&C Yellow No. 6.

- PCE (erythromycin particles in tablets). The coating protects the antibiotic from the inactivating effects of gastric acidity and permits efficient absorption of the antibiotic in the small intestine. PCE is available in two strengths containing either 333 or 500 mg of erythromycin base. PCE 500-mg tablets contain no synthetic dyes or artificial colors. Inactive ingredients: PCE 333-mg tablets: Cellulosic polymers, citrate ester, colloidal silicon dioxide, D&C Red No. 30, hydrogenated vegetable oil wax, lactose, magnesium stearate, microcrystalline cellulose, povidone, propylene glycol, sodium starch glycolate, stearic acid, and vanillin. PCE 500-mg tablets: Cellulosic polymers, citrate ester, colloidal silicon dioxide, crospovidone, hydrogenated vegetable oil wax, iron oxide, microcrystalline cellulose, polyethylene glycol, povidone, propylene glycol, stearic acid, talc, titanium dioxide, and vanillin.
- PEGANONE (ethotoin tablets, USP) are available in a dosage strength of 250 mg. Inactive ingredients Acacia, lactose, sodium carboxymethylcellulose, stearic acid, and talc.
- Peri-Colace® (docusate sodium and standardized senna concentrate) is a combination stimulant laxative and stool softener. Peri-Colace® tablets contains the following active ingredient: 50 mg of docusate sodium and 8.6 mg of sennosides. Inactive ingredients: carnauba wax, colloidal silicon dioxide, croscarmellose sodium, dicalcium phosphate, FD&C Blue No. 2, FD&C Red No. 40, hypromellose, magnesium stearate, microcrystalline cellulose, PEG 400, sodium benzoate, stearic acid, and titanium dioxide.
- Phenergan. Each tablet of Phenergan contains 12.5, 25, or 50 mg promethazine HCl. The inactive ingredients present are lactose, magnesium stearate, and methylcellulose. Each dosage strength also contains the following: 12.5 mg—FD&C Yellow 6 and saccharin sodium; 25 mg—saccharin sodium; 50 mg—FD&C Red 40. Each rectal suppository of Phenergan contains 12.5, 25, or 50 mg promethazine HCl with ascorbyl palmitate, silicon dioxide, white wax, and cocoa butter.
- PLAVIX (clopidogrel bisulfate) for oral administration is provided as pink, round, biconvex, debossed film-coated tablets containing 97.875 mg of clopidogrel bisulfate, which is the molar equivalent of 75 mg of clopidogrel base. Each tablet contains hydrogenated castor oil, hydroxypropyl cellulose, mannitol, microcrystalline cellulose, and polyethylene glycol 6000 as inactive ingredients. The pink film coating contains ferric oxide, hypromellose 2910, lactose monohydrate, titanium dioxide, and triacetin. The tablets are polished with Carnauba wax.
- PLENDIL (felodipine) is available as tablets containing 2.5, 5, or 10 mg of felodipine for oral administration. In addition to the active ingredient felodipine, the tablets contain the following inactive ingredients: 2.5-mg tablets-–hydroxypropyl cellulose, lactose, FD&C Blue 2, sodium stearyl fumarate, titanium dioxide, yellow iron oxide, and other ingredients. 5- and 10-mg tablets—cellulose, red and yellow oxide, lactose, polyethylene glycol, sodium stearyl fumarate, titanium dioxide, and other ingredients.
- PLETAL (cilostazol) tablets for oral administration are available in 50 mg triangular and 100 mg round, white debossed tablets. Each tablet, in addition to the active ingredient, contains the following inactive ingredients: carboxymethylcellulose calcium, cornstarch, hydroxypropyl methylcellulose 2910, magnesium stearate, and microcrystalline cellulose.
- PRANDIN® (repaglinide) tablets contain 0.5, 1, or 2 mg of repaglinide. In addition each tablet contains the following inactive ingredients: calcium hydrogen phosphate (anhydrous), microcrystalline cellulose, maize starch, polacrilin potassium, povidone, glycerol (85%), magnesium stearate, meglumine, and poloxamer. The 1- and 2-mg tablets contain iron oxides (yellow and red, respectively) as coloring agents.
- PreCare® Chewables are prescription prenatal multivitamin/mineral nutritional supplement tablets. Each orange colored, flavored, oval, chewable tablet contains: Folic Acid, USP, 1 mg; vitamin B6 (pyridoxine HCl), 2 mg; vitamin C (as Ester-C®)*, 50 mg; vitamin D3 (cholecalciferol), 6 mcg; vitamin E (dl-tocopheryl acetate), 3.5 IU; calcium (calcium carbonate), 250 mg; copper (cupric oxide), 2 mg; iron (including MicroMask® ferrous fumarate), 40 mg; magnesium (magnesium oxide, USP), 50 mg; zinc (zinc oxide, USP), 15 mg.* Ester-C® is a patented pharmaceutical grade material consisting of calcium ascorbate and calcium threonate. Inactive ingredients: Citric acid, FD&C yellow #6 lake, flow agents, natural and artificial nonnutritive and nutritive sweetening agents, and natural and artificial flavors.
- PreCare® Prenatal is a prescription prenatal multivitamin/mineral nutritional supplement. Each dye-free, peach film-coated caplet contains Folic Acid, USP 1 mg; vitamin B1 (thiamine mononitrate, USP) 3 mg; vitamin B2 (riboflavin, USP) 3.4 mg; vitamin B3 (niacinamide) 20 mg; vitamin B6 (pyridoxine HCl, USP) 50 mg; vitamin B12 (cyanocobalamin) 12 mcg; vitamin C (as Ester-C) 50 mg; vitamin D3 (cholecalciferol) l6 mcg; vitamin E (dl-tocopheryl acetate) 3.5 IU; Calcium (as CalciPure™ calcium carbonate) 250 mg; Copper (cupric oxide) 2 mg; Iron (as MicroMask® ferrous fumarate) 40 mg; Magnesium (magnesium oxide, USP) 50 mg; Zinc (zinc oxide, USP) 15 mg. Inactive ingredients: Natural oils, natural wax, cellulose polymers, flow agents, and other ingredients. Dye free.
- PRECOSE® (acarbose tablets) is available as 25-, 50-, and 100-mg tablets for oral use. The inactive ingredients are starch, microcrystalline cellulose, magnesium stearate, and colloidal silicon dioxide.
- PREFEST regimen provides for a single oral tablet to be taken once daily. The estrogenic component of PREFEST is estradiol, USP. It is a white, crystalline solid. The progestational component of PREFEST is micronized norgestimate, a white powder. Each tablet for oral administration contains 1.0 mg estradiol alone or 1.0 mg estradiol and 0.09 mg of norgestimate, and the following inactive ingredients: croscarmellose sodium, microcrystalline cellulose, magnesium stearate, ferric oxide red, and lactose monohydrate.
- Prelief tablets : Each tablet contains 345 mg calcium glycerophosphate (65 mg of elemental calcium). The tablets also contain 0.25% magnesium stearate as a processing aid.

