
Preface

(AHFS primary)

An Evidence-based Foundation for Safe and Effective Drug Therapy

The mission of *AHFS Drug Information*® (*AHFS DI*®) is to provide an evidence-based foundation for safe and effective drug therapy. 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, *AHFS DI*® has remained true to its mission for over 50 years. This notable achievement of more than 5 decades of evidence-based medical publishing has gained *AHFS DI*® the unique distinction of being the longest published federally designated drug compendium issued by a scientific and professional society. As such, *AHFS DI*® maintains a unique role in establishing medically accepted uses of drugs, both labeled and off-label.

With the 2014 edition, the *American Hospital Formulary Service*® (*AHFS*™) marks its 56th year of continuous publication by the American Society of Health-System Pharmacists (ASHP). First published in 1959, the *Formulary Service*™ has evolved to address increasingly complex issues related to drug therapy and formulary management.

AHFS DI® is a collection of drug monographs kept current by ongoing electronic updates (e.g., information on new molecular entities, MedWatch notices, <http://www.ahfsdruginformation.com>) and by a revised master print volume issued each year. The *AHFS DI*® database is maintained continuously throughout the year for the purpose of disseminating comprehensive, evaluative drug information to the entire medical and paramedical community, and updates are issued frequently on an ongoing basis in electronic formats.

AHFS™ was first published in 1959 as an adaptation from the *Hospital Formulary of Selected Drugs* by Don E. Francke. *AHFS*™ had its roots in the hospital formulary system, which was intended to establish a sound therapeutic and economic basis for drug policy. Originally, the *Formulary Service*™ was conducted through the Committee of Pharmacy and Pharmaceuticals of the American Society of Hospital (now Health-System) Pharmacists to assist the pharmacy and therapeutics committee of each hospital in preparing its hospital formulary. Since then, *AHFS DI*® has developed beyond its original purpose to become the most comprehensive, authoritative source of evaluative, evidence-based drug information available. Paramount to providing such information is the critical, evidence-based evaluation of pertinent clinical data concerning drugs, with a focus on assessing thoroughly the advantages and disadvantages of various therapies, including interpretation of various claims of drug efficacy.

As a result of its foundation in a professional and scientific society, the values, editorial standards, and professional priorities of *AHFS DI*® differ importantly from those of commercial drug information publishers. The critical evidence-based assessment and provision of drug information is a core professional activity of ASHP and competency of its members. Despite increased emphasis on provision of evidence-based drug information in all pharmacy practice settings, ASHP and its members remain at the forefront of disseminating such information. As a professional society, ASHP takes a leadership position in influencing health policy, practice, and education toward the goal of assuring that patient care is grounded in accurate, timely, unbiased, and evidence-based drug information. ASHP has been at the forefront of efforts to improve medication use and enhance patient safety for 70 years.

■ AHFS Consumer Medication Information (CMI)

ASHP has a long history of providing patients with meaningful information about medications. AHFS CMI had its origins in 1976 as a collaboration among ASHP, the American Hospital Association (AHA), the US Department of Health, Education, and Welfare (DHEW; now DHHS), and the US Center for Disease Control (CDC; now the Centers for Disease Control and Prevention) and is the only trusted and objective compendium-based database of CMI published by a professional and scientific society in the US. CMI also has been referred to as patient medication information (PMI).

Credibility of sources has been ranked by physicians and other clinicians as the most important characteristic of the Internet related to health information. Consumers also are emphasizing credibility of the health information they obtain on the Internet, trusting safe and effective treatment information from professional societies like ASHP the most and that from pharmaceutical companies the least. AHFS has a clear reputation for credible, valid information based on its history, references, and evidence basis. AHFS CMI, hosted by the National Institutes of Health (NIH), is one of only a few such sites of trusted accurate medication information.

