

USERS GUIDE

AHFS Drug Information® Users Guide

ORGANIZATION OF CONTENT

AHFS Drug Information® (*AHFS® DI*™) is a collection of drug monographs on virtually every single-drug entity available in the United States. *AHFS Drug Information*® is a tested and proven source of comparative, unbiased, and evaluative drug information.

AHFS® DI™ 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 8:12.20) when the combinations are considered important because of therapeutic rationale and/or frequency of use. There also are general statements on groups of drugs (e.g., Salicylates 28:08.04.24) whose activities and uses permit their discussion as a class. Information on older and prototype drugs is another feature of *AHFS® DI*™.

Organization of the Book

In the annual print edition of *AHFS® DI*™, drug monographs are arranged by the widely recognized and used *AHFS® Pharmacologic-Therapeutic Classification*®. (See p. xix.) This arrangement permits easy review of information on a group of drugs with similar activities and uses and allows the reader to determine quickly the similarities and differences among drugs within a group.

A *table of contents* precedes each major class of drugs (e.g., 8:00 Anti-infective Agents) in the book. The table of contents lists each drug monograph included in that major class according to the specific subclass (e.g., Cephalosporins 8:12.06). Within each subclass, monographs are arranged alphabetically by nonproprietary (generic) name and are preceded by the general statement, when present, for that subclass. The names of the drugs are the United States Adopted Names (USAN) and other names for drugs as described in the *USP Dictionary of USAN and International Drug Names*.

In the print edition of *AHFS® DI*™, a monograph must be printed within a single class section. However, multiple classifications may apply to a drug (based on its pharmacology or therapeutic uses); these are represented by cross-references provided in the table of contents for each class to the location of the monograph in the book. Although the print version of *AHFS® DI*™ does not include reference notations, all statements appearing in the publication are documented. (See the discussion on References.)

Information on a particular drug can be located via the Index by looking up the drug by its proprietary (trade) or nonproprietary (generic) name. The Index also includes entries for the major *AHFS® Pharmacologic-Therapeutic Classification*® terms. Once the table of contents for a specific major class of drugs

has been located, the page number for the beginning of each drug monograph is listed alongside the monograph title in the table; thus, the list of drug monographs in a given subclass can be quickly scanned to locate a specific drug or drugs of interest.

Some monographs have been omitted from the print version of *AHFS® DI*™ because of space limitations. Associated index entries and listings in the table of contents for each major class of drugs in the printed book refer users to the website www.ahfsdruginformation.com to see these monographs. A username and password are required to access these electronic-only monographs.

Each year after publication of the print edition of *AHFS® DI*™, new monographs are created, and revisions to existing monographs continue. At the end of the subscription year, any new or revised monographs that were published electronically usually will become incorporated into the upcoming annual edition of *AHFS® DI*™ within the appropriate *AHFS® Pharmacologic-Therapeutic class*®. Revised monographs carry the statement "Selected Revisions January 2022" or some other appropriate revision date in the Copyright notice at the end of the monograph. Because information about a drug frequently changes, the manufacturer's labeling should be reviewed periodically.

Organization of Full-length Monographs

Information within each full-length drug monograph is divided into the sections and subsections described below; the types of information that may be included in each major section and subsection within a monograph also are described. Not all sections or subsections are included in each monograph; such subdivisions are used when applicable and necessary. Some information may appear in one or more sections, depending on the type of discussion (e.g., pharmacogenomics information may appear under Dosage, Cautions, and/or Pharmacokinetics depending on the specific information presented). Individual monographs may not contain all of the information described below, or other subsections may be used as needed to organize the text; the absence of specific information within an individual monograph does not imply that such information is unavailable.

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

● Monograph Title and Synonyms

Lists the USAN name or other name for the drug(s) described; salts generally are included even when omitted from the USAN name. If multiple forms (e.g., salts, esters) of the same drug are available, all forms are described within the monograph; the title may include all forms (if only a few) or just the base (active moiety). Occasionally, when several drug entities are described in a single monograph, an alternative title descriptive of the group (e.g., Antacids 56:04) is used. Common synonyms for the drug are listed alongside the USAN or other names.

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When recommended by the US Food and Drug Administration (FDA) or the Institute for Safe Medication Practices (ISMP), "tall man" (mixed case) lettering is used for drug names in titles or synonyms (e.g., "diazepam").

When a graphic formula of the drug or prototype (if multiple drugs) is present, it is in the style adopted by the USAN Council and United States Pharmacopeial Convention.