Two tablets are equivalent to 690 mg calcium glycerophosphate (130 mg of elemental calcium).

- Premarin® (conjugated estrogens tablets, USP) for oral administration contains a mixture of conjugated estrogens obtained exclusively from natural sources, occurring as the sodium salts of water-soluble estrogen sulfates blended to represent the average composition of material derived from pregnant mares' urine. It is a mixture of sodium estrone sulfate and sodium equilin sulfate. It contains as concomitant components, as sodium sulfate conjugates, 17α-dihydroequilenin, 17α-estradiol, and 17β-dihydroequilenin. Tablets for oral administration are available in 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, and 1.25 mg strengths of conjugated estrogens. Premarin 0.3-, 0.45-, 0.625-, 0.9-, and 1.25-mg tablets also contain the following inactive ingredients: calcium phosphate tribasic, hydroxypropyl cellulose, microcrystalline cellulose, powdered cellulose, hypromellose, lactose monohydrate, magnesium stearate, polyethylene glycol, sucrose, and titanium dioxide. The 0.3-mg tablets also contain D&C Yellow No. 10 and FD&C Blue No. 2. The 0.45-mg tablets also contain FD&C Blue No. 2. The 0.625-mg tablets also contain FD&C Blue No. 2 and FD&C Red No. 40. The 0.9-mg tablets also contain: D&C Red No. 30 and D&C Red No. 7. The 1.25-mg tablets also contain black iron oxide, D&C Yellow No. 10, and FD&C Yellow No. 6.
- PremCal is a combination calcium and vitamin D nutritional supplement that offers three different strengths of vitamin D3 per tablet—500 IU, 750 IU, and 1000 IU with 500 mg of elemental calcium as the carbonate. PremCal is indicated in those requiring higher than the currently recommended doses of vitamin D such as vitamin D deficiency, premenstrual syndrome, osteoporosis, osteomalacia, or malabsorption. Ingredients: PremCal tablets are supplied in three different strengths of vitamin D3 (light, 500 IU; regular, 750 IU; extra strength,1000 IU) with a constant amount of calcium 500 mg as calcium carbonate and 15 mg of magnesium oxide. Each tablet also contains hypromellose, croscarmellose sodium, malto dextrin, povidone, stearic acid, magnesium stearate, triacetin, polyethylene glycol, and silicon dioxide. Free of sugar, soy, wheat, gluten, corn, shellfish, and artificial colors.
- PremesisRx®. Each blue tablet contains vitamin B6 (as pyridoxine HCl), 75 mg; vitamin B12 (cyanocobalamin), 12 mcg; folic acid, USP, 1 mg; calcium (as calcium carbonate), 200 mg. Inactive ingredients: Natural waxes, cellulose polymers, FD&C blue No. 1 aluminum lake, D&C yellow No. 10 aluminum lake, flow agents, and other ingredients.
- PREMPRO™ 0.3 mg/1.5 mg therapy consists of a single tablet containing 0.3 mg of the conjugated estrogens (CE) found in Premarin® tablets and 1.5 mg of medroxyprogesterone acetate (MPA) for oral administration. PREMPRO 0.45 mg/1.5 mg therapy consists of a single tablet containing 0.45 mg of the conjugated estrogens found in Premarin tablets and 1.5 mg of medroxyprogesterone acetate for oral administration. PREMPRO 0.625 mg/2.5 mg therapy consists of a single tablet containing 0.625 mg of the conjugated estrogens found in Premarin tablets and 2.5 mg of medroxyprogesterone acetate for oral administration. PREMPRO 0.625 mg/5 mg therapy consists of a single tablet containing 0.625 mg of the conjugated estrogens found in Premarin tablets and 5 mg of medroxyprogesterone acetate for oral administration. PREMPHASE® therapy consists of two separate tablets, a maroon Premarin tablet containing 0.625 mg of conjugated estrogens that is taken orally on days 1 through 14 and a light-blue tablet containing 0.625 mg of the conjugated estrogens found in Premarin tablets and 5 mg of medroxyprogesterone acetate that is taken orally on days 15 through 28. Premarin (conjugated estrogens tablets, USP) for oral administration contains a mixture obtained exclusively from natural sources, occurring as the sodium salts of water-soluble estrogen sulfates blended to represent the average composition of material derived from pregnant mares' urine. It is a mixture of sodium estrone sulfate and sodium equilin sulfate. It contains as concomitant components, as sodium sulfate conjugates, 17 (α)-dihydroequilenin, 17 (α)-estradiol, and 17 (β)-dihydroequilenin.
- PREVACID® NapraPAC™ 375 is a combination package containing NAPROSYN 375-mg tablets and PREVACID 15-mg capsules. PREVACID® NapraPAC™ 500 is a combination package containing NAPROSYN 500-mg tablets and PREVACID 15-mg capsules. NAPROSYN tablets contain 250, 375, or 500 mg of naproxen (active ingredient) and croscarmellose sodium, iron oxides, povidone, and magnesium stearate (inactive ingredients). PREVACID capsules contain enteric-coated granules consisting of lansoprazole (15 mg) [active ingredient], hydroxypropyl cellulose, low substituted hydroxypropyl cellulose, colloidal silicon dioxide, magnesium carbonate, methacrylic acid copolymer, starch, talc, sugar sphere, sucrose, polyethylene glycol, polysorbate 80, and titanium dioxide [inactive ingredients]. Components of the gelatin capsule include gelatin, titanium dioxide, D&C Red No. 28, FD&C Blue No. 1, FD&C Green No. 3, and FD&C Red No. 40 [inactive ingredients]. PREVACID I.V. The active ingredient in PREVACID I.V. (lansoprazole) for injection is a substituted benzimidazole, 2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)-2-pyridyl] methyl] sulfinyl] benzimidazole, a compound that inhibits gastric acid secretion. PREVACID I.V. for injection contains 30 mg of the active ingredient lansoprazole, 60-mg mannitol, 10-mg meglumine, and 3.45-mg sodium hydroxide and is supplied as a sterile, lyophilized powder for I.V. (intravenous) use. The solution of PREVACID I.V. for injection has a pH of approximately 11 following the first reconstitution with sterile water for injection, USP, and approximately 10.2, 10.0, or 9.5 after further dilution with either 0.9% sodium chloride injection, USP, lactated Ringer's injection, USP, or 5% dextrose injection, USP, respectively.
- PREVACID for delayed-release orally disintegrating tablets contain the active ingredient, lansoprazole in the form of enteric-coated microgranules. The tablets are available in 15-mg and 30-mg dosage strengths. Each tablet contains lansoprazole and the following inactive ingredients: lactose monohydrate, microcrystalline cellulose, magnesium carbonate, hydroxypropyl cellulose, hypromellose, titanium dioxide, talc, mannitol, methacrylic acid, polyacrylate, polyethylene glycol, glyceryl monostearate, polysorbate 80, triethyl citrate, ferric oxide, citric acid, crospovidone, aspartame, artificial strawberry flavor, and magnesium stearate.
- ProAmatine® (midodrine hydrochloride) tablets. Dosage form: 2.5-, 5-, and 10-mg tablets for oral administration. Active ingredient: Midodrine hydrochloride, 2.5, 5, and 10 mg. Inactive ingredients: colloidal silicone dioxide NF, cornstarch NF, FD&C Blue No. 2 Lake (10-mg tablets), FD&C Yellow No. 6 Lake (5-mg tablet), magnesium stearate NF, microcrystalline cellulose NF, Talc USP.
- Proflavanol 90 tablet contains the following: vitamin C (Poly C, a blend of calcium, zinc, potassium, and magnesium ascorbates), 300 mg; grape seed extract, 90 mg; ascorbyl palmitate, 12 mg.

