

# AHFS DI<sup>®</sup> Essentials<sup>™</sup> Users Guide

(AHFS primary)

## Organization of the Content

Since 1959, the American Society of Health-System Pharmacists (ASHP) has been building its evidence-based foundation for safe and effective drug therapy through its premier drug compendium—*AHFS Drug Information*<sup>®</sup>. With *AHFS DI<sup>®</sup> Essentials<sup>™</sup>*, ASHP continues to build on that foundation by providing a resource that focuses on the *essential*, evidence-based information that allows pharmacists, nurses, physicians, and other health-care providers to access quickly, in a straight-forward fashion, the specific guidance needed to safely and effectively prescribe and monitor drug therapy. Because it is derived from the authoritative *AHFS DI<sup>®</sup>*, the well-respected information development process, evidence analysis, and expert advice of authoritative reviewers are encapsulated and summarized in the highly structured format of *Essentials<sup>™</sup>*.

*AHFS DI<sup>®</sup> Essentials<sup>™</sup>* monographs are written principally on single-drug entities; information on various trademarked preparations and brands of a drug is contained in a single monograph. Drug *combinations* are described in the monographs on the principal ingredients or, rarely, appear as separate monographs (e.g., Co-trimoxazole, Levodopa/Carbidopa) when the combinations are considered important because of therapeutic rationale and/or frequency of use.

### ■ Scope

*AHFS DI<sup>®</sup> Essentials<sup>™</sup>* is designed to offer clinicians easy access to knowledge that is critical at the point of care. *Essentials<sup>™</sup>* monographs draw on the meticulously evidence-based guidance from the full *AHFS DI<sup>®</sup>* database, distilling for the clinician the essential information on prescription and key over-the-counter (OTC) drugs in an easy-to-use, highly structured outline format.

Clinically important information that is needed to help clinicians provide safe and effective drug therapy is included. *AHFS DI<sup>®</sup> Essentials<sup>™</sup>* is not intended to provide the “full disclosure” safety information provided by US Food and Drug Administration (FDA)-approved professional labeling. Instead, it provides a summary of critical information intended to provide quick, point-of-care answers to common prescribing and monitoring questions. More detailed information generally can be found in the full-length *AHFS DI<sup>®</sup>* monographs also published by ASHP (see <http://www.ahfsdruginformation.com> for information on subscribing to this resource) and the manufacturers’ professional labeling. Users should refer to these resources for more complete information. Information on multiple products containing the same drug (either singly or in combination) often is included in the same *Essentials<sup>™</sup>* monograph, incorporating key elements from a variety of professional labeling and other references (e.g., authoritative therapeutic guidelines).

*Essentials<sup>™</sup>* monographs also include information that is outside the manufacturers’ labeling (“off-label,” “unlabeled”). This information is drawn from the full *AHFS DI<sup>®</sup>* database, which is widely trusted for its established record in refuting unfounded efficacy claims, its rigorous science-based editorial process, and its independence from the influence of pharmaceutical manufacturers.

*Essentials<sup>™</sup>* includes a subset of drugs from the full *AHFS DI<sup>®</sup>* database. Drugs were selected from those most widely used in hospital (including most parenteral drugs) and outpatient (including key OTC products) settings, new molecular entities (NMEs) introduced into the US market in recent years, and drugs requiring particular attention for safe use (e.g., those with boxed warnings).

The presence or absence of a particular drug or use should *not* be interpreted as indicating any judgment by *AHFS DI* on its merits.

*AHFS DI<sup>®</sup> Essentials<sup>™</sup>* is designed to serve as an aid to, not a substitute for, sound, informed clinical judgment.

### ■ Organization of Full-length Monographs

Information within each drug monograph is divided into the sections and subsections listed below.

Not all sections or subsections are included in each monograph. The information is divided only when applicable and necessary. Other subsections not listed above also are used within sections.

Described below are the types of information that may be included in each major section and subsection within a monograph. Individual monographs may not contain all of the information described below, and the absence of specific information within an individual monograph does not imply that such information is unavailable.