Occasionally, certain synonyms (e.g., pharmacy equivalent names [PENs]) that apply to specific preparations or combinations rather than to the drug itself are noted parenthetically alongside various preparation headings. (See the discussion on Preparations.)

● **Introductory Description**

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

● **REMS**

Provides a brief description of a Risk Evaluation and Mitigation Strategy (REMS) approved by FDA. 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 that requires the REMS.

● **Uses**

Provides information on uses that are included in the labeling approved by FDA and those that are not (i.e., "off-label" [unlabeled] uses). Off-label uses are identified with dagger† within the text of the monograph; a footnote that describes the use as unlabeled appears at the end of the monograph. The authority of *AHFS® DITM* to establish medically accepted uses of drugs is recognized through designation as an official federal compendium. (See the Preface for additional information.) Comparisons with other forms of therapy and limitations on use are included when appropriate. This section usually is subdivided by major indication.

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 has been reviewed by FDA; other uses for which the sponsor has chosen not to submit data to 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 sponsor 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.

Accordingly, *AHFS® DITM* monographs attempt to describe most uses for a drug, whether or not they are included in FDA-approved labeling; however, the presence or absence of a particular use should *not* be interpreted as indicating any judgment by *AHFS® DITM* on its merits. Coverage of off-label uses in *AHFS Drug Information®*, an official Federal drug compendium, has been recognized by the US Congress (e.g., in OBRA 90 and OBRA 93), the Centers for Medicare & Medicaid Services (CMS; Section 1861 and 1927 of the Social Security Act), third-party health-care providers, and others. (See Off-label Uses at www.ahfsdruginformation.com for additional information.)

AHFS® DITM is the longest published official drug compendium and the only remaining one published by a non-commercial, nonprofit scientific and professional society. ASHP is an IRS 501(c)(6) tax-exempt entity.

Drugs designated as orphan drugs by FDA 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. An orphan drug also may be a vaccine, diagnostic drug, or preventive drug if the individuals to whom it will be administered in the US are fewer than 200,000 per year.

AHFS Grades of Recommendation

During 2008, *AHFS® DITM* introduced a new process for publishing structured, codified, evidence-based determinations for off-label cancer uses. In some monographs that subsequently were revised based on Final Off-label Determinations for cancer uses, text describing such uses based on *AHFS®* Grades of Recommendation may be noted. 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; or may be harmful)

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● *Dosage and Administration*

Includes information on preparation and administration of specific dosage forms and on dosage. In addition, pretreatment screening, patient monitoring, premedication and prophylaxis, dispensing and administration precautions, and certain Risk Evaluation and Mitigation Strategies (REMS) program requirements are described in discrete sections to allow quick retrieval of pertinent dosage and administration information.

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. For injectable drugs or other dosage forms requiring reconstitution, the Administration subsection is replaced by the Reconstitution and Administration subsection. 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. Generally, compatibility and stability information is described under Chemistry and Stability.

The Dosage subsection describes recommended and alternative dosage schedules for each dosage form and route of administration and condition being treated. Information in this subsection often is divided by use. When applicable, dosage equivalencies are described. The initial, maintenance, and maximum dosages are given. When available and applicable, specific dosages for children, geriatric or debilitated patients, or patients with renal and/or hepatic impairment are described. 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. Because information about a drug frequently changes, the manufacturer's labeling should be reviewed periodically.

● *Cautions*

Includes information about adverse effects, precautions and contraindications, pediatric and geriatric precautions, mutagenicity and carcinogenicity, and pregnancy, fertility, and lactation precautions.

Adverse reactions of a drug 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 general Adverse Effects subsection usually is replaced by multiple subsections that are specifically divided by body system affected (e.g., GI, CNS, Hematologic) or by type of effect (e.g., Sensitivity Reactions).

The Precautions and Contraindications subsection includes any special care to be taken by practitioners and/or patients 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. Additional precautions and contraindications are included in other appropriate sections of the drug monograph (e.g., Pediatric Precautions; Pregnancy, Fertility, and Lactation; Drug Interactions). Because precautionary information about a drug frequently changes, the manufacturer's labeling should be reviewed periodically.

The Pediatric Precautions subsection 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 associated with use of the drug in pediatric age groups also are described.

The Geriatric Precautions subsection includes precautions, warnings, and contraindications associated with use of the drug in geriatric individuals and provides some perspective regarding study and experience in this population, including factors that may affect response and tolerance.