The trust placed in AHFS CMI has resulted in strategic alliances with groups such as the National Library of Medicine (MedlinePlus® and MedlinePlus® Connect) and Consumers Union (Consumer Reports Health and Best Buy Drugs), groups that also place a high priority on the credibility that AHFS CMI provides. In collaboration with Consumer Reports Best Buy Drugs, ASHP has developed a series of off-label drug use reports through a grant from the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by a multistate settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin® (gabapentin). When accessing any of these sites, consumers can be assured that they are receiving the most trusted and credible medication information available. AHFS CMI also is accessible through ASHP's own website—<http://www.safemedication.com>.

AHFS CMI also has been adopted as the trusted source of patient medication information by the two leading providers of bedside patient engagement and education resources in hospitals—GetWellNetwork® and Sonifi® Healthcare (formerly LodgeNet® Healthcare). These services focus on improving patient satisfaction, outcomes, and quality as measured by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey, Care Measures, and other indicators.

■ Off-Label Drug Reviews for Oncology

In 2008, *AHFS DI*® introduced a process for publishing structured, codified, evidence-based determinations for off-label cancer uses. The decision to create a separate method resulted from the unique characteristics of evidence-based decisions that are applied to serious and life-threatening conditions such as cancer. This process supplements the long-standing evidence-based process used by AHFS to evaluate off-label uses of drugs and biologics, and incorporates the desirable characteristics for cancer-specific compendia outlined by the Medicare Evidence Development and Coverage Advisory Committee (MedCAC). The cancer-specific codified method developed by AHFS is consistent with distinctions applied to evidence-based assessments of cancer treatments by other authoritative sources such as the National Cancer Institute (NCI) and FDA.

The principles of the *AHFS DI*® evidence-based editorial development process have not changed with this oncology process. However, the codified determinations supplement and enhance the traditional *AHFS DI*® evaluation of off-label uses with structured determinations that summarize ongoing assessments of new and changing evidence. ASHP appointed an Oncology Expert Committee, comprised of oncologists, oncology pharmacists, and oncology nurses, to assist with the independent review and final recommendations for off-label cancer determinations. Final decisions are made solely by the Oncology Expert Committee for determinations emanating from this supplementary process for oncology uses and by AHFS staff for other information, taking into account the advice of other expert reviewers. All processes related to the review and publication of determinations are transparent and designed to mitigate any potential conflict of interest in order to preserve the integrity of *AHFS DI*® and to minimize bias.

Federal regulations for transparency and conflict of interest disclosure and management became effective January 1, 2010 for off-label oncology determinations. AHFS employs a process for evaluating therapies that is publicly transparent as defined by CFR Section 414.930(a) and that includes criteria used to evaluate the use, a listing of evidentiary materials reviewed by the compendium, and a listing of all individuals who participated substantively in the development, review, or disposition of the request. In the case of balloted determinations made by the AHFS Oncology Expert Committee as of this date, conflict of interest disclosure policies follow the definition of a publicly transparent process for identifying potential conflicts of interest as established in this section of the CFR.

Documents describing this process for off-label oncology uses, including levels of evidence, transparency, and conflict of interest disclosure and management, may be viewed under the Off-label Uses section of the *AHFS DI*® website at <http://www.ahfsdruginformation.com>. Subscribers may access details about specific determinations of medical acceptance for these uses at this website location.

■ Editorial Independence

Information included in *AHFS DI*® shapes treatment decisions made by clinicians and influences public and private health-care policies and decisions. As a result, it is important that the information be authoritative, objective, and free of undue influence from pharmaceutical companies and other third parties who may seek to use the compendium to promote their own vested interests. Editorial decisions are evidence-based and made independent of such third parties.

AHFS DI® is the only remaining official drug compendium published by a non-commercial, nonprofit professional and scientific society. ASHP is an IRS 501(c)(6) tax-exempt entity. ASHP is the national professional organization that represents pharmacists who provide patient care services in hospitals, health systems, ambulatory clinics, and other settings spanning the full spectrum of medication use. ASHP has a long history of fostering evidence-based medication use as well as patient medication safety. *AHFS DI*® and Consumer Medication Information are published in part to support the mission of pharmacists in helping people achieve optimal health outcomes.