### ■ Monograph Title and Introductory Information

- Special Alerts
- Boxed Warning
- REMS
- Introductory Description

- Class (AHFS and VA)
- Brands (common brand names)
- Synonyms

### ■ Uses

#### *Specific Indications (Diseases/Conditions)*

### ■ Dosage and Administration

#### *General*

#### *Administration*

- Specific Routes.**
  - Reconstitution
  - Dilution
  - Rate of Administration

#### *Dosage*

- Pediatric Patients.**
  - Specific Indications (Diseases/Conditions)
  - Specific Routes
- Adults.**
  - Specific Indications (Diseases/Conditions)
  - Specific Routes

#### *Prescribing Limits*

- Pediatric Patients.**
  - Specific Indications (Diseases/Conditions)
  - Specific Routes
- Adults.**
  - Specific Indications (Diseases/Conditions)
  - Specific Routes

#### *Special Populations*

- Hepatic Impairment
- Renal Impairment
- Geriatric Patients

### ■ Cautions

#### *Contraindications*

#### *Warnings/Precautions*

- Warnings.**
- Sensitivity Reactions.**
- Other Warnings and Precautions.**
- Specific Populations.**
  - Pregnancy
  - Lactation
  - Pediatric Use
  - Geriatric Use
  - Hepatic Impairment
  - Renal Impairment

#### *Common Adverse Effects*

### ■ Interactions

#### *Specific Drugs, Foods, and Tests (alphabetically)*

### ■ Pharmacokinetics

#### *Absorption*

- Bioavailability.**
- Onset.**
- Duration.**
- Food.**
- Plasma Concentrations.**
- Special Populations.**

#### *Distribution*

- Extent (e.g., placental, lactation, blood-brain barrier).**
- Plasma Protein Binding.**
- Special Populations.**

#### *Elimination*

- Metabolism.**
- Elimination Route.**
- Half-life.**
- Special Populations.**

### ■ Stability

#### *Storage*

- Specific Routes.**
  - Specific Dosage Forms

#### *Compatibility*

- Parenteral.**
  - Solution Compatibility
  - Compatible

- Incompatible
- Variable
- Drug Compatibility
- Compatible
- Incompatible
- Variable
- Y-site Compatibility
- Compatible
- Incompatible
- Variable

## ■ Actions (or Actions and Spectrum)

## ■ Advice to Patients

## ■ Preparations

### **Generic Drug Name (Single-entity or Combination)**

#### **Routes (alphabetically).**

#### Dosage Forms (alphabetically)

—Strength/Concentration (in ascending order)

—Product Listings (alphabetically by Brand Names & Manufacturers)

## ■ Monograph Footnotes (e.g., off-label use footnote)

## ■ Copyright Notice, Selected Revision Date

## ■ References

## ■ Monograph Title and Introductory Information

Lists the USAN name or other name for the drug(s) described; the title includes only the base drug name.

“Tall man” (mixed case) lettering is used for drug names in titles or synonyms (e.g., “CISplatin”) when recommended by FDA or the Institute for Safe Medication Practices (ISMP).

If multiple forms (e.g., salts, esters) of the same drug are available, information about the forms is described throughout the monograph, where applicable. The specific various forms are listed as headings within the Preparations section, with the respective products described under each associated heading.

Occasionally, when several drug entities are described in a single monograph, an alternative title descriptive of the group (e.g., Antacids) is used.

### **Introductory Description**

Provides a brief chemical, structural, and/or pharmacologic/therapeutic description for the purpose of orientation and introduction.

### **Class**

Lists the applicable AHFS and VA pharmacologic and therapeutic classes for the drug. Occasionally, multiple classes for the same drug appear.

### **Brands**

Lists common brand (trade) names for single-entity and combination products alphabetically. By comparison in the Preparations section, the brand names are listed with each specific product description, which are organized by ingredients, route, formulation, and strength.