Pediatric and geriatric information also may be described within the appropriate major sections of the monograph. For example, information on age-dependent pharmacokinetics of the drug would be described within the Pharmacokinetics section and that on age-specific dosage recommendations would be described in the Dosage and Administration section of the monograph. When relevant information on use of the drug in pediatric or geriatric patients is readily available in the medical literature and/or the drug is labeled specifically for use in this age group, details about efficacy generally are described in the Uses section.

The Mutagenicity and Carcinogenicity subsection describes data derived from long-term animal studies evaluating carcinogenic potential of the drug as well as data derived from in vitro tests of mutagenic potential. Pertinent evidence from human data regarding the mutagenic and/or carcinogenic potential of the drug also is included.

The Pregnancy, Fertility, and Lactation subsection describes the safety of the drug in pregnant and/or lactating women and any potential effects on male and female reproduction capacity. Precautionary information regarding use of the drug during pregnancy, which is based on FDA's previously designated pregnancy categories A, B, C, D, and X, is included when available. (See Overviews: Pregnancy Precautions for a description of the previously used FDA categories.) In 2014, FDA amended the requirements for pregnancy and lactation labeling, eliminating these long-recognized lettered categories and replacing the letters with a narrative structure for pregnancy labeling. Therefore, *AHFS® DI™* monographs may have varying styles depending on the available information. Additional pertinent information regarding use of the drug during pregnancy or effects on labor and delivery also is presented.

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

Evidence from animal studies regarding effects of the drug on fertility is given, and relevant advice regarding the importance of these animal findings is included when available. Pertinent evidence from humans regarding effects of the drug on fertility also is described.

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● **Acute Toxicity**

Describes toxic effects of the drug associated with intentional or accidental ingestion or administration of a large dose. Information on the amount of drug in a single dose that usually is associated with symptoms of overdosage and the amount of drug in a single dose that is likely to be life-threatening is included when available. Manifestations, laboratory findings, and potential complications of acute overdosage are described. Plasma concentrations associated with toxicity are included when well described.

Recommendations for management of acute toxicity, including those for supportive and symptomatic treatment, are described.

● **Chronic Toxicity**

Includes well-described toxic effects of the drug associated with prolonged use. When information on chronic toxicity is limited, it often is described in the appropriate subsection under Cautions. The pathogenesis, manifestations, and treatment of chronic toxic effects are discussed. Also included is a description of tolerance to and/or physical or psychological dependence on the drug. Adverse effects associated with abrupt withdrawal of the drug are described, and appropriate measures for management are included.

● **Drug Interactions**

Describes clinically important drug/drug and drug/food interactions, including adverse and therapeutically useful interactions. The mechanism of the interaction, associated clinical importance, precautions to be observed, and management of the interaction are described. Generally, potential interactions supported only by animal or in vitro data are not described. Occasionally, theoretical interactions are 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.

● **Laboratory Test Interferences**

Includes information on common, well-established drug/laboratory test interferences. The mechanism of the interaction, effects on test results, and effects on interpretation of these results are included. Alternative laboratory tests are described when appropriate. Alterations in laboratory test results that reflect a pathologic effect of the drug (e.g., aminoglycoside-induced increase in serum creatinine concentration) are described in the appropriate subsections under Cautions. Because of the nature of information on laboratory tests, appropriate specialized references on laboratory methods should be consulted when detailed information is required.

● **Pharmacology**

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. Expanded descriptions of pharmacologic activities and effects are included. When relevant to human pharmacology and therapeutics, animal or in vitro data are presented. Data from human studies are not specified as such unless needed for clarification. Quantitative

and qualitative comparative (with other drugs) information is provided when appropriate. Pharmacology usually is subdivided by pharmacologic effect (e.g., Anti-inflammatory, Analgesic) and/or body system affected (e.g., CNS, GI, Hematologic).

For anti-infectives, pharmacology is described under Mechanism of Action, Spectrum, and Resistance.

● **Mechanism of Action**

Describes the mechanism of anti-infective activity for anti-infective agents.

● **Spectrum**

Describes the in vitro spectra of activity of anti-infectives. The subsection on Susceptibility Testing describes factors (e.g., pH, test media, inoculum size) affecting susceptibility tests and defines susceptible and resistant organisms in terms of in vitro susceptibility test results (e.g., zone diameters for the Kirby-Bauer method, MICs for the tube dilution method). MIC values for clinically important organisms are included in the spectra subsections. Spectra often are divided according to class of organism (e.g., Gram-negative Bacteria, Anaerobic Bacteria).

