AMA DRUG EVALUATIONS

FIFTH EDITION

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Preface

AMA Drug Evaluations (AMA-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. AMA-DE is intended to serve as a reference source for practical, comparative, evaluative information on drug therapy. Basic pharmacologic information, principles of therapeutics, and pathogenesis of disease are presented only to the extent deemed necessary to facilitate the use of drugs in patients.

In addition to publishing this volume, the American Medical Association is exploring new methods of supplying drug information. To that end and as a complement to the more detailed and comparative evaluations contained in AMA-DE, the AMA Division of Drugs is developing an on-line drug data base for more rapid update and convenient access to drug information. Also, the AMA Patient Medication Instruction Program was instituted recently to assist practicing physicians in instructing their patients on the effective and safe use of prescribed medicines.

Evaluative Process for AMA-DE: The fifth edition of AMA-DE continues the successful cooperative effort of the AMA Division of Drugs and the American Society for Clinical Pharmacology and Therapeutics (ASCPT). The American Medical Association is grateful to the ASCPT for their assistance in the preparation of this book. As in previous editions, the initial drafts of the 84 chapters were written by the professional staff of the Division of Drugs. These drafts were reviewed by more than 500 distinguished consultants and the medical staffs of the appropriate pharmaceutical manufacturers. Following consensus revision, the chapters were finally reviewed by designees or members of the ASCPT. 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 comparative and individual drug evalutions contained therein represent a distillation of the current scientific literature plus the combined wisdom of many experienced clinicians.

Drugs selected for individual evaluation are those most commonly prescribed or administered by physicians in the United States, both single-entity and mixtures, as well as other agents, including some investigational drugs, that are judged to be of particular importance to complete a discussion of a therapeutic category. Other nationally distributed preparations that are not evaluated individually are listed and indexed to give information about their therapeutic category, composition, and availability. 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.

Drug evaluations are based upon the most recent information available. Every effort has been made to include, as close as possible to the publication date, investigational drugs and those newly introduced to the market. In a project of this scope, however, the inadvertent omission of some products and the inclu-

sion of others no longer marketed, although regretted, are inevitable.

The inclusion of a particular drug in *AMA Drug Evaluations* does not imply endorsement by the American Medical Association, nor should it be a criterion for approving use of that drug in any institution or for any other purpose. The principal goal of this volume is to provide the medical profession with information on selected drugs and drug classes based on the available evidence. An *evaluation* may be favorable, unfavorable, or a combination of both and represents a statement of the general merits of the preparation, not its specific usefulness in a given patient. The physician should determine in each individual patient the relevance of the limitations of use, adverse reactions, contraindications, precautions, or dosage discussed in the text.

The evaluative or interpretive information in the book, particularly on controversