



DRUG

EVALUATIONS

6th edition

*American Medical
Association*



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6th edition

**Prepared by the
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and Technology**

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Preface

Drug Evaluations (DE) is now in its second decade of use, and its original goal is unaltered: To provide physicians and other health care professionals with up-to-date, unbiased information on the *clinical* use of drugs. *DE* is intended to serve as a reference source for practical, comparative, evaluative information on drug therapy.

Evaluative Process for Drug Evaluations (DE): After chapters are prepared by the professional staff of the AMA Department of Drugs on the basis of the current scientific literature, they are reviewed by consultants and the medical staffs of the appropriate pharmaceutical manufacturers. Following consensus revision, the chapters are then reviewed by designees or members of the American Society for Clinical Pharmacology and Therapeutics (ASCPT). For this edition, 512 distinguished consultants contributed their comments to the drafts of the chapters. Thus, this publication is a joint scientific contribution to the field of applied therapeutics by the AMA, a large consultant body, and the ASCPT. The principles of therapeutics and comparative information contained in the introductions to the chapters and the individual drug evaluations that follow thus represent a distillation of the current scientific literature plus the combined wisdom of many experienced clinicians.

Drug evaluations are based upon the most recent information available. Every effort has been made to include information on newly introduced drugs and dosage forms and on significant investigational drugs. In a project of this scope, however, the inadvertent omission of some products and the inclusion of others no longer marketed are inevitable.

The inclusion of a particular drug in *DE* does not imply endorsement by the American Medical Association, nor should it be a criterion for approving use of that drug in any institution. An *evaluation* may be favorable, unfavorable, or both and represents a statement of the general merits of the preparation, not its specific usefulness in a given patient. The limitations of use, adverse reactions, contraindications, precautions, or dosage should be considered for each patient.

The opinions expressed in this book, particularly on controversial matters, may disagree with those from other sources. Statements are based on information from the scientific literature, unpublished data, the advice of consultants, and the opinions of reviewers representing the ASCPT. For other information, for basic data, and even for varying points of view, the physician is encouraged to consult other sources of information on drugs.

Scope and Organization of Drug Evaluations (DE): Like previous editions of *DE*, the sixth edition has been organized into sections and chapters that are based, insofar as possible, on therapeutic classifications. The three initial chapters contain *general information* on therapeutic principles or prescribing practices (ie, prescription practices and regulatory agencies, drug response variation and dosing information, drug interactions and adverse drug reactions).

In most of the remaining chapters, the introductions contain a discussion on the basic pharmacologic information, principles of therapeutics, pathogenesis of disease to the extent deemed necessary to facilitate the use of drugs in patients, and *comparative drug evaluations* within a pharmacologic or therapeutic category. Drug selection is based principally on the severity of the disease or disorder, the pharmacologic profile of each drug, and individual patient considerations. When possible, drugs of choice are recommended within the therapeutic or pharmacologic class. Discussions on the comparative merits of drugs have been expanded considerably for many of the chapters, and the utilization of tables for ready reference continues to increase.

The introductory section of each chapter is followed by *individual drug evaluations*, including selected mixtures. Information on investigational drugs and uses usually appears in the introductory section of the chapter; however, if an investigational drug's approval is deemed likely in the near future, an individual evaluation of the agent may appear. Evaluations on 76 new drugs marketed since the fifth edition and 103 investigational agents and uses have been added to the sixth edition. Listings of these newly marketed and investigational drugs follow the Acknowledgment Section.

Generally, titled headings in the evaluations include *Actions, Uses, Adverse Reactions and Precautions, Pharmacokinetics, and Dosage and Preparations*.

Discussion of drug *action* is limited to that deemed necessary to facilitate clinical drug use.

FDA-approved labeling limits the *use* of a drug for purposes of marketing and advertising, but does not constrain a physician's use of the drug in individual patients; therefore, because indications approved for labeling by the FDA may lag behind both the world literature and good medical practice, *DE* describes recognized uses of drugs regardless of their status in approved labeling.