### **Synonyms**

Lists common synonyms, acronyms, former names, and other names for the drug.

## ■ Special Alerts

May be temporarily inserted in an *AHFS DI<sup>®</sup> Essentials<sup>™</sup>* monograph to inform users of emerging safety information about possible new toxicities (e.g., FDA MedWatch alerts).

## ■ Boxed Warning

Describes information required by FDA to appear in a prominently displayed box in the manufacturer’s professional labeling (prescribing information).

FDA currently is unable to provide a list of all drugs requiring such warnings. As a result, while a reasonable attempt was made to include these warnings in a box at the beginning of the respective *Essentials<sup>™</sup>* monograph, the information occasionally may appear elsewhere in the monograph (e.g., in the Warnings section) or not at all.

Boxed Warning information describes special problems, particularly those that may lead to death or serious injury.

Although such boxed warnings usually appear at the beginning of labeling, they can appear anywhere in the manufacturer’s labeling at FDA’s prerogative.

## ■ REMS

Provides a brief description of a Risk Evaluation and Mitigation Strategy (REMS) approved by FDA, including a list of the components. Because REMS frequently are modified or rescinded, a cross reference to FDA’s list of “Approved Risk Evaluation and Mitigation Strategies (REMS)” is provided to refer users to the most current information. REMS for drug *combinations* are described in the monographs on the principal ingredient.

## ■ Uses

Provides information on uses included in the labeling approved by FDA and those that are not (“off-label”, unlabeled uses).

“Off-label” uses are identified with daggers† within the text of the monograph; a footnote that describes the use as such appears at the end of the monograph.

Comparisons with other forms of therapy and limitations on use are included when appropriate.

The Uses section is subdivided by major indication (disease/condition).

Under the Federal Food, Drug, and Cosmetic (FD&C) Act, the labeling approved by FDA for a drug is limited to those uses for which the sponsor has submitted information regarding the safety and efficacy of that product and which information has been reviewed by the FDA; other uses for which the sponsor has chosen not to submit data to the FDA may be demonstrated in the clinical literature before and after the product is approved by FDA. The FD&C Act does not, however, limit the manner in which a clinician may use an approved drug. Once a drug has been approved for marketing, the clinician may prescribe it for uses or in treatment regimens or patient populations (e.g., children) that are not included in approved labeling.

Such “off-label” uses may be appropriate and rational, and may reflect approaches to drug therapy that have been reported extensively in the medical literature. Valid new uses for drugs often are first discovered via serendipitous observations and therapeutic innovations, and then subsequently may be confirmed by well-designed and controlled studies. Inclusion of such new uses in the FDA-approved labeling for a drug may take considerable time and, without the initiative of the manufacturer whose product is involved, may never occur. Therefore, accepted medical practice (state-of-the-art) often includes drug use that is not included in FDA-approved labeling.

*AHFS DI<sup>®</sup> Essentials<sup>™</sup>* monographs include the principal “off-label” uses developed for the full *AHFS DI<sup>®</sup>* database via its respected evidence-based process.

Coverage of “off-label” uses in *AHFS DI<sup>®</sup>* monographs has been recognized by the US Congress (e.g., in OBRA 90, OBRA 93), federal agencies and programs (e.g., CMS; sections 1861 and 1927 of the Social Security Act), third-party health-care providers, and others, designating it through legislation, regulation, and other official guidance documents as an “official” compendium for information on medically accepted uses of drugs.