AHFS DI[®] is published by ASHP under the authority of its elected Board of Directors. As such, the Board exercises oversight through its ongoing Society considerations as well as through its Committee on Publications. This oversight by the Board also involves review and approval of relevant recommendations originating from its appointed Council on Therapeutics and the advisory and best practices developments of its other Councils, House of Delegates, and other policy-recommending bodies.

In addition, hundreds of experts, principally physicians but also other clinicians, medical scientists, pharmacists, pharmacologists, and other professionally qualified individuals, participate in an ongoing extramural review process for *AHFS DI*[®]. Participation is solicited but voluntary, and no honorarium nor other benefit other than limited access to the *AHFS DI*[®] database is provided. These experts must provide full disclosure of interest, including any affiliation with or financial involvement with the manufacturer of the drug(s) under consideration and directly competitive products.

ASHP considers it essential that interactions between AHFS staff and pharmaceutical companies be limited to the legitimate exchange of the scientific and medical information needed to fulfill the mission of *AHFS DI*[®]. To maintain independence from the undue influence of the promotional interests of pharmaceutical companies, communications are directed to the scientific and medical information areas within the companies; contact with marketing areas is avoided.

ASHP holds in high regard the responsibilities attendant to the public and private trust placed in the evidence-based editorial deliberations of *AHFS DI*[®]. As such, ASHP also considers it essential to protect the integrity and independence of the editorial decisions of AHFS staff by separating the Society's business activities with pharmaceutical companies (e.g., exhibits at educational meetings, journal advertising) from the editorial activities of its drug compendium. An editorial independence statement, approved by ASHP's Board of Directors and available at <http://www.ahfsdruginformation.com>, outlines the principles that AHFS staff apply in ensuring such independence.

■ Comparative, Unbiased, Evaluative Drug Information

AHFS DI[®] is a tested and proven source of comparative, unbiased, and evidence-based drug information containing a monograph on virtually every molecular drug entity available in the US. Drug monographs are prepared by a professional editorial and analytical staff, who critically evaluate published evidence on the drug. The monographs incorporate the advice of leading medical experts in the specific field of therapy under consideration, including experts from major research and clinical institutions as well as public bodies such as the National Institutes of Health (NIH) and US Centers for Disease Control and Prevention (CDC) and professional associations with therapeutic authority. It is this preparation by a professional staff and the exhaustive review process that make *AHFS DI*[®] monographs unbiased and authoritative.

Using an independent, evidence-based, evaluative process, *AHFS DI*[®] monographs incorporate information from pertinent references in the literature and expert therapeutic guidelines. The monographs also address the labeling approved by the FDA, in some cases challenging outdated and clinically irrelevant information that may persist in the approved labeling. *AHFS DI*[®] monographs continue to include information on uses, dosages, and routes and/or methods of administration that may not be included in the FDA-approved labeling for the drug ("off-label/unlabeled uses"). (See Uses in the Users Guide, p. xiii.) A typical monograph on a new drug incorporates information from several hundred published references, and some general statements and individual monographs incorporate information from several thousand references.

The current *AHFS DI*[®] database includes more than 85,000 uniquely cited references linked to more than 618,000 statements. Tens-of-thousands of additional references from the *AHFS*[™] archives provide support for monographs on drugs introduced into the US market prior to 1984. It is this point-by-point analysis and evaluation of the literature that make *AHFS DI*[®] monographs comprehensive, evaluative, and considerably beyond the FDA-approved labeling in their scope.

■ Widely Vetted Editorial Process in Support of Compendial Recognition

The *American Hospital Formulary Service*[®] grew out of the concept of the Formulary System in institutions. The ASHP Minimum Standard for Pharmacies in Hospitals, which described principles of the formulary system, was approved in 1951 by ASHP and the American Pharmaceutical Association, American Hospital Association, American Medical Association, and American College of Surgeons and served as the cornerstone for Joint Commission standards on formularies.

The broad-based vetting and recognition of ASHP's editorial standards over several decades are unparalleled. (See also the section "Highly Recognized Authority" below.)