Information on *adverse reactions* and *precautions* usually represents that most essential for use of the drugs. Accordingly, rare, minor, or unconfirmed reactions or precautions that relate to obvious or remote situations are sometimes omitted.

Pharmacokinetic information, especially that in the evaluations, continues to expand. Therapeutic drug blood concentrations are included when relevant.

The *dosage* information cited in *DE* falls within the ranges suggested by manufacturers and the FDA or that considered appropriate by other authorities. For many drugs, however, the correct dosage depends upon the size, age, and condition of the patient; response to treatment; sensitivity or tolerance; and the possible synergistic or antagonistic effect of concomitant medication. If the clinical situation permits, establishment of the dose should be cautious and exploratory unless a wide margin of safety prevails. However, if immediate disaster threatens because of therapeutic failure, treatment should be

aggressive. In either situation, the physician should remember that improper dosage of the proper drug is probably as common a cause of inadequate response or therapeutic failure as the use of an improper drug. Accordingly, many doses are stated as ranges, but even the limits of these ranges are not inviolable. The upper limits given for most ranges, however, do suggest that larger amounts either may increase the risks of toxicity beyond what is ordinarily acceptable or may fail to provide a significant degree of additional therapeutic effect. Similarly, the lower limits often indicate that smaller doses will not provide therapeutic effects for most patients. For some drugs, no dosage is suggested.

The *preparations* listed for each drug, including those available generically, appear at the end of each evaluation. However, clinical experience often is limited to products of one or only a few manufacturers. Adequate clinical comparisons of all brands of the same drug are rarely available. For this reason, a valid comparison of brands has rarely been possible or attempted. Although most drugs described in this volume are dispensed exclusively or principally by prescription, many, of course, *can* be sold without prescription and these are so indicated.

The number of *cited* and/or *selected* references at the end of each chapter has increased considerably in the sixth edition. Specific statements in the evaluations often are cited, but general references also may be included for additional information.

The single comprehensive index that includes drug names (both generic and trademark), indications, and adverse reactions has been expanded to improve access to the information in this text.

An important addition to the sixth edition is Chapter 65, Antimicrobial Therapy and Chemoprophylaxis of Infectious Diseases. This initial chapter in the section on Anti-Infective Agents presents an overview of antimicrobial drug therapy and guidelines for drug selection for many common infectious diseases, including specific information on the treatment of sexually transmitted diseases and antimicrobial chemoprophylaxis for ambulatory and surgical patients. Another significant addition is Chapter 57, which furnishes background information and an update on the immune system to aid the physician in the selection and use of immunoreactive substances. These and the many other extensively revised chapters enhance the usefulness of the sixth edition for the practicing physician. The larger size and the new type face also increase the book's readability.

We hope that *DE* will continue to be a valuable reference for the medical profession and others who provide medical care. Suggestions for improving the usefulness of future editions are welcome.

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New Drugs and Uses Evaluated for Sixth Edition