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 of current approved bacterial names (e.g., List of Prokaryotic Names with Standing in Nomenclature/Prokaryotic Nomenclature Up-to-date at <https://www.dsmz.de/services/online-tools/prokaryotic-nomenclature-up-to-date>), as described by the American Society for Microbiology in Instructions to Authors for *Antimicrobial Agents and Chemotherapy*, also are used. When available, in vitro susceptibility information generally is described according to the Clinical and Laboratory Standards Institute (CLSI) and/or the manufacturer's labeling.

● **Resistance**

Describes the mechanism of resistance of microorganisms to anti-infective agents. Microbiologic tolerance to these agents also is described. Information on cross-resistance with other anti-infective agents is included. Definition of resistance in terms of in vitro susceptibility test results is described in the Spectrum section. Descriptions of resistant organisms are included in the Resistance section and/or in the spectra subsections of Spectrum.

Resistance of cells to antineoplastic agents generally is described in the Pharmacology section. Resistance or tolerance to the pharmacologic and/or therapeutic effects (e.g., tachyphylaxis) of other drugs generally is described in Pharmacology and/or Uses. Tolerance to the pharmacologic effects of some drugs (e.g., opiate agonists) also may be described in the Chronic Toxicity section.

● **Pharmacokinetics**

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

The Absorption subsection includes information on extent (bioavailability) and rate of absorption by usual routes of

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administration and factors (e.g., product formulation) that might influence them. Applicable comparative information on doses, dosage forms, and routes of administration is included. Information on serum concentrations achieved and on the period of time for onset, peak, and duration of pharmacologic and/or therapeutic effect also is 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 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 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.

● *Chemistry and Stability*

Includes a brief chemical, structural, and/or pharmacologic description, often compared with other similar drugs, for the purpose of orientation and introduction. Structure-activity relationships are described when applicable. A physical description of drug entities includes physical appearance, taste, odor, and solubility. Solubilities are described according to USP descriptive terms (see the current edition of the *United States Pharmacopeia–National Formulary [USP–NF]*) or as appropriate specific solubilities (i.e., amount of solute per volume of solvent).

If the drug is ionizable, the pK_a is given. Other chemical and/or physical constants such as pH and osmolarity/osmolality of commercially available preparations are included. Preservatives and other important excipients in a commercial preparation also are described. Dosage equivalencies (e.g., units per mg of drug, mg of base per mg of salt) are given when the dosage of a drug differs from the commercially available form (e.g., salt, ester). Amounts of important ions (e.g., mg/mEq of potassium, sodium) in commercial preparations also are included.

Applicable stability information such as the effect of pH, autoclaving, heat, light, moisture, air, freezing, and microwave thawing is described. Storage requirements (i.e., recommended environmental storage conditions) also are described. Stability information about reconstituted and/or diluted preparations is provided. Physical and/or chemical compatibility information may be included. Additional detailed compatibility information on injectable drugs is available in the *ASHP® Injectable Drug Information™* (available from the American Society of Health-System Pharmacists; go to www.ashp.org for details).

● *Preparations*

Lists commercially available preparations of the drug. Preparations are described under the appropriate heading by USAN or other nonproprietary (generic) name. Combination preparations are described under a separate heading (e.g., Aspirin

Combinations) following the appropriate single-entity subsection (e.g., Aspirin); official USP combination names (e.g., Metoprolol Tartrate and Hydrochlorothiazide) are used whenever possible.

Although USP has changed its naming conventions to eliminate salt forms in many official monograph titles (active moiety nomenclature concept), ASHP continues to oppose this nomenclature change because of resulting confusion and loss of important chemical identity cues, and therefore *AHFS® DI™* will continue to include salts in the Preparations headings for clarity. When recommended by FDA or the Institute for Safe Medication Practices (ISMP), "tall man" (mixed case) lettering is used for generic or brand (trade) names (e.g., "diazepam").

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 proprietary (trade) names are listed alphabetically and include the corresponding manufacturers. Generally, preparations that are available by nonproprietary (generic) name do not include the names of the manufacturers/labelers; these preparations are listed under the generic name and described as being "available by nonproprietary name."