- ProSom (estazolam), tablets are scored and contain either 1 or 2 mg of estazolam. Inactive ingredients: colloidal silicon dioxide, lactose, povidone, stearic acid, and sodium starch glycolate. In addition, the 2-mg tablets contain FD&C Red No. 40.
- PROTONIX® (pantoprazole sodium) delayed-release tablets is supplied as a delayed-release tablet for oral administration, available in 2 strengths. Each delayed-release tablet contains 45.1 or 22.6 mg of pantoprazole sodium sesquihydrate (equivalent to 40 or 20 mg pantoprazole, respectively) with the following inactive ingredients: calcium stearate, crospovidone, hypromellose, iron oxide, mannitol, methacrylic acid copolymer, polysorbate 80, povidone, propylene glycol, sodium carbonate, sodium lauryl sulfate, titanium dioxide, and triethyl citrate.
- PROVIGIL (modafinil) tablets contain 100 or 200 mg of modafinil and the following inactive ingredients: lactose, microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, povidone, and magnesium stearate.
- Prozac® (fluoxetine hydrochloride) contains fluoxetine hydrochloride equivalent to 10 mg (32.3 μmol), 20 mg (64.7 μmol), or 40 mg (129.3 μmol) of fluoxetine. The Pulvules also contain starch, gelatin, silicone, titanium dioxide, iron oxide, and other inactive ingredients. The 10- and 20-mg Pulvules also contain FD&C Blue No. 1, and the 40-mg Pulvule also contains FD&C Blue No. 1 and FD&C Yellow No. 6. Each tablet contains fluoxetine hydrochloride equivalent to 10 mg (32.3 μmol) of fluoxetine. The tablets also contain microcrystalline cellulose, magnesium stearate, crospovidone, hypromellose, titanium dioxide, polyethylene glycol, and yellow iron oxide. In addition to the above ingredients, the 10-mg tablet contains FD&C Blue No. 1 aluminum lake, and polysorbate 80.
- PURINETHOL (mercaptopurine) tablet contains 50 mg of mercaptopurine and the inactive ingredients corn and potato starch, lactose, magnesium stearate, and stearic acid.
- Ranexa™ (ranolazine) film-coated, extended-release tablets containing 500 mg of ranolazine. Inactive ingredients of the 500-mg tablet include carnauba wax, hypromellose, magnesium stearate, methacrylic acid copolymer (Type C), microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium hydroxide, titanium dioxide, and FD&C Yellow #6 Lake.
- Rapamune® (sirolimus) is available as a white, triangular-shaped tablet containing 1-mg sirolimus, and as a yellow to beige triangular-shaped tablet containing 2-mg sirolimus, ascorbyl palmitate, and polysorbate 80. Rapamune the inactive ingredients in Rapamune® tablets include sucrose, lactose, polyethylene glycol 8000, calcium sulfate, microcrystalline cellulose, pharmaceutical glaze, talc, titanium dioxide, magnesium stearate, povidone, poloxamer 188, polyethylene glycol 20, 000, glyceryl monooleate, carnauba wax, and other ingredients. The 2-mg dosage strength also contains iron oxide yellow 10 and iron oxide brown 70.
- RELAFEN (nabumetone) oval-shaped, film-coated tablet contains 500 or 750 mg of nabumetone. Inactive ingredients consist of hypromellose, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium lauryl sulfate, sodium starch glycolate, and titanium dioxide. The 750-mg tablets also contain iron oxides.
- RELPAX® (eletriptan) tablets for oral administration contains 24.2 or 48.5 mg of eletriptan hydrobromide equivalent to 20 or 40 mg of eletriptan, respectively. Each tablet also contains the inactive ingredients microcrystalline cellulose NF, lactose NF, croscarmellose sodium NF, magnesium stearate NF, titanium dioxide USP, hypromellose, triacetin USP and FD&C Yellow No. 6 aluminum lake.
- REQUIP (ropinirole hydrochloride) film-coated TILTAB® tablet with beveled edges contains ropinirole hydrochloride equivalent to ropinirole, 0.25, 0.5, 1, 2, 3, 4, or 5 mg. Inactive ingredients consist of: croscarmellose sodium, hydrous lactose, magnesium stearate, microcrystalline cellulose, and one or more of the following: carmine, FD&C Blue No. 2 aluminum lake, FD&C Yellow No. 6 aluminum lake, hypromellose, iron oxides, polyethylene glycol, polysorbate 80, and titanium dioxide.
- RESCRIPTOR tablets contain delavirdine mesylate. Each RESCRIPTOR tablet, for oral administration, contains 100 or 200 mg of delavirdine mesylate (henceforth referred to as delavirdine). Inactive ingredients consist of lactose, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide, and carnauba wax. In addition, the 100-mg tablet contains Opadry White YS-1-7000-E and the 200-mg tablet contains hypromellose, Opadry White YS-1-18202-A and Pharmaceutical Ink Black.
- RETROVIR (zidovudine) film-coated tablet contains 300 mg of zidovudine and the inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide.
- REVATIO™ is the citrate salt of sildenafil. REVATIO (sildenafil citrate) is formulated as white, film-coated round tablets equivalent to 20 mg of sildenafil for oral administration. In addition to the active ingredient, sildenafil citrate, each tablet contains the following inactive ingredients: microcrystalline cellulose, anhydrous dibasic calcium phosphate, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide, lactose monohydrate, and triacetin.
- RILUTEK® (riluzole) is a member of the benzothiazole class. RILUTEK is available as a capsule-shaped, white, film-coated tablet for oral administration containing 50 mg of riluzole. Each tablet is engraved with "RPR 202" on one side. Inactive ingredients (core): anhydrous dibasic calcium phosphate, USP; microcrystalline cellulose, NF; anhydrous colloidal silica, NF; magnesium stearate, NF; croscarmellose sodium, NF. Inactive ingredients (film coating): hypromellose, USP; polyethylene glycol 6000; titanium dioxide, USP.
- Ritalin-SR®: Ritalin hydrochloride, methylphenidate hydrochloride USP, is available as tablets of 5, 10, and 20 mg for oral administration; Ritalin-SR is available as sustained-release tablets of 20 mg for oral administration. Inactive ingredients (Ritalin tablets): D&C Yellow No. 10 (5- and 20-mg tablets), FD&C Green No. 3 (10-mg tablets), lactose, magnesium stearate, polyethylene glycol, starch (5- and 10-mg tablets), sucrose, talc, and tragacanth (20-mg tablets). Inactive ingredients (Ritalin-SR tablets): Cellulose compounds, cetostearyl alcohol, lactose, magnesium stearate, mineral oil, povidone, titanium dioxide, and zein.
- ROZEREM™ (ramelteon) tablet includes the following inactive ingredients: lactose monohydrate, starch, hydroxypropyl cellulose, magnesium stearate, hypromellose, copovidone, titanium dioxide, yellow ferric oxide, polyethylene glycol 8000, and ink containing shellac and synthetic iron oxide black.
- Seasonale® (levonorgestrel/ethinyl estradiol tablets) is an extended-cycle oral contraceptive consisting of 84 pink