In the mid-1960s through the mid-1970s, recommendations from the US Department of Health, Education, and Welfare (DHEW), including DHEW's Task Force on Prescription Drugs and FDA's Bureau of Drugs, proposed the creation of a Federal drug compendium. Key people involved in promoting the concept of

a national formulary included FDA Commissioner James Goddard and DHEW Secretary Caspar Weinberger. Congressional Committees involved included the Senate Monopoly Committee (Senator Gaylord Nelson, Chair) and the Senate Subcommittee on Health. Various physician proponents of the quality and scope of *AHFS*[™] and others corresponded and met with most of the Federal principals involved in these deliberations and proposed *AHFS*[™] as meeting the goals for such a compendium. ASHP also provided comments at the Drug Information Association's symposium on a Federal Drug Compendium held in Washington, DC June 11-12, 1970. At the time, *AHFS*[™] was "the only constantly updated compendium of edited, organized, unbiased, and evaluated information on virtually all drugs used in the United States."

The National Academy of Sciences-National Research Council (NAS-NRC) was contracted by FDA in 1966 to evaluate efficacy claims being made by manufacturers for drugs cleared for marketing from 1938-1962 (prior to Kefauver-Harris amendments). Analysis of existing conclusions in *AHFS*[™] found remarkable similarities with the NAS-NRC findings and spoke well for *AHFS*[™] as an evaluative, unbiased drug compendium. (*Am J Hosp Pharm.* 1968; 25:483-4.)

Based on ASHP's demonstrated expertise as a scientifically based group that reviewed drug data in an ongoing program and that could provide a continuum of experience and evaluation of drug information, FDA contracted with ASHP in 1975 to develop a class prescription labeling system. ASHP exhaustively applied this system to 20 major therapeutic classes and subclasses of drugs (e.g., antipsychotics, antidepressants, various anti-infective and endocrine classes, analgesics, antihypertensives), developing standard, objective professional class labeling for safe and effective use that FDA applied to numerous individual drug products included in these classes. At the time, pharmaceutical company labeling for drug products within the same class and even for the same generic drug included inconsistent information, including that about efficacy of the drugs.

The Medicare Catastrophic Health Coverage Act of 1988 (Public Law 100-360) required that the Secretary of the Department of Health and Human Services (DHHS) establish outpatient standards for prescribing drugs that were based on accepted medical practice. In establishing such, the Secretary was directed to incorporate standards from current authoritative compendia for the prescribing, dispensing, and utilization of covered outpatient drugs. The editorial policies and procedures, scope, and evidence-based analyses applied to *AHFS DI*[®] content were exhaustively scrutinized by Congressional staff as part of this process. To assist the Secretary in making a determination of official compendial designation, *AHFS DI*[®] was required to establish that it met the criteria identified by the Conference Committee as an appropriate source of information for establishing the prescribing standards based on accepted medical practice. The activities surrounding this legislation, including intense analysis by Congressional staff and that of the Health Care Financing Administration (HCFA; now the Centers for Medicare & Medicaid Services [CMS]), ultimately resulted in the designation of *AHFS DI*[®] as a source for establishing these drug prescribing standards. This set the precedent for recognition by Federal, State, and private sector entities of *AHFS DI*[®] as an authoritative source for establishing drug use standards in subsequent legislation (e.g., Omnibus Budget Reconciliation Act [OBRA] of 1990 and 1993) and guidelines. Federal compendial recognition continues under part 456 of CMS regulations governing utilization control for Medicaid and under section 1927 of the Social Security Act.