*AHFS DI<sup>®</sup> Essentials<sup>™</sup>* monographs include findings from structured, codified, evidence-based determinations for off-label cancer uses published in *AHFS DI<sup>®</sup>* under a process initiated in 2008. Details about specific determinations of medical acceptance for these uses are available under the Off-label Uses section of the *AHFS DI<sup>®</sup>* website (<http://www.ahfsdruginformation.com>). Documents describing the current process for off-label oncology uses, including levels of evidence, may be viewed at this website location. Following are the categories of AHFS Grades of Recommendation and the definitions of each:

- A: Recommended (Accepted) (e.g., should be used, is recommended/indicated, is useful/effective/beneficial in most cases)
- B: Reasonable Choice (Accepted, with Possible Conditions) (e.g., treatment option) (e.g., is reasonable to use under certain conditions [e.g., in certain patient groups], can be useful/effective/beneficial, is probably recommended/indicated)
- C: Not Fully Established (Unclear risk/benefit, equivocal evidence, inadequate data and/or experience) (e.g., usefulness/effectiveness unknown/unclear/uncertain or not well established relative to standard of care)
- D: Not Recommended (Unaccepted) (e.g., considered inappropriate, obsolete, or unproven; is not recommended/indicated/useful/effective/beneficial; may be harmful)

Drugs designated as orphan drugs by FDA and those otherwise considered as orphans are described. An orphan drug is one that is used for the treatment of a rare disease or condition that either occurs in fewer than 200,000 individuals in the US or is more prevalent but for which there is no reasonable expectation that the cost of developing and marketing the drug in the US for such disease or condition would be recovered from US sales.

## ■ Dosage and Administration

Includes information on the various applicable routes of administration for specific dosage forms of a drug and on its reconstitution, dilution, and administration. Also includes information on various applicable dosages and regimens. May describe restricted distribution programs for certain drugs when requirements for prescribing and dispensing exist or where distribution is otherwise limited (e.g., orphan drugs).

### **Administration**

The Administration subsection describes the routes of administration and, when necessary for clarity, the appropriate dosage form for each route. Instructions for administering the drug (e.g., after meals, with food) and specialized methods of administration are given.

Occasionally, instructions for extemporaneous preparation of a dosage form that is not commercially available (e.g., preparation of a pediatric oral suspension from the contents of capsules) are included.

In addition to information described for the Administration subsection, instructions for reconstitution and, when applicable, further dilution of the dosage form are

presented. The rate of injection or infusion of the drug is described, as well as any precautions associated with administration.

Compatibility and stability information is described under the Stability section toward the end of the monograph.

#### **Reconstitution.**

For injectable drugs and other dosage forms requiring reconstitution, this subsection describes the recommended methods.

#### **Dilution.**

For injectable drugs and other dosage forms requiring further dilution, this subsection describes the recommended methods.

#### **Rate of Administration.**

For injectable drugs and other dosage forms, this subsection describes the recommended rates of administration (e.g., for direct IV injection, for IV infusion).

### **Dosage**

The Dosage subsection describes recommended and alternative dosage schedules for each dosage form and route of administration, age of the patient, and condition being treated.

Information in this subsection is divided by age, indication, and route.

When applicable, dosage equivalencies are described (e.g., dosage of fosphenytoin is expressed in terms of phenytoin equivalents [PEs]).

When available and applicable, specific dosages for special populations (e.g., geriatric patients, patients with renal and/or hepatic impairment) are described in appropriately headed subsections of Special Populations under Dosage and Administration.

The initial and maintenance dosages are given. When available and applicable, maximum recommended dosages are described under the Prescribing Limits subsection of Dosage and Administration.

Occasionally, when use of a fixed-dosage combination preparation or concomitant use of the drug with another drug is considered rational, specific regimens may be described.

#### **Pediatric Patients.**

Describes age-specific dosages from the neonatal period through adolescence.

Dosages are further subdivided by specific indications (conditions/diseases).

Dosages for specific indications are subdivided further by specific routes of administration.

#### **Adults.**

Describes specific dosages for adults. Special dosages that apply to elderly adults are described under the Geriatric Patients subsection of Special Populations under Dosage and Administration.

Dosages are further subdivided by specific indications (conditions/diseases).

Dosages for specific indications are subdivided further by specific routes of administration.

### **Prescribing Limits**

When available and applicable, maximum recommended dosages for specific patient populations (e.g., age groups), routes of administration, and uses are described.

### **Special Populations**

When available and applicable, specific dosages for special populations (e.g., hepatic impairment, renal impairment, geriatric patients) are described in appropriately headed subsections.