active tablets each containing 0.15 mg of levonorgestrel, a synthetic progestogen, and 0.03 mg of ethinyl estradiol as well 7 white inert tablets (without hormones). Each pink active tablet contains the following inactive ingredients: anhydrous lactose NF, FD&C Blue No. 1, FD&C Red No. 40, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, polyethylene glycol NF, magnesium stearate NF, polysorbate 80 NF, and titanium dioxide USP. Each white inert tablet contains the following inactive ingredients: anhydrous lactose NF, hydroxypropyl methylcellulose USP, microcrystalline cellulose NF, and magnesium stearate NF.

- Sedapap®Butalbital and acetaminophen is supplied in tablet form for oral administration. Each Sedapap® tablet contains Butalbital (50 mg) and acetaminophen (650 mg). In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid.
- SENOKOT tablets: Each tablet contains 8.6 mg of sennosides. Active ingredient: Standardized Senna Concentrate. Inactive ingredients: croscarmellose sodium, dicalcium phosphate, hypromellose, magnesium stearate, microcrystalline cellulose, and mineral oil. SENOKOT-S tablets: Each tablet contains 8.6 mg sennosides and 50 mg of docusate sodium. Active ingredients: Docusate Sodium and standardized senna concentrate. Inactive ingredients: carnauba wax, colloidal silicon dioxide, croscarmellose sodium, dicalcium phosphate, D&C Yellow #10, FD&C Yellow #6, hypromellose, magnesium stearate, microcrystalline cellulose, PEG 8000, sodium benzoate, stearic acid, and titanium dioxide.
- Sensipar™ (cinacalcet hydrochloride) tablets are formulated as light-green, film-coated, oval-shaped tablets for oral administration in strengths of 30, 60, and 90 mg of cinacalcet HCl as the free base equivalent (33, 66, and 99 mg as the hydrochloride salt, respectively). Inactive ingredients: Sensipar™ tablets are composed of the active ingredient, and the following inactive ingredients: pregelatinized starch, microcrystalline cellulose, povidone, crospovidone, colloidal silicon dioxide, and magnesium stearate. Tablets are coated with color (Opadry® II green) and clear film-coat (Opadry® clear), carnauba wax, and Opacode® black ink.
- SEROQUEL (quetiapine fumarate) is supplied for oral administration as 25 mg (round, peach), 50 mg (round, white), 100 mg (round, yellow), 200 mg (round, white), 300 mg (capsule-shaped, white), and 400 mg (capsule-shaped, yellow) tablets. Inactive ingredients are povidone, dibasic dicalcium phosphate dihydrate, microcrystalline cellulose, sodium starch glycolate, lactose monohydrate, magnesium stearate, hypromellose, polyethylene glycol, and titanium dioxide. The 25-mg tablets contain red ferric oxide and yellow ferric oxide and the 100-mg tablets contain only yellow ferric oxide.
- SPECTRACEF® tablets contain cefditoren pivoxil. The tablets contain 200 mg of cefditoren as cefditoren pivoxil and the following inactive ingredients: croscarmellose sodium, D-mannitol, hydroxypropyl cellulose, hypromellose, magnesium stearate, sodium caseinate (a milk protein), and sodium tripolyphosphate. The tablet coating contains carnauba wax, hypromellose, polyethylene glycol, and titanium dioxide. Tablets are printed with ink containing D&C Red No. 27, FD&C Blue No. 1, propylene glycol, and shellac.
- Stalevo® (carbidopa, levodopa, and entacapone) is a combination of carbidopa, levodopa, and entacapone. Stalevo® (carbidopa, levodopa, and entacapone) is supplied as tablets in three strengths: Stalevo 50, containing 12.5 mg of carbidopa, 50 mg of levodopa, and 200 mg of entacapone; Stalevo 100, containing 25 mg of carbidopa, 100 mg of levodopa, and 200 mg of entacapone; Stalevo 150, containing 37.5 mg of carbidopa, 150 mg of levodopa, and 200 mg of entacapone. The inactive ingredients of the Stalevo tablet are cornstarch, croscarmellose sodium, glycerol 85%, hypromellose, magnesium stearate, mannitol, polysorbate 80, povidone, sucrose, red iron oxide, titanium dioxide, and yellow iron oxide.
- Starlix® (nateglinide) biconvex tablets contain 60 mg, or 120 mg, of nateglinide for oral administration. Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl methylcellulose, iron oxides (red or yellow), lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, talc, and titanium dioxide.
- Striant® is a white to off-white colored, monoconvex, tablet-like, mucoadhesive buccal system. Striant® adheres to the gum tissue above the incisors, with the flat surface facing the cheek mucosa. The active ingredient in Striant® is testosterone. Each buccal system contains 30 mg of testosterone. Other pharmacologically inactive ingredients in Striant® are anhydrous lactose NF, carbomer 934P, hypromellose USP, magnesium stearate NF, lactose monohydrate NF, polycarbophil USP, colloidal silicon dioxide NF, starch NF, and talc USP.
- SULAR® (nisoldipine) is an extended-release tablet dosage form of the dihydropyridine calcium channel blocker nisoldipine. SULAR tablets consist of an external coat and an internal core. Both coat and core contain nisoldipine, the coat as a slow-release formulation and the core as a fast-release formulation. SULAR tablets contain either 10, 20, 30 or 40 mg of nisoldipine for once-a-day oral administration. Inert ingredients in the formulation are: hydroxypropyl cellulose, lactose, cornstarch, crospovidone, microcrystalline cellulose, sodium lauryl sulfate, povidone, and magnesium stearate. The inert ingredients in the film coating are: hypromellose, polyethylene glycol, ferric oxide, and titanium dioxide.
- SYNTHROID® (levothyroxine sodium tablets, USP). Inactive ingredients: acacia, confectioner's sugar (contains cornstarch), lactose monohydrate, magnesium stearate, povidone, and talc. The following are the color additives by tablet strength: 25 FD&C Yellow No. 6 Aluminum Lake; 50 None; 75 FD&C Red No. 40 Aluminum Lake; FD&C Blue No. 2 Aluminum Lake; 88 FD&C Blue No. 1 Aluminum Lake; FD&C Yellow No. 6 Aluminum Lake; D&C Yellow No. 10 Aluminum Lake; 100 D&C Yellow No. 10 Aluminum Lake; FD&C Yellow No. 6 Aluminum Lake; 112 D&C Red No. 27 & 30 Aluminum Lake; 125 FD&C Yellow No. 6 Aluminum Lake; FD&C Red No. 40 Aluminum Lake, FD&C Blue No. 1 Aluminum Lake; 137 FD&C Blue No. 1 Aluminum Lake; 150 FD&C Blue No. 2 Aluminum Lake; 175 FD&C Blue No. 1 Aluminum Lake, D&C Red No. 27 & 30 Aluminum Lake; 200 FD&C Red No. 40 Aluminum Lake; 300 D&C Yellow No. 10 Aluminum Lake; FD&C Yellow No. 6 Aluminum Lake; and FD&C Blue No. 1 Aluminum Lake.
- TABLOID scored tablet contains 40 mg of thioguanine and the inactive ingredients gum acacia, lactose, magnesium stearate, potato starch, and stearic acid.
- TAGAMET (cimetidine) film-coated tablet contains cimetidine as follows: 300 mg—round, debossed with the product name TAGAMET, SB and 300; 400 mg—oval Tiltab®