In January 1989, HCFA began developing regulations to implement section 202 of the Medicare Catastrophic Coverage Act of 1988 aimed at establishing standards for prescribing outpatient drugs based on accepted medical practice. In establishing these standards, HCFA required ASHP to describe the extent to which *AHFS DI*[®] met each of the criteria outlined in the Congressional Conference Report. HCFA was required by Congress to designate as official only those compendia that based such medical practice standards on review of published scientific and medical information and that provided adequate assurances that the expert reviewers who assisted in establishing the standards were free of financial (or other) conflicts of interest. ASHP participated in a public hearing conducted by HCFA's Bureau of Eligibility, Reimbursement, and Coverage on the use of authoritative compendia to determine prescribing standards for the new Medicare outpatient drug coverage. In September 1989, HCFA published its determination that *AHFS DI*[®] met the selection criteria as an official compendium. HCFA's determination was subject to broad-based public scrutiny and comment via the *Federal Register* (1989; 172:37190-246). HCFA also established the expectation that such designation of any compendium in the future would require evaluation by the Agency as to whether the compendium met the established standards as well as publication for public comment in the *Federal Register* of their selection decision in the form of a proposed rule.

In 1989, the Health Insurance Association of America (HIAA; now America's Health Insurance Plans [AHIP]) recommended that insurers use *AHFS DI*[®] as well as certain other resources (e.g., peer-reviewed literature, medical specialty organizations, consultants) for making determinations about off-label uses. In 1994, ASHP met with the HIAA Health Care Technology Committee regarding the use of *AHFS DI*[®] as a standard for making determinations on reimbursement of off-label uses.

In 1989, ASHP also was invited to the National Blue Cross and Blue Shield Association's Technology Management Conference for the purpose of addressing the individual member Plan Medical Directors and senior Plan management regarding the use of the compendia for evaluating the efficacy of off-label uses. As a result, the National Blue Cross and Blue Shield Association changed its previous position that off-label uses be considered investigational and therefore ineligible for reimbursement. The revised position stated that off-label uses should be eligible for reimbursement based on evaluation of efficacy and that *AHFS DI*[®] was a valuable resource for use in the evaluation process.

In September 1991, ASHP was invited to participate in Medicaid's National Medical Directors' Conference to provide information on the use of *AHFS DI*[®] for making decisions regarding which drugs to pay for and under what clinical circumstances. This conference was a forum for the medical directors to discuss HCFA's national drug coverage determination.

Section 4401 of OBRA 90 (Public Law 101-508) specified requirements for a Drug Use Review program as part of Medicaid. As a result of OBRA 90, section 1927(g) of Title XIX of the Social Security Act required State Medicaid programs to assess data on drug use against standards established by ASHP, American Medical Association (AMA), and the United States Pharmacopeia (USP) (the latter 2 no longer publish a drug compendium). Once again, the *Federal Register* (1992; 57:49397-412) provided an opportunity for public comment; the rule was finalized in September 1994.

Section 9401 of HCFA's State Medicaid Manual required that State Medicaid programs use *AHFS DI*[®] as a predetermined standard against which to assess drug use. In June 1992, this revision to the Manual was submitted to the State Medicaid Directors for comment prior to being finalized. The authority of *AHFS DI*[®] as an official compendium was further recognized under OBRA 93 for use by State Medicaid programs for information on medically accepted off-label uses of drugs and under the Medicare provisions of this Act for medically accepted indications of antineoplastic drugs.

Section 1861(t) of the Social Security Act established *AHFS DI*[®] as an official compendium for use in determining medically accepted indications of drugs and biologics used in anti-cancer chemotherapeutic regimens under Medicare Part B and section 1927(k) established such compendial recognition for all Medicare Part D drugs.

Because of its long-standing record in evidence-based evaluation of information on drug use, ASHP was requested by FDA in 1993 to assist the Agency in attempting to identify important off-label uses. ASHP was the only professional pharmacy organization requested to assist FDA in this effort.

In 2003, *AHFS DI*[®] was specified by the National Association of Insurance Commissioners as a standard reference compendia in their model Health Carrier Prescription Drug Benefit Management Act that provides standards for the establishment, maintenance, and management of prescription drug formularies and other pharmaceutical benefit management procedures used by health plans that provide prescription drug benefits.