#### **■ Cautions**

Includes information about contraindications, warnings and precautions, precautions for specific populations (e.g., pregnancy, fetal/neonatal morbidity and mortality, lactation, pediatric use, geriatric use, hepatic impairment, renal impairment), and common adverse effects. Information on general warnings and precautions is subdivided into content-specific subsections.

The Cautions section describes any special care required for safe and effective use of the drug and describes serious adverse effects and potential safety hazards, limitations on use imposed by them, and actions that should be taken if they occur. Those situations or conditions for which the drug should not be used because the risk clearly outweighs any possible benefit also are described.

Because precautionary information about a drug frequently changes, the manufacturer's labeling should be reviewed periodically.

### **Specific Populations**

#### **Pregnancy.**

Describes the safety of the drug in pregnant women. FDA's previously designated lettered categories (A, B, C, D, or X) describing pregnancy precautions are included when available. In 2014, FDA amended the pregnancy labeling requirements, eliminating these lettered categories and replacing the letters with a narrative structure. During the transition period, labeling may contain either the letters designating categories of risk or a text description. Therefore, *AHFS DI<sup>®</sup> Essentials*<sup>™</sup> monographs also may have varying styles depending on the available information. Following are definitions of FDA's previously designated categories:

**Category A:** Adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester and there is no evidence of risk

in later trimesters. If the drug were used during pregnancy, the possibility of fetal harm appears remote.

**Category B:** Either animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women or animal reproduction studies have shown an adverse effect (other than on fertility) but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester and there is no evidence of risk in later trimesters. In either case, the drug should be used during pregnancy only when clearly needed.

**Category C:** Either animal reproduction studies have revealed evidence of an adverse fetal effect and there are no adequate and well-controlled studies in pregnant women or animal reproduction studies have not been performed and it is not known whether the drug can cause fetal harm when administered to pregnant women. In the first case, the drug should be used during pregnancy only when the potential benefits justify the possible risks to the fetus. In the latter case, the drug should be used during pregnancy only when clearly needed.

**Category D:** There is positive evidence of human fetal risk based on adverse reaction data from investigational or postmarketing experience or studies in humans, but the potential benefits from use of the drug in pregnant women may be acceptable in certain conditions despite the possible risks to the fetus. The drug should be used during pregnancy only in life-threatening situations or severe disease for which safer drugs cannot be used or are ineffective. When the drug is administered during pregnancy or if the patient becomes pregnant while receiving the drug, the patient should be informed of the potential hazard to the fetus.

**Category X:** The drug may (can) cause fetal toxicity when administered to pregnant women based on animal or human studies demonstrating fetal abnormalities or positive evidence of human fetal risk from adverse reaction data from investigational or postmarketing experience, or both, and the risk of use of the drug during pregnancy clearly outweighs any benefit (e.g., safer drugs or alternative therapies are available). Since the risks clearly outweigh any possible benefits in women who are or may become pregnant, the drug is contraindicated in such women. If the drug is inadvertently administered during pregnancy or if the patient becomes pregnant while receiving the drug, the patient should be informed of the potential hazard to the fetus.

#### **Lactation.**

A description of whether the drug is distributed into milk is included when available, and any associated precautions regarding use of the drug in lactating women are described. Effects of the drug on lactation and/or the nursing infant also are described.

#### **Pediatric Use.**

Describes those pediatric age groups for which safety and/or efficacy of the drug have not been established from adequate and well-controlled studies. Risks and limitations associated with use of the drug in pediatric age groups also are described.

#### **Geriatric Use.**

Describes precautionary information associated with the drug in geriatric individuals and provides some perspective regarding study and experience in this population, including factors that may affect response and tolerance. In addition to the Geriatrics Use subsection, geriatric information also may be described in the Geriatric Patients subsection of Special Populations under Dosage and Administration as well as within other appropriate sections (e.g., Pharmacokinetics) of the monograph.