tablets, debossed with the product name TAGAMET, SB and 400. Inactive ingredients consist of cellulose, D&C Yellow No. 10, FD&C Blue No. 2, FD&C Red No. 40, FD&C Yellow No. 6, hypromellose, iron oxides, magnesium stearate, povidone, propylene glycol, sodium lauryl sulfate, sodium starch glycolate, starch, titanium dioxide, and trace amounts of other inactive ingredients.

- TAMBOCOR TM (flecainide acetate) is available in tablets of 50, 100 or 150 mg for oral administration. Flecainide acetate is a white crystalline substance with a pK_a of 9.3. It has an aqueous solubility of 48.4 mg/mL at 37°C. TAMBOCOR tablets also contain croscarmellose sodium, hydrogenated vegetable oil, magnesium stearate, microcrystalline cellulose, and starch.
- TARCEVA (erlotinib) is a Human Epidermal Growth Factor Receptor Type 1/Epidermal Growth Factor Receptor (HER1/EGFR) tyrosine kinase inhibitor. TARCEVA tablets are available in three dosage strengths containing erlotinib hydrochloride (27.3, 109.3, and 163.9 mg) equivalent to 25, 100, and 150 mg erlotinib and the following inactive ingredients: lactose monohydrate, hypromellose, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, sodium lauryl sulfate, and titanium dioxide. The tablets also contain trace amounts of color additives, including FD&C Yellow #6 (25 mg only) for product identification.
- TARCEVA (erlotinib) tablets are available in three dosage strengths containing erlotinib hydrochloride (27.3, 109.3, and 163.9 mg) equivalent to 25, 100, and 150 mg erlotinib and the following inactive ingredients: lactose monohydrate, hypromellose, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, sodium lauryl sulfate, and titanium dioxide. The tablets also contain trace amounts of color additives, including FD&C Yellow #6 (25 mg only) for product identification.
- TARKA® (trandolapril/verapamil hydrochloride ER). The tablet strengths are trandolapril 2 mg/verapamil hydrochloride ER 180 mg, trandolapril 1 mg/verapamil hydrochloride ER 240 mg, trandolapril 2 mg/verapamil hydrochloride ER 240 mg, and trandolapril 4 mg/verapamil hydrochloride ER 240 mg. The tablets also contain the following ingredients: cornstarch, dioctyl sodium sulfosuccinate, ethanol, hydroxypropyl cellulose, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, purified water, silicon dioxide, sodium alginate, sodium stearyl fumarate, synthetic iron oxides, talc, and titanium dioxide.
- TASMAR® is available as tablets containing 100 or 200 mg tolcapone. Inactive ingredients (core): lactose monohydrate, microcrystalline cellulose, dibasic calcium phosphate anhydrous, povidone K-30, sodium starch glycolate, talc, and magnesium stearate. Inactive ingredients (film coating): hydroxypropyl methylcellulose, titanium dioxide, talc, ethylcellulose, triacetin, and sodium lauryl sulfate, with the following dye systems: 100 mg of yellow and red iron oxide and 200 mg of red iron oxide.
- Tegretol, carbamazepine USP is available for oral administration as chewable tablets of 100 mg, tablets of 200 mg, XR tablets of 100, 200, and 400 mg, and as a suspension of 100 mg/5 mL (teaspoon). Inactive ingredients (tablets): Colloidal silicon dioxide, D&C Red No. 30 Aluminum Lake (chewable tablets only), FD&C Red No. 40 (200-mg tablets only), flavoring (chewable tablets only), gelatin, glycerin, magnesium stearate, sodium starch glycolate (chewable tablets only), starch, stearic acid, and sucrose (chewable tablets only). Inactive ingredients (suspension): Citric acid, FD&C Yellow No. 6, flavoring, polymer, potassium sorbate, propylene glycol, purified water, sorbitol, sucrose, and xanthan gum. Tegretol-XR tablets: cellulose compounds, dextrates, iron oxides, magnesium stearate, mannitol, polyethylene glycol, sodium lauryl sulfate, and titanium dioxide (200-mg tablets only).
- TENORMIN® (atenolol) is available as 25-, 50-, and 100-mg tablets for oral administration. Inactive ingredients: Magnesium stearate, microcrystalline cellulose, povidone, and sodium starch glycolate.
- Thioridazine hydrochloride is available as tablets for oral administration containing 10, 25, 50, or 100 mg. Each tablet for oral administration contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium lauryl sulfate, titanium dioxide, and FD&C Yellow #6 Aluminum Lake.
- Thyrolar tablets (Liotrix tablets, USP) contain triiodothyronine (T3 liothyronine) sodium and tetraiodothyronine (T4 levothyroxine) sodium. The inactive ingredients are calcium phosphate, colloidal silicon dioxide, cornstarch, lactose, and magnesium stearate. The tablets also contain the following dyes: Thyrolar 1/4—FD&C Blue #1 and FD&C Red #40; Thyrolar 1/2—FD&C Red #40 and D&C Yellow #10; Thyrolar 1—FD&C Red #40; Thyrolar 2—FD&C Blue #1, FD&C Red #40, and D&C Yellow #10; Thyrolar 3—FD&C Red #40 and D&C Yellow #10. Thyrolar tablets (Liotrix tablets, USP) are available in five potencies coded as follows: 3.1 mcg/12.5 mcg, 6.25 mcg/25 mcg, 12.5 mcg/50 mcg, 25 mcg/100 mcg, and 37.5 mcg/150 mcg.
- Tinidazole is a synthetic antiprotozoal agent. Tindamax pink film-coated oral tablets contain 500 or 250 mg of tinidazole. Inactive ingredients include croscarmellose sodium, FD&C Red 40 lake, FD&C Yellow 6 lake, hypromellose, magnesium stearate, microcrystalline cellulose, polydextrose, polyethylene glycol, pregelatinized cornstarch, titanium dioxide, and triacetin.
- TRACLEER® (bosentan) is available as 62.5 and 125 mg film-coated tablets for oral administration, and contains the following excipients: cornstarch, pregelatinized starch, sodium starch glycolate, povidone, glyceryl behenate, magnesium stearate, hydroxypropyl methylcellulose, triacetin, talc, titanium dioxide, iron oxide yellow, iron oxide red, and ethylcellulose. Each TRACLEER® 62.5-mg tablet contains 64.541 mg of bosentan, equivalent to 62.5 mg of anhydrous bosentan. Each TRACLEER® 125-mg tablet contains 129.082 mg of bosentan, equivalent to 125 mg of anhydrous bosentan.
- TRANXENE T-TAB tablets contain either 3.75, 7.5, or 15 mg of clorazepate dipotassium for oral administration. Tranxene-SD and Tranxene-SD Half Strength tablets contain 22.5 and 11.25 mg of clorazepate dipotassium, respectively. Tranxene-SD and Tranxene-SD Half Strength tablets gradually release clorazepate and are designed for once-a-day administration in patients already stabilized on TRANXENE T-TAB tablets. Inactive ingredients for TRANXENE T-TAB® tablets: Colloidal silicon dioxide, FD&C Blue No. 2 (3.75 mg only), FD&C Yellow No. 6 (7.5 mg only), FD&C Red No. 3 (15 mg only), magnesium oxide, magnesium stearate, microcrystalline cellulose, potassium carbonate, potassium chloride, and talc. Inactive ingredients for TRANXENE-SD and TRANXENE-SD HALF STRENGTH tablets: Castor oil