■ Widely Used in Print and Electronic Formats

AHFS DI[®] and its point-of-care derivative database *AHFS DI*[®]Essentials are used widely as sources of authoritative drug information by physicians, pharmacists, dentists, nurses, and other health-care professionals and by schools of pharmacy, nursing, and medicine and are available in a variety of formats. Electronic formats include Lexicomp ONLINE with *AHFS*[®]; First DataBank's (FDB Health's) *AHFS Drug Information* monographs available from multiple vendors (e.g., McKesson); *AHFS Drug Information*[®] from STAT!Ref[®]; Pepid's Pharmacist Pro with *AHFS DI*[®], and MedicinesComplete[®]; *Drug Information Fulltext*[®] (*DIF*[®]); ePocrates Rx Online[™] + *AHFS DI*[®]; and *AHFS DI*[®] Powered by Skyscape. *AHFS DI*[®]Essentials is available electronically for access via computer desktops and mobile smart phone (i.e., iPhone[®], Android[®]) and tablet (i.e., iPad[®], Android[®]) applications.

In hospitals, extended-care facilities, nursing homes, health maintenance organizations, and other organized health-care settings, *AHFS DI*[®] as print and/or electronic databases is accessible in patient-care areas for ready use by physicians, nurses, pharmacists, and other health-care professionals. *AHFS DI*[®] also is used in community pharmacies, chain drugstores (e.g., CVS), and other professional practice settings and is available in most medical libraries.

■ Highly Recognized Authority

AHFS DI[®] is supported solely through subscriptions. *AHFS DI*[®] has been officially adopted by the US Public Health Service and the Department of Veterans Affairs; recommended by the National Association of Boards of Pharmacy as part of the standard reference library; recommended by the American College of Physicians as part of a library for internists; included in the Standards for Medicare; approved by the American Pharmaceutical (now Pharmacists) Association, American Health Care Association, American Hospital Association, and Catholic Health Care Association of the United States; recognized by the US Congress, CMS, AHIP, National Blue Cross and Blue Shield Association, National Association of Insurance Commissioners, and various third-party health-care insurance providers for coverage decisions on off-label

(unlabeled) uses; and included as a required or recommended standard reference for pharmacies in many states.

The authority of *AHFS DI*[®] also includes Federal recognition through legislation and regulation as an "official" compendium for information on medically accepted uses of drugs. The Federal compendial recognition for *AHFS DI*[®] originated in the Medicare Catastrophic Coverage Act. HCFA (now CMS) determined that *AHFS DI*[®] met the compendial selection criteria established by Congress and adopted the compendium for carrying out certain aspects of the Act and in meeting the need of the US Secretary of HHS to establish standards based on accepted medical practice for the prescribing, dispensing, and utilization of covered drugs. This established the Federal precedent for use of *AHFS DI*[®] as a compendial standard in subsequent legislative and regulatory initiatives, including for drug coverage under Medicaid and Medicare Parts B and D.

For additional information on official recognition, see the section on Widely Vetted Editorial Process in Support of Compendial Recognition above.

Highlights of 2014 Revisions

The 2014 edition has been updated extensively, incorporating revised information on uses, therapeutic perspectives, cautions, drug interactions, new products, and other new developments. In addition, the coverage in the 2014 edition has been expanded by 34 new drug monographs.

■ Recognition and Increased Granularity of the AHFS

Pharmacologic-Therapeutic Classification[®]

The *AHFS*[™] Pharmacologic-Therapeutic Classification[®] is the most widely used formulary-structure drug classification in the US and Canada. The AHFS classification is maintained continuously by ASHP and allows the grouping of drugs with similar pharmacologic, therapeutic, and/or chemical characteristics in a 4-tier hierarchy.