#### **Hepatic Impairment.**

Describes specific precautions applicable to patients with impaired hepatic function.

Recommendations for specific adjustment to dosage are described in the Special Populations subsection of Dosage and Administration, and alterations in pharmacokinetics of the drug secondary to hepatic impairment are described in the Pharmacokinetics section.

#### **Renal Impairment.**

Describes specific precautions applicable to patients with impaired renal function.

Recommendations for specific adjustment to dosage are described in the Special Populations subsection of Dosage and Administration, and alterations in pharmacokinetics of the drug secondary to renal impairment are described in the Pharmacokinetics section.

### **Common Adverse Effects**

Adverse reactions are undesirable effects, reasonably associated with use of the drug, that may occur as part of its pharmacologic action or may be unpredictable in occurrence. The common adverse effects subsection is not intended to be all inclusive. Potentially serious adverse effects usually are described under the Warnings and Precautions subsections under specific headed topics.

#### **■ Interactions**

Describes clinically important drug/drug, drug/food, and drug/laboratory test interactions, including adverse and therapeutically useful interactions. The mechanism of the interaction, associated clinical importance, precautions to be observed, and management of the interaction may be described briefly in the accompanying tables.

The Interactions tables list information alphabetically by interacting drug or drug class, food (usually specific food types [e.g., grapefruit juice]), and test (under Test and then alphabetically by specific test name).

Generally, potential interactions supported only by animal or in vitro data are not described. Theoretical interactions may be presented because of the likelihood of their occurrence (e.g., based on evidence from similar drugs) or the potential severity of the effect should it occur.

Information on physical and/or chemical incompatibility of parenteral drugs and solutions is described in the Compatibility section of Stability.

## ■ Pharmacokinetics

Describes absorption, distribution, and elimination (biotransformation and excretion) characteristics of a drug.

The Absorption subsection includes key information on extent (bioavailability) and rate of absorption by usual routes of administration and factors (e.g., product formulation) that might influence them. Applicable comparative information on doses, dosage forms, and routes of administration may be included. Information on serum concentrations achieved and on the period of time for onset, peak, and duration of pharmacologic and/or therapeutic effect also may be included, even when an absorption phase per se does not occur (e.g., following IV administration). Ranges for therapeutic and/or toxic concentrations (e.g., plasma, serum) of the drug are described when established.

The Distribution subsection describes key information on the usual distribution of the drug into body tissue and fluids. Information describing the drug's propensity to cross the blood-brain barrier and placenta and to distribute into milk is included. Protein binding characteristics are presented.

The Elimination subsection describes key information on the biotransformation and excretory characteristics of the drug. Information on elimination half-life and factors influencing it, clearance, site and extent of biotransformation, metabolic products and their activities, and routes of elimination from the body (e.g., urine, feces via bile) and factors affecting them is included. The effect of peritoneal dialysis and hemodialysis on elimination of the drug also is discussed.

## Absorption

### Bioavailability.

Describes extent and rate of systemic absorption of a drug from various routes of administration (e.g., oral, IM, transdermal, buccal).

Describes whether the drug undergoes first-pass metabolism.

Describes whether a drug is a prodrug.

### Onset.

Describes the onset of various effects of the drug, specific to various routes of administration when available.

### Duration.

Describes the duration of various effects of the drug, specific to various routes of administration when available.

### Food.

Describes the effect of food on absorption of the drug.

### Plasma Concentrations.

Describes plasma concentrations associated with specific therapeutic or toxic effects of the drug.

### Special Populations.

Describes specific absorption characteristics (e.g., serum concentrations, systemic exposure) of the drug in special populations.

## Distribution

### Extent.

Describes distribution of the drug into various tissues (e.g., placenta, eyes, organs) and fluids (e.g., breast milk, CSF).

### Plasma Protein Binding.

Describes extent of drug binding to plasma proteins (e.g., albumin,  $\alpha_1$ -acid glycoprotein).