wax, FD&C Blue No. 2 (SD Half Strength, 11.25 mg only), iron oxide (SD, 22.5 mg only), lactose, magnesium oxide, magnesium stearate, potassium carbonate, potassium chloride, and talc.

- TRECATOR TABLET. Ethionamide tablets contain 250 mg of ethionamide. The inactive ingredients present are croscarmellose sodium, FD&C Yellow #6, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, povidone, silicon dioxide, talc, and titanium dioxide.
- Triamterene capsule for oral use, with opaque red cap and body, contains triamterene, 50 or 100 mg, and is imprinted with the product name DYRENIUM, strength (50 or 100) and WPC 002 (for the 50 mg strength) and WPC 003 (for the 100 mg strength). Inactive ingredients consist of D&C Red No. 33, FD&C Yellow No. 6, gelatin NF, lactose NF, magnesium stearate NF, sodium lauryl sulfate NF, titanium dioxide USP, and silicon dioxide NF.
- TRICOR (fenofibrate tablets) is available as tablets for oral administration. Each tablet contains 48 or 145 mg of fenofibrate. Inactive ingredients: Each tablet contains hypromellose 2910 (3cps), docusate sodium, sucrose, sodium lauryl sulfate, lactose monohydrate, silicified microcrystalline cellulose, crospovidone, and magnesium stearate. In addition, individual tablets contain the following ingredients: 48-mg tablets—polyvinyl alcohol, titanium dioxide, talc, soybean lecithin, xanthan gum, D&C Yellow #10 aluminum lake, FD&C Yellow #6/sunset yellow FCF aluminum lake, and FD&C Blue #2/indigo carmine aluminum lake. 145-mg tablets—polyvinyl alcohol, titanium dioxide, talc, soybean lecithin, and xanthan gum.
- TRIGLIDE™ (fenofibrate) tablets contains 50 or 160 mg of fenofibrate. Inactive ingredients: Each tablet also contains crospovidone, lactose monohydrate, mannitol, maltodextrin, carboxymethylcellulose sodium, egg lecithin, croscarmellose sodium, sodium lauryl sulfate, colloidal silicon dioxide, magnesium stearate, and monobasic sodium phosphate.
- Trileptal® (oxcarbazepine) is available as 150, 300, and 600 mg film-coated tablets for oral administration. Trileptal film-coated tablets contain the following inactive ingredients: colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, talc, titanium dioxide, and yellow iron oxide.
- Triphasil cycle of 28 tablets consists of three different drug phases as follows: Phase 1 composed of 6 brown tablets, each containing 0.050 mg of levonorgestrel (*d*(-)-13 β-ethyl-17-α-ethinyl-17-β-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.030 mg of ethinyl estradiol (19-nor-17(α)-pregna-1,3,5(10)-trien-20-yne-3,17-diol); phase 2 composed of 5 white tablets, each containing 0.075 mg levonorgestrel and 0.040 mg ethinyl estradiol; and phase 3 composed of 10 light-yellow tablets, each containing 0.125 mg levonorgestrel and 0.030 mg ethinyl estradiol; then followed by 7 light-green inert tablets. The inactive ingredients present are cellulose, FD&C Blue 1, iron oxides, lactose, magnesium stearate, polacrilin potassium, polyethylene glycol, titanium dioxide, and hydroxypropyl methylcellulose.
- ULTRAM® ER (tramadol hydrochloride) tablets contain 100, 200 or 300 mg of tramadol HCl in an extended-release formulation. The tablets are white in color and contain the inactive ingredients ethylcellulose, dibutyl sebacate, polyvinyl pyrrolidone, sodium stearyl fumarate, colloidal silicon dioxide, and polyvinyl alcohol.
- ULTRAM® ODT (tramadol hydrochloride) orally disintegrating tablets is supplied as orally disintegrating tablets containing 50 mg of tramadol hydrochloride for oral administration. The tablets are white in color and contain the inactive ingredients aspartame, copovidone, crospovidone, ethylcellulose, magnesium stearate, mannitol, mint flavor, and silicon dioxide.
- Uniphyl® (theophylline, anhydrous) tablets in a controlled-release system allows a 24-hour dosing interval. Each controlled-release tablet for oral administration, contains 400 or 600 mg of anhydrous theophylline. Inactive ingredients: cetostearyl alcohol, hydroxyethyl cellulose, magnesium stearate, povidone, and talc.
- Uniretic® (moexipril hydrochloride/hydrochlorothiazide) is a combination of an angiotensin-converting enzyme (ACE) inhibitor, moexipril hydrochloride, and a diuretic, hydrochlorothiazide. Uniretic® is available for oral administration in three tablet strengths. The inactive ingredients in all strengths are lactose, magnesium oxide, crospovidone, magnesium stearate, and gelatin. The film coating in all strengths contains hydroxypropyl cellulose, hypromellose, polyethylene glycol 6000, magnesium stearate, and titanium dioxide. In addition, the film coating for Uniretic® 7.5 mg/12.5 mg and Uniretic® 15 mg/25 mg contains ferric oxide.
- Univasc® (moexipril hydrochloride) is supplied as scored, coated tablets containing 7.5 and 15 mg of moexipril hydrochloride for oral administration. In addition to the active ingredient, moexipril hydrochloride, the tablet core contains the following inactive ingredients: lactose, magnesium oxide, crospovidone, magnesium stearate, and gelatin. The film coating contains hydroxypropyl cellulose, hypromellose, polyethylene glycol 6000, magnesium stearate, titanium dioxide, and ferric oxide.
- Urocit®-K is a citrate salt of potassium. Urocit®-K is supplied as wax matrix tablets containing 5 mEq (540 mg) and 10 mEq (1080 mg) of potassium citrate each, for oral administration.
- UROQID-Acid® No.2 tablet contains methenamine mandelate (500 mg) and sodium acid phosphate, monohydrate (500 mg). Inactive ingredients Calcium phosphate, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate, starch, sugar, syloid, and talc.
- VAGIFEM® (estradiol vaginal tablets) are small, white, film-coated tablets containing 25.8 μg of estradiol hemihydrate equivalent to 25 μg of estradiol. Each tablet contains the following inactive ingredients: hypromellose, lactose monohydrate, maize starch, and magnesium stearate. The film coating contains hypromellose and polyethylene glycol. Each white tablet is 6 mm in diameter and is placed in a disposable applicator. Each tablet-filled applicator is packaged separately in a blister pack. 17(β)-estradiol hemihydrate is a white, almost white or colorless crystalline solid, chemically described as estra-1,3,5(10)-triene-3,17,diol.
- VESIcare® (solifenacin succinate) tablet contains 5 or 10 mg of solifenacin succinate and is formulated for oral administration. In addition to the active ingredient solifenacin succinate, each VESIcare tablet also contains the following inert ingredients: lactose monohydrate, cornstarch, hypromellose 2910, magnesium stearate, talc, polyethylene glycol 8000, and titanium dioxide with yellow ferric oxide (5 mg VESIcare tablet) or red ferric oxide (10 mg VESIcare tablet).
- VFEND tablets contain 50 or 200 mg of voriconazole. The inactive ingredients include lactose monohydrate,