Additional subdivision of the *AHFS*[™] Pharmacologic-Therapeutic Classification[®] to provide more specific subgroupings of certain drugs along therapeutic and pharmacologic lines is implemented with the 2014 edition. New this year are subclasses: 68:20.17 Sodium-glucose Cotransporter 1 (SGLT1) Inhibitors, 68:20.18 Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors, 68:29.04 Somatostatin Agonists, 68:29.08 Somatostatin Antagonists, 86:12.04 Antimuscarinics, 86:12.08 β_3 -Adrenergic Agonists, and 86:12.08.12 Selective β_3 -Adrenergic Agonists. In addition, the name of class 92:20 Biologic Response Modifiers was changed to Immunomodulatory Agents. **For additional details on the new subclasses and affected drug monographs, see the link to the AHFS Classification on the homepage at <http://www.ahfsdruginformation.com>.**

In the printed version of the classification in *AHFS DI*[®], a drug monograph generally is only printed under one classification. Multiple classifications for a drug in print are represented by cross-references in the table of contents for each chapter/class. If cross-referenced, the drug name is given followed by the classification number that it is printed under. Electronically, all applicable classes for a drug are listed.

CMS' "Guidelines for Reviewing Prescription Drug Plan Formularies and Procedures" and "Medicare Prescription Drug Benefit Manual: Part D Drugs and Formulary Requirements" describe use of the *AHFS*[®] Pharmacologic-Therapeutic Classification[®] as the only named alternative to USP's Model Guidelines for use by prescription drug plans (PDPs) in implementing the formulary portion of the outpatient prescription drug benefit in the Medicare Modernization Act (MMA) of 2003. These Guidelines are part of the MMA Final Guidelines for Formularies that address the "CMS Strategy for Affordable Access to Comprehensive Drug Coverage."

The AHFS Classification is a registered external code system in the HL7 Vocabulary Repository. (OID: 2.16.840.1.113883.6.234.)

The AHFS Classification also is an approved value code of the External Code List for use in the Formulary & Benefit, Telecommunication, Post-Adjudication, & SCRIPT e-Prescribing standards of the National Council for Prescription Drug Programs (NCPDP).

■ Evolving Therapeutic Guidance and Perspective

A comprehensive revision of the Cephalosporins class of antibiotics (8:12.06) was completed for the 2014 edition. Included in this comprehensive revision were CDC treatment recommendations for gonorrhea resulting from increasing resistance of *Neisseria gonorrhoeae* and concerns about emergence of potential high-level resistance. Also included were the current recommendations of the *American Academy of Pediatrics (AAP)* for the diagnosis and management of uncomplicated acute otitis media (AOM) and acute bacterial sinusitis and those of the *Infectious Diseases Society of America (IDSA)* for streptococcal pharyngitis and acute bacterial rhinosinusitis.

Incorporation of revised American College of Obstetricians and Gynecologists (ACOG) recommendations on the management of preterm labor was completed for the 2014 edition.

Comprehensive update of antifungal monographs to address their use in the treatment of *Exserohilum rostratum* infections caused by contaminated extemporaneously compounded methylprednisolone injections. These monographs

also were updated with new recommendations from *CDC, NIH, and the HIV Medicine Association of IDSA* regarding the prevention and treatment of opportunistic infections.

Some other notable updates for *AHFS DI*[®] include:

- denosumab for osteoporosis in men and for the treatment of giant cell tumor of bone in adults and skeletally mature adolescents
- the first new antituberculosis agent in over 40 years—bedaquiline fumarate—under FDA's accelerated access program as an orphan drug for multidrug-resistant tuberculosis; the drug has a novel mechanism of action
- a novel once-daily fixed-combination antiretroviral agent—elvitegravir, cobicistat, emtricitabine, and tenofovir—that can be used alone for initial treatment of HIV infection in antiretroviral-naïve patients for the treatment of certain types of melanoma.
- a new topical pediculocide—ivermectin—for resistant lice infections
- varicella zoster immune globulin, which previously was available in the US only under an IND expanded access protocol, as an orphan for passive immunization in high-risk patients
- the first pharmacologic treatment for symptomatic vitreomacular adhesion—ocriplasmin—under priority review because of the sight-threatening nature of the disease
- a novel drug—teduglutide—as an orphan for the management of short bowel syndrome
- a novel antineoplastic—ado-trastuzumab emtansine—for the treatment of metastatic breast cancer with over-expression of HER2 protein
- a new first-line treatment for relapsing multiple sclerosis—dimethyl fumarate
- everolimus as the first new drug for preventing allograft rejection in liver transplant recipients in over 10 years
- apixaban for stroke and systemic embolism reduction in patients with nonvalvular atrial fibrillation
- a novel drug—prothrombin complex concentrate—for rapid reversal of warfarin anticoagulation
- a novel antidiabetic agent—canagliflozin
- the first therapy for atypical hemolytic syndrome—eculizumab
- the second drug in the US—pasireotide—as second-line therapy for Cushing's disease when pituitary surgery fails or is contraindicated