## Elimination

### Metabolism.

Describes principal metabolic pathways for the drug and any associated pharmacologic or toxic activity.

### Elimination Route.

Describes the principal routes of elimination for the drug (e.g., urine, feces, expired air).

### Half-life.

Describes the elimination half-lives for the drug.

### Special Populations.

Describes specific elimination characteristics (e.g., elimination half-life, clearance) of the drug in special populations (e.g., hepatic impairment, renal impairment, geriatric patients).

## ■ Stability

Applicable stability information such as the effect of heat, light, moisture, air, and freezing may be described. Stability information about reconstituted and/or diluted preparations is provided. Physical and/or chemical compatibility information is included.

## Storage

Describes storage requirements (i.e., recommended environmental storage conditions) for products and formulations. Also describes storage conditions and associated stability for reconstituted and diluted preparations.

## Compatibility

Describes compatibility information for parenteral preparations, including commercially available injections and reconstituted and diluted solutions.

The information may include a general discussion and several tables organized by solution compatibility, drug compatibility, and Y-site compatibility. Within each table, information is subdivided according to whether the drug is compatible, incompatible, or variably compatible.

Information in the compatibility section summarizes complex information from multiple sources in an easy-to-use, reliable format. Designed with the input of nurses and pharmacists, the tables greatly simplify quick location of specific information on the compatibility of parenteral drugs when diluted with common IV infusion solutions, admixed with other drugs in IV solutions, or run through a common Y-site. The absence of specific solutions or drugs does not imply compatibility or incompatibility.

Additional detailed compatibility information on injectable drugs is available in specialized references such as the *Handbook on Injectable Drugs (HID)*, available from ASHP; go to [www.ashp.org](http://www.ashp.org) for details). Solutions and drugs are listed as variably compatible because their compatibility differed based on environmental (e.g., exposure to various light and temperature conditions) and other (e.g., concentration, pH, formulation) conditions or there was conflicting evidence under similar conditions. It is particularly important to consult such specialized references when the solution or drug compatibility is listed as *variable*, since details on the conditions under which they are likely to be compatible versus incompatible will be described there.

Only a small amount of information on compatibility of drugs mixed in the same syringe is included; consult specialized references for additional information.

A cross-reference at the beginning of the compatibility section advises users that information on systemic interactions of drugs is described in the Interactions section.

### Solution Compatibility.

Lists alphabetically by IV infusion solution name (under 3 separate portions of the table) solutions in which the drug is compatible, incompatible, or variably compatible.

### Drug Compatibility.

Lists alphabetically by admixed drug (under 3 separate portions of the table) combinations that are compatible, incompatible, or variably compatible when admixtures are prepared in common IV solutions.

### Y-site Compatibility.

Lists alphabetically by admixed drug (under 3 separate portions of the table) combinations that are compatible, incompatible, or variably compatible when flowing through the common portion of IV administration set below the Y-site. Consult specialized references for additional details.

## ■ Actions (or Actions and Spectrum)

Information is presented in a bulleted format.

Includes a brief statement of pharmacologic activity and/or mechanism of action, often compared with other similar drugs, for the purpose of orientation and introduction. More specific brief descriptions of important pharmacologic activities and effects follow.

For anti-infectives, the important in vitro spectra of activity is summarized.

In general, nomenclature for microorganisms follows that presented in *Bergey's Manual of Systematic Bacteriology* and the "Approved Lists of Bacterial Names" and validation lists and notification lists published in the *International Journal of Systematic and Evolutionary Bacteriology*. Other standard sources, as described by the American Society for Microbiology in the Instructions to Authors for *Antimicrobial Agents and Chemotherapy*, also are used.

## ■ Advice to Patients

Information is presented in a bulleted format.

Includes important information to advise patients and/or their caregivers concerning risks of therapy, special instructions for use and monitoring, and other guidance.

It generally is important that all patients be advised to inform their clinicians about concomitant therapies and diseases and for women of childbearing potential if they are or plan to become pregnant or plan to breast-feed.