pregelatinized starch, croscarmellose sodium, povidone, magnesium stearate and a coating containing hypromellose, titanium dioxide, lactose monohydrate, and triacetin.

- VIAGRA®, an oral tablet, is the citrate salt of sildenafil. VIAGRA (sildenafil citrate) is formulated as blue, film-coated rounded-diamond-shaped tablets equivalent to 25, 50, and 100 mg of sildenafil for oral administration. In addition to the active ingredient, sildenafil citrate, each tablet contains the following inactive ingredients: microcrystalline cellulose, anhydrous dibasic calcium phosphate, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide, lactose, triacetin, and FD & C Blue #2 aluminum lake.
- VICODIN HP (hydrocodone bitartrate and acetaminophen) is supplied in tablet form for oral administration. Each VICODIN HP tablet contains hydrocodone bitartrate (10 mg) and acetaminophen (660 mg). In addition each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid. Meets USP Dissolution Test 2. Each VICODIN ES tablet contains hydrocodone bitartrate (7.5 mg) and acetaminophen (750 mg). In addition each tablet contains the following inactive ingredients: Colloidal silicon dioxide, pregelatinized starch, magnesium stearate, croscarmellose sodium povidone, and stearic acid. Meets USP Dissolution Test 2. Each VICODIN tablet contains hydrocodone bitartrate (5 mg) and acetaminophen (500 mg). In addition each tablet contains the following inactive ingredients: colloidal silicon dioxide, starch, croscarmellose sodium, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, povidone, and stearic acid. Meets USP Dissolution Test 2.
- VICOPROFEN® tablet contains hydrocodone bitartrate, USP (7.5 mg), and ibuprofen, USP (200 mg). Inactive ingredients in VICOPROFEN tablets include: colloidal silicon dioxide, cornstarch, croscarmellose sodium, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, and titanium dioxide.
- VIRACEPT® (nelfinavir mesylate) tablets are available for oral administration as a light blue, capsule-shaped tablet with a clear film coating in 250-mg strength (as nelfinavir free base) and as a white oval tablet with a clear film coating in 625-mg strength (as nelfinavir free base). Each tablet contains the following common inactive ingredients: calcium silicate, crospovidone, magnesium stearate, hypromellose, and triacetin. In addition, the 250-mg tablet contains FD&C blue #2 powder and the 625-mg tablet contains colloidal silicon dioxide.
- Voltaren® (diclofenac sodium enteric-coated tablets). Voltaren is available as Delayed-Release (enteric-coated) tablets of 25 mg (yellow), 50 mg (light brown), and 75 mg (light pink) for oral administration. The inactive ingredients in Voltaren include hydroxypropyl methylcellulose, iron oxide, lactose, magnesium stearate, methacrylic acid copolymer, microcrystalline cellulose, polyethylene glycol, povidone, propylene glycol, sodium hydroxide, sodium starch glycolate, talc, titanium dioxide, D&C Yellow No. 10 Aluminum Lake (25-mg tablet only), and FD&C Blue No. 1 Aluminum Lake (50-mg tablet only).
- Voltaren® -XR, (diclofenac sodium extended-release tablets are available as extended-release tablets of 100 mg (light pink) for oral administration. The inactive ingredients in Voltaren-XR include cetyl alcohol, hydroxypropyl methylcellulose, iron oxide, magnesium stearate, polyethylene glycol, polysorbate, povidone, silicon dioxide, sucrose, talc, and titanium dioxide.
- VYTORIN contains ezetimibe. VYTORIN is available for oral use as tablets containing 10 mg of ezetimibe, 10 mg of simvastatin (VYTORIN 10/10), 20 mg of simvastatin (VYTORIN 10/20), 40 mg of simvastatin (VYTORIN 10/40), or 80 mg of simvastatin (VYTORIN 10/80). Each tablet contains the following inactive ingredients: butylated hydroxyanisole NF, citric acid monohydrate USP, croscarmellose sodium NF, hydroxypropyl methylcellulose USP, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, and propyl gallate NF.
- VYTORIN contains ezetimibe. VYTORIN is available for oral use as tablets containing 10 mg of ezetimibe, 10 mg of simvastatin (VYTORIN 10/10), 20 mg of simvastatin (VYTORIN 10/20), 40 mg of simvastatin (VYTORIN 10/40), or 80 mg of simvastatin (VYTORIN 10/80). Each tablet contains the following inactive ingredients: butylated hydroxyanisole NF, citric acid monohydrate USP, croscarmellose sodium NF, hydroxypropyl methylcellulose USP, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, and propyl gallate NF.
- YASMIN provides an oral contraceptive regimen consisting of 21 active film-coated tablets each containing 3.0 mg of drospirenone and 0.030 mg of ethinyl estradiol and 7 inert film-coated tablets. The inactive ingredients are lactose monohydrate NF, cornstarch NF, modified starch NF, povidone 25000 USP, magnesium stearate NF, hydroxypropyl methylcellulose USP, macrogol 6000 NF, talc USP, titanium dioxide USP, ferric oxide pigment, and yellow NF. The inert film-coated tablets contain lactose monohydrate NF, cornstarch NF, povidone 25000 USP, magnesium stearate NF, hydroxypropyl methylcellulose USP, talc USP, and titanium dioxide USP.
- Zelnorm® (tegaserod maleate) tablets contain tegaserod as the hydrogen maleate salt. Each 1.385 mg of tegaserod as the maleate is equivalent to 1 mg of tegaserod. Zelnorm is available for oral use in the following tablet formulations: 2- and 6-mg tablets (blister packs) containing 2 and 6 mg of tegaserod, respectively, and the following inactive ingredients: crospovidone, glyceryl monostearate, hypromellose, lactose monohydrate, poloxamer 188, and polyethylene glycol 4000; 6-mg tablets (bottles) containing 6 mg of tegaserod and the following inactive ingredients: crospovidone, glyceryl behenate, hypromellose, lactose monohydrate, and colloidal silicon dioxide.
- ZESTORETIC® (lisinopril and hydrochlorothiazide) combines an angiotensin converting enzyme inhibitor, lisinopril, and a diuretic, hydrochlorothiazide. ZESTORETIC is available for oral use in three tablet combinations of lisinopril with hydrochlorothiazide: ZESTORETIC 10-12.5 containing 10 mg of lisinopril and 12.5 mg of hydrochlorothiazide; ZESTORETIC 20-12.5 containing 20 mg of lisinopril and 12.5 mg of hydrochlorothiazide; and, ZESTORETIC 20-25 containing 20 mg of lisinopril and 25 mg of hydrochlorothiazide. Inactive ingredients: 10-12.5 tablets—calcium phosphate, magnesium stearate, mannitol, red ferric oxide, starch, and yellow ferric oxide. 20-12.5 tablets—calcium phosphate, magnesium stearate, mannitol, and starch. 20-25 tablets—calcium phosphate, magnesium stearate, mannitol, red ferric oxide, starch, and yellow ferric oxide.
- ZESTRIL (lisinopril) is supplied as 2.5-, 5-, 10-, 20-, 30-, and 40-mg tablets for oral administration. Inactive ingredients: 2.5-mg tablets-–calcium phosphate, magnesium stearate, mannitol, and starch. 5-, 10-, 20-, and 30-mg