Drug	Indication/Classification
Acebutolol Hydrochloride [Sectral]	Hypertension/Arrhythmias
Acetohydroxamic Acid [Lithostat]	Urinary calculus inhibitor
Acyclovir [Zovirax]	Antiviral agent, oral
Amdinocillin [Coactin]	Penicillin
Amiodarone Hydrochloride [Cordarone]	Arrhythmias
Ammonium Lactate [Lac-Hydrin]	Dermatologic agent
Amoxicillin/Clavulanate Potassium [Augmentin]	Antibacterial preparation
Amrinone Lactate [Inocor]	Inotropic agent
Atracurium Besylate [Tracrium]	Neuromuscular blocking agent
Auranofin [Ridaura]	Arthritis
Betaxolol Hydrochloride [Betoptic]	Glaucoma
Bitolterol Mesylate [Tornalate]	Bronchodilator
Bromocriptine Mesylate [Parlodel]	Acromegaly
Bumetanide [Bumex]	Diuretic
Buprenorphine Hydrochloride [Buprenex]	Analgesic
Butoconazole Nitrate [Femstat]	Antifungal agent
Cefonicid Sodium [Monocid]	Cephalosporin
Cefotetan Disodium [Cefotan]	Cephalosporin
Ceftazidime [Fortaz, Tazicef, Tazidime]	Cephalosporin
Ceftizoxime Sodium [Cefizox]	Cephalosporin
Ceftriaxone Sodium [Rocephin]	Cephalosporin
Ceforanide [Precef]	Cephalosporin
Cefuroxime Sodium [Zinacef]	Cephalosporin
Cellulose Sodium Phosphate [Calcibind]	Urinary calculus inhibitor
Chenodioid [Chenix]	Gallstone dissolution
Chymopapain [Chymodiactin, Discase]	Herniated lumbar disc
Ciclopirox Olamine [Loprox]	Antifungal agent
Clobetasol Propionate [Temovate]	Corticosteroid, topical
Cromolyn Sodium [Nasal crom, Intal]	Allergy prophylaxis
Cromolyn Sodium [Opticrom]	Allergy, ocular
Cyclosporine [Sandimmune]	Immunomodulator
Diflorasone Diacetate [Florone, Maxiflor]	Corticosteroid, topical
Digoxin Immune Fab [Digibind]	Allergic rhinitis/Asthma
Dronabinol [Marinol]	Antiemetic
Econazole Nitrate [Spectazole]	Antifungal agent
Enalapril Maleate [Vasotec]	Hypertension/Congestive heart failure
Etomidate [Amidate]	Intravenous anesthetic
Etoposide [VePesid]	Antineoplastic agent
Flecainide Acetate [Tambacor]	Arrhythmias
Glipizide [Glucotrol]	Oral hypoglycemic agent
Glyburide [DiaBeta, Micronase]	Oral hypoglycemic agent
Gonadorelin Hydrochloride [Factrel]	Releasing hormone
Haemophilus B Polysaccharide Vaccine [b CAPSA I, Hib-Immune, HibVax]	Immunologic agent
Hemin for Injection [Panhematin]	Porphyrias
Imipenem/Cilastatin [Primaxin]	Antibacterial preparation
Indapamide [Lozol]	Hypertension/Diuretic
Indomethacin Sodium Trihydrate [Indocin IV]	Patent ductus arteriosus
Interferon, alfa A	Antineoplastic agent

Ketoprofen [Orudis]
 Labetalol Hydrochloride [Trandate, Normodyne]
 Levobunolol Hydrochloride [Betagan]
 Leuprolide Acetate [Lupron]
 Mexiletine Hydrochloride [Mexitil]
 Midazolam Hydrochloride [Versed]
 Monooctanoin [Mocetanin]
 Nabilone [Cesamet]
 Naltrexone Hydrochloride [Trexan]
 Netilmicin Sulfate [Netromycin]
 Nicotine Polacrilex [Nicorette]
 Pentamidine Isethionate [Pentam 300]
 Pentoxifylline [Trental]
 Pimozide [Orap]
 Polyethylene Glycol Electrolyte Preparation [Colyte, GoLYTELY]
 Praziquantel [Biltricide]
 Quazepam [Dormalin]
 Ranitidine Hydrochloride [Zantac]
 Ribavirin [Virazole]
 Somatrem [Protoprin]
 Suprofen [Suprol]
 Sufentanil Citrate [Sufenta]
 Terfenadine [Seldane]
 Ticarcillin Disodium/Clavulanate Potassium [Timentin]
 Tocainide Hydrochloride [Tonocard]
 Trientine Hydrochloride [Cuprid]
 Trilostane [Modrastane]
 Vecuronium Bromide [Norcuron]