The Cautions section and any Boxed Warning also should be consulted for other precautionary information that may be relevant to the patient and/or their caregivers.

## ■ Preparations

Detailed product descriptions in the style of *AHFS Drug Information*®.

Lists commercially available preparations of the drug. Combination preparations are described under a separate heading (e.g., Aspirin Combinations) following the appropriate single-entity subsection (e.g., Aspirin).

Preparations are described under the appropriate heading by USAN or other generic (nonproprietary) name.

"Tall man" (mixed case) lettering is used for generic or brand (trade) names when recommended by FDA or ISMP.

Preparations are listed hierarchically by route of administration (alphabetically), dosage form (alphabetically), and strength (in order of increasing strength). When

potency is described in terms other than those listed in the drug heading (e.g., potency of cefotaxime sodium is expressed in terms of cefotaxime), the labeled moiety is described parenthetically after the strength [e.g., 1 g (of cefotaxime)].

Route of administration and dosage form listings may be modified (e.g., Injection, for IM use only; Tablets, chewable; Capsules, extended-release).

Following each preparation description, the trade (proprietary) names are listed alphabetically and include the corresponding manufacturers. Generally, multiple-source preparations that are available by generic (nonproprietary) name do not include the manufacturers/labelers; these preparations are described as being “available generically.”

When established by USP, pharmacy equivalent names (PENs) (e.g., co-careldopa for levodopa and carbidopa) are listed parenthetically alongside the corresponding combination heading. PENs are short and simple names that can be used for convenience by practitioners when it would be impractical to use the complete nonproprietary combination name. PENs are informational rather than official (USP/NF), but are offered by USP as standardized terms intended to discourage the proliferation of trivial names and undefined abbreviations for combinations. This abbreviated nomenclature was pioneered by the British Pharmacopoeia (BP) and subsequently adopted by USP.

Generally, dosage forms used in the Preparations sections are the pharmaceutical dosage forms described in USP. (See the current edition of the *United States Pharmacopoeia*.) Several dosage forms (i.e., elixir, extract, fluidextract, spirit, tincture) are used only when the preparation is official (USP or NF). Solution generally is used to describe all liquid preparations of dissolved drug, regardless of solvent; although syrups occasionally are official (USP or NF), these are listed as solutions and syrup is included only as part of the proprietary name.

Applicable legal descriptions (e.g., drugs subject to control under the Federal Controlled Substances Act of 1970 [i.e., C-II, C-III, C-IV, and C-V], drugs subject to restricted distribution programs) are included.

#### ■ **AHFSfirstReleases™**

Certain monographs in *AHFS DI® Essentials™* are designated as *AHFSfirstReleases™*. This designation appears in a boldface notice before the Preparations section for the respective monograph. *AHFSfirstReleases™* disseminate timely information on new molecular entities (NMEs) in an expedited format as soon as possible after FDA approval; the principal limitation is availability of final labeling from the manufacturer.

#### **Scope**

*AHFSfirstReleases™* are descriptions about new molecular entities (NMEs) that include select information drawn principally from the manufacturer’s labeling (package insert); however, the descriptions are not intended to be comprehensive. When additional information on such drugs is needed before publication of a more detailed monograph, the manufacturer’s labeling should be consulted.

*AHFS First Releases®* are intended to provide subscribers with descriptions on NMEs that can answer typical basic questions about newly approved drugs. The descriptions are limited to highlights of boxed warnings in labeling; a brief description of a REMS approved by FDA; the brand name; an introductory sentence providing a brief pharmacologic/therapeutic description; highlights of labeled dosage and administration information; highlights of labeled contraindications; labeled warnings and precautions, including those for specific populations; highlights of common adverse effects; highlights of interactions; highlights of the actions and spectrum of the drug; manufacturer-recommended advice to patients; and a product description. As a result, the *AHFS First Releases®* do not provide full disclosure about the respective drugs, and therefore it is essential that the manufacturer’s labeling be consulted for more detailed information on usual uses, dosage and administration, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.