tablets—calcium phosphate, magnesium stearate, mannitol, red ferric oxide, and starch. 40-mg tablets—calcium phosphate, magnesium stearate, mannitol, starch, and yellow ferric oxide.

- ZETIA (ezetimibe) is available as a tablet for oral administration containing 10 mg of ezetimibe and the following inactive ingredients: croscarmellose sodium NF, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, povidone USP, and sodium lauryl sulfate NF.
- ZETIA (ezetimibe) is available as a tablet for oral administration containing 10 mg of ezetimibe and the following inactive ingredients: croscarmellose sodium NF, lactose monohydrate NF, magnesium stearate NF, microcrystalline cellulose NF, povidone USP, and sodium lauryl sulfate NF.
- Zileuton tablets for oral administration are supplied in one dosage strength containing 600 mg of zileuton. Inactive ingredients: crospovidone, hydroxypropyl cellulose, hypromellose, magnesium stearate, microcrystalline cellulose, pregelatinized starch, propylene glycol, sodium starch glycolate, talc, and titanium dioxide.
- ZITHROMAX® tablets contain azithromycin dihydrate equivalent to 600 mg azithromycin. The tablets are supplied as white, modified oval-shaped, film-coated tablets. They also contain the following inactive ingredients: dibasic calcium phosphate anhydrous, pregelatinized starch, sodium croscarmellose, magnesium stearate, sodium lauryl sulfate and an aqueous film coat consisting of hypromellose, titanium dioxide, lactose, and triacetin.
- ZOLOFT® (sertraline hydrochloride) is supplied for oral administration as scored tablets containing sertraline hydrochloride equivalent to 25, 50, and 100 mg of sertraline and the following inactive ingredients: dibasic calcium phosphate dihydrate, D & C Yellow #10 aluminum lake (in 25-mg tablet), FD & C Blue #1 aluminum lake (in 25-mg tablet), FD & C Red #40 aluminum lake (in 25-mg tablet), FD & C Blue #2 aluminum lake (in 50-mg tablet), hydroxypropyl cellulose, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, synthetic yellow iron oxide (in 100-mg tablet), and titanium dioxide.
- ZOMIG® (zolmitriptan) tablets and ZOMIG-ZMT® (zolmitriptan) orally disintegrating tablets contain zolmitriptan, available as 2.5 mg (yellow) and 5 mg (pink) film-coated tablets for oral administration. The film-coated tablets contain anhydrous lactose NF, microcrystalline cellulose NF, sodium starch glycolate NF, magnesium stearate NF, hydroxypropyl methylcellulose USP, titanium dioxide USP, polyethylene glycol 400 NF, yellow iron oxide NF (2.5-mg tablet), red iron oxide NF (5-mg tablet), and polyethylene glycol 8000 NF. ZOMIG-ZMT® orally disintegrating tablets are available as 2.5 and 5.0 mg white uncoated tablets for oral administration. The orally disintegrating tablets contain mannitol USP, microcrystalline cellulose NF, crospovidone NF, aspartame NF, sodium bicarbonate USP, citric acid anhydrous USP, colloidal silicon dioxide NF, magnesium stearate NF, and orange flavor SN 027512.
- ZYPREXA (olanzapine) tablet contains olanzapine equivalent to 2.5 mg (8 μmol), 5 mg (16 μmol), 7.5 mg (24 μmol), 10 mg (32 μmol), 15 mg (48 μmol), or 20 mg (64 μmol). Inactive ingredients are carnauba wax, crospovidone, hydroxypropyl cellulose, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, and other inactive ingredients. The color coating contains titanium dioxide (all strengths), FD&C Blue No. 2 Aluminum Lake (15 mg), or synthetic red iron oxide (20 mg). The 2.5, 5.0, 7.5, and 10-mg tablets are imprinted with edible ink which contains FD&C Blue No. 2 Aluminum Lake.
- ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) contains olanzapine equivalent to 5 mg (16 μmol), 10 mg (32 μmol), 15 mg (48 μmol), or 20 mg (64 μmol). It begins disintegrating in the mouth within seconds, allowing its contents to be subsequently swallowed with or without liquid. ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) also contains the following inactive ingredients: gelatin, mannitol, aspartame, sodium methyl paraben, and sodium propyl paraben.
- ZYRTEC® (tablets and syrup) is cetirizine hydrochloride. ZYRTEC tablets are formulated as white, film-coated, rounded-off rectangular shaped tablets for oral administration and are available in 5- and 10-mg strengths. Inactive ingredients are lactose, magnesium stearate, povidone, titanium dioxide, hypromellose, polyethylene glycol, and cornstarch. ZYRTEC chewable tablets are formulated as purple round tablets for oral administration and are available in 5- and 10-mg strengths. Inactive ingredients of the chewable tablets are acesulfame potassium, artificial grape flavor, betadex NF, blue dye, colloidal silicon dioxide, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose, natural flavor, and red dye (carmine).
- ZYRTEC-D 12 HOUR™ (cetirizine hydrochloride (5 mg) and pseudoephedrine hydrochloride (120 mg)) extended-release tablets for oral administration contain 5 mg of cetirizine hydrochloride for immediate release and 120 mg of pseudoephedrine hydrochloride for extended release in a bilayer tablet. Tablets also contain as inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, and microcrystalline cellulose.

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