Arthritis
 Hypertension
 Glaucoma
 Antineoplastic agent
 Arrhythmias
 Anesthetic induction agent
 Gallstone dissolution
 Antiemetic
 Opioid abuse deterrent
 Aminoglycoside
 Smoking deterrent
 Antiprotozoal agent
 Intermittent claudication
 Tourette's syndrome

Laxative preparation
 Anthelmintic
 Sedative/Hypnotic
 Peptic ulcer therapy
 Antiviral agent
 Human growth hormone
 Analgesic
 Adjunct to anesthesia
 Antihistamine
 Antibacterial preparation
 Arrhythmias
 Chelating agent
 Cushing's syndrome
 Neuromuscular blocking agent

Investigational Drugs and Uses Evaluated in Sixth Edition

Drug

Acecainide Hydrochloride [NAPA]
 Aclarubicin
 Acrivastine
 Altretamine (Hexamethylmelamine)
 Aminothiadiazole (A-TDA)
 Amsacrine (m-AMSA) [Amsidyl]
 Astemizole [Hismanal]
 Azacitidine [Mylosar]
 Aziridinybenzoquinone (A2Q)
 Aztreonam [Azactam]
 BCG Vaccine
 Budesonide [Rhinocort]
 Buspirone Hydrochloride [Buspar]
 Carboplatin (CBDCA)
 CHIP
 Cholestyramine Resin [Questran]
 Clofazimine [Lamprene]
 Compactin (Mevastatin)
 Corynebacterium Parvum (CP)
 Cyproheptadine Hydrochloride [Periactin]
 Cytomegalovirus Immune Globulin
 4 -Deoxydoxorubicin (DxDx)
 Dexamethasone, Dexamethasone Sodium Phosphate
 Dialyzable Transfer Factor
 Difluoromethylornithine (DFMO)
 Domperidone [Motilium]
 Encainide [Enkaid]
 Enviroxime
 Epoprostenol Sodium [Cyclo-Prostin]
 Ethionamide [Trecator-SC]
 Etretnate [Tegison]
 Fenoterol Hydrobromide [Berotec]
 Fludarabine Phosphate
 Fluocortin Butyl
 Flunitrazepam [Rohypnol]
 Foscarnet Sodium
 Guanfacine
 Haemophilus Influenzae Type b
 Polysaccharide-Diphtheria Toxoid Conjugate Vaccine (PRP-D)
 Homoharringtonine
 Ifosamide [Ifex]
 Indoramin Hydrochloride [Baratol]
 Inosiplex [Isoprinosine]
 Interferons
 Interleukin-2
 Ipratropium Bromide [Atrovent]
 Isotretinoin [Accutane]

Indication/Classification

Arrhythmias
 Antineoplastic agent
 Antihistamine
 Antineoplastic agent
 Antineoplastic agent
 Antineoplastic agent
 Antihistamine
 Antineoplastic agent
 Antineoplastic agent
 Antibacterial agent
 Immunostimulant
 Rhinitis/Asthma
 Anxiety
 Antineoplastic agent
 Antineoplastic agent
 Hyperoxaluria
 Leprosy
 Hyperlipidemia
 Immunostimulant
 Cushing's disease
 Immunologic agent
 Antineoplastic agent
 Antiemetic (with cancer chemotherapy)
 Immunostimulant
 Antineoplastic agent
 Antiemetic
 Antiarrhythmic agent
 Antiviral agent
 Vasodilator/Antithrombotic agent
 Leprosy
 Psoriasis
 Asthma
 Antineoplastic agent
 Rhinitis
 Anesthetic premedication
 Antiviral agent
 Hypertension

 Immunologic agent
 Antineoplastic agent
 Antineoplastic agent
 Hypertension
 Immunostimulant/Antiviral agent
 Antiviral agent
 Antineoplastic agent
 Asthma/Chronic bronchitis
 Keratinization disorders/Antineoplastic agent