■ Major Cautionary Information

For the 2014 edition of *AHFS DI*[®], Risk Evaluation and Mitigation Strategy (REMS) information was revised to reflect various changes as well as rescinded REMS. Through semi-automated processes, this information is updated on an ongoing basis in electronic versions of the database to reflect more contemporaneously changes made by FDA. Forty-three monographs were revised to address new MedWatch notices issued by FDA during 2013.

Information on magnesium sulfate fetal risk was revised, including hypocalcemia, and related skeletal abnormalities, when used beyond 5–7 days for tocolysis in pregnant women and a change in the FDA pregnancy category from A to D.

The imidazoline nasal and ophthalmic vasoconstrictor monographs were revised to address the risk of accidental ingestion in children (e.g., coma, bradycardia, decreased respiration, somnolence)

Zolpidem dosage was revised to address the potential risk of impaired alertness in the morning (e.g., could affect driving). Patients may be impaired even if they feel fully awake. Women appear to be more susceptible to next-day impairment because of slower drug clearance, resulting in a lowering of recommended bedtime dosages in women.

Fluoroquinolone monographs were revised to expand boxed warnings on these antibiotics concerning the risk of potentially irreversible peripheral neuropathy.

Other major cautionary information added or revised for *AHFS DI 2014*[®] includes dozens of FDA MedWatch notices affecting 43 monographs and other new safety information (e.g., REMS), such as risk of serious, potentially fatal hepatic injury with tolvaptan; delayed sprue-like enteropathy with olmesartan; rare but serious skin reactions with acetaminophen; ocular abnormalities and blue skin discoloration with ezogabine; rare cases of death following long-acting olanzapine and revised post-injection delirium sedation risk discussion; first case of progressive multifocal leukoencephalopathy with fingolimod; potential for dispensing and prescribing errors with Kadcyla and Herceptin because of the common trastuzumab root in their names; increased risk of mortality, severe renal injury, and excessive bleeding with hetastarch; strengthened warnings against valproic acid use during pregnancy and change in FDA pregnancy category from D to X; and potentially fatal serious skin reactions with combined telaprevir, peginterferon alfa, and ribavirin in patients with chronic hepatitis C.

This is just a small sampling of the numerous revisions that are included in *AHFS Drug Information 2014*[®].

■ www.ahfsdruginformation.com

With the 2014 edition, *AHFS DI*[®] print subscribers will continue to have free access to ASHP's www.ahfsdruginformation.com, a companion website designed to provide timely ongoing updates as part of their subscription service.

The username and password will be required to access the subscriber-only portions of the website.

By providing post-publication updates to *AHFS DI*[®] electronically via this website, timely notification of critical updates (e.g., MedWatch information) as well as

information on newly approved drugs (same-day coverage for most drugs) will be ensured. Information on new molecular entities (NMEs) will be posted on the website as soon as possible following FDA approval, initially as part of the news service and then in the form of an Overview monograph.

Some monographs have been omitted from the print version of *AHFS DI*[®] because of space limitations. Associated index entries for these monographs are followed by “see www.ahfsdruginformation.com.” Copies of these monographs are available on the “For Subscribers” page of the AHFS Drug Information website, www.ahfsdruginformation.com, in the “Electronic Only Monographs” section. For the 2014 edition, the username and password for accessing electronic-only content are as follows:

- **username:** ahfsdi
- **password:** ASHP84691

The Editorial staff wishes to express appreciation to the many consultants and reviewers for their excellent guidance and cooperation and to our subscribers for their support and comments.