Generally, dosage forms used in the Preparations sections are the pharmaceutical dosage forms described in USP. (See the current edition of the *United States Pharmacopeia–National Formulary*.) Several dosage forms (i.e., elixir, extract, fluid extract, 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, drugs subject to restricted distribution programs) are included.

● *References*

Includes the bibliography for cited references. Information included in *AHFS® DI™* is thoroughly referenced. Access to referenced statements and the References section of individual drug monographs for *AHFS® DI™* and its point-of-care derivative database *AHFS® DI™ Essentials™* can be gained through electronic versions (e.g., AHFS® Clinical Drug Information™ [AHFS® CDI™], eBroselow's SafeDose®, Lexicomp® Online®, First DataBank's AHFS Drug Information® monographs available from multiple vendors; *AHFS Drug Information®* from STAT!Ref®, Pepid's Pharmacist Pro with AHFS DI®, and MedicinesComplete®; *Drug Information Full-text® [DIF®]*; *AHFS® DI™ Powered by Skyscape Medpresso*).

Reference citations currently are electronically accessible for all monographs published after March 1984. For monographs originally published prior to that time, bibliographic citations are accessible only for selected revisions occurring since 1984. To

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determine whether a monograph was published or revised after March 1984, see the copyright notice at the end of the monograph in question. In electronic versions of *AHFS® DI™*, approximately 90% of the monographs currently are completely or partially referenced.

For additional information on searching the electronic versions of *AHFS® DI™*, contact ASHP Customer Service by phone at 1-866-279-0681 or by email at custserv@ashp.org.

AHFS® *firstReleases*™

Certain monographs in *AHFS® DI™* are designated as *AHFS® firstReleases™*. This designation appears in a boldface footnote preceding the Preparations section of the monograph. The *AHFS® firstReleases™* 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

AHFS® firstReleases™ are descriptions about new molecular entities that include information drawn 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® firstReleases™* are intended to provide information that can answer typical basic questions about newly approved drugs. As such, the descriptions are limited to highlights of boxed warnings in labeling; a brief description of a REMS (if one is approved by FDA for the drug); 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® firstReleases™* 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. Sections for Preparations and References are similar to those previously described for full-length monographs.

Overviews

Certain monographs in *AHFS® DI™* are designated as Overviews. This designation appears in a boldface footnote preceding the Preparations section of the monograph.

● Scope

The Overview drug monographs are summary descriptions that include information drawn principally from the manufacturer's labeling (package insert) and the principal clinical studies that

supported approval of the drug. Pertinent information from other sources such as authoritative therapeutic guidelines, secondary references (e.g., review articles), and a limited number of primary references also are included.

The Overviews are intended to provide subscribers to *AHFS® DI™* with summaries on new molecular entities (NMEs) that can answer most common questions about these drugs. As such, the Overviews are limited to basic information on the drugs, including brief descriptions (chemical and pharmacologic) of the type of drug, its labeled uses and associated dosages, administration instructions, product availability, cautionary information (e.g., contraindications; warnings and precautions; sensitivity reactions; cautions applicable to specific populations, common adverse effects), drug interactions, and important advice for patients. Some Overviews have been expanded to include important "unlabeled/off-label" uses. While selected information appears in these monographs, the scope of the Overview format limits the extent of discussion. As a result, the Overviews 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 pharmacodynamics, pharmacokinetics, adverse reactions, laboratory test interferences, and acute and chronic toxicity. Sections for Preparations and References are similar to those previously described for full-length monographs.

● Pregnancy Precautions

The pregnancy precautions in the Overviews historically have followed FDA's lettered categories (A, B, C, D, or X), as stated in the manufacturer's labeling. Because of the summary format of the Overviews, only the letter designation previously appeared. However, as noted previously FDA amended the requirements for pregnancy and lactation labeling in 2014, eliminating these lettered categories and replacing the letters with a narrative structure for pregnancy labeling. Therefore, some *AHFS® DI™* Overviews now contain text descriptions of information about use of a drug during pregnancy when the lettered category has not been provided in the labeling.

Following are definitions of the categories FDA previously had designated:

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.

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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.

SumMons®

Certain monographs in *AHFS® DI™* are designated as SumMons® (summary monographs). This designation appears in a bold-face footnote preceding the Preparations section of the monograph. SumMons® are summary descriptions about a drug, which include information that is drawn principally from the manufacturer's labeling (package insert) and/or other pertinent information (such as secondary references [e.g., review articles] and a limited number of primary references [e.g., the principal clinical studies]); however, no attempt is made to be complete, and the

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