Ketanserlin
 Levamisole [Ergamisol]
 Lidoflazine [Angex]
 Lorazepam [Ativan]
 Lorcainide
 Menogaril (7-Omen)
 Meptazinol
 Methyl-glyoxalbis-guanylhydrazone (MGBG)
 Methylprednisolone Sodium Succinate [Solu-Medrol]
 Metrifonate
 Metyrapone Tartrate [Metopirone]
 Mevinolin
 Milrinone
 Minoxidil [Regaine]
 Misoprostol [Cytotec]
 Mitolactol (Dibromodulcitol)
 Mitoxantrone Hydrochloride
 Moricizine (Ethmozin) [Ethmozone]
 Muramyl Dipeptide
 Muromonab CD3 (Murine Monoclonal Antibody,
 Anti-CD3) [Orthoclone OKT3]
 N-Methylformamide (N-MF)
 Niridazole [Ambilhar]
 Norfloxacin [Noroxin]
 Oxandrolone [Anavar]
 Oxymetazoline [Oxylin]
 PCNU
 Pentostatin [Potentiator]
 Pergolide Mesylate
 Pirmenol
 Potassium Citrate [Urocit-K]
 Praziquantel [Biltricide]
 Procaterol [Beta-Air]
 Propafenone [Rytmonorm]
 Quinidine Gluconate
 Razoxane
 Recombinant Human Tissue-Type Plasminogen
 Activator (tPA) [TPA]
 Recombinant Yeast DNA Hepatitis B Vaccine
 Rifampin [Rifadin, Rimactane]
 Rotavirus Vaccine Live Oral Attenuated
 Selegiline (Deprenyl) [Eldepryl]
 Semustine (Methyl CCNU)
 Spirogermanium (NSC) [Spiro 32]
 Suramin Sodium
 Tegafur (Ftorafur)
 Teniposide (VM-26)
 Terazosin Hydrochloride [Vasocard]
 Tetrabenazine [Nitoman]
 Thymic Hormones
 Thymoxamine Hydrochloride
 Tiopronin [Thiola]
 Trimazosin [Cardovar]
 Typhoid Vaccine Live Oral
 Ursodeoxycholic Acid
 Varicella-Zoster Vaccine Live Attenuated
 Verapamil Hydrochloride [Calan, Isoptin]
 Vindesine Sulfate [Eldisine]
 Zoladex

Hypertension
 Immunostimulant
 Angina
 Antiemetic (with cancer chemotherapy)
 Arrhythmias
 Antineoplastic agent
 Analgesic
 Antineoplastic agent
 Antiemetic (with cancer chemotherapy)
 Schistosomiasis
 Cushing's syndrome
 Hyperlipidemia
 Inotropic drug
 Alopecia
 Peptic ulcer
 Antineoplastic agent
 Antineoplastic agent
 Arrhythmias
 Immunostimulant

 Immunosuppressant
 Antineoplastic agent
 Schistosomiasis
 Antibacterial agent
 Hyperlipidemia
 Ocular decongestant
 Antineoplastic agent
 Antineoplastic agent
 Parkinson's disease
 Arrhythmias
 Hyperoxaluria
 Cestodiasis
 Asthma
 Arrhythmias
 Malaria
 Antineoplastic agent

 Thrombolytic agent
 Immunologic agent
 Leprosy
 Immunologic agent
 Parkinson's disease
 Antineoplastic agent
 Antineoplastic agent
 Onchocerciasis
 Antineoplastic agent
 Antineoplastic agent
 Hypertension
 Extrapyrimalidal movement disorders
 Immunostimulants
 Alpha blocker, ophthalmic
 Cystinuria
 Hypertension
 Immunologic agent
 Gallstone dissolving agent
 Immunologic agent
 Migraine headache
 Antineoplastic agent
 Antineoplastic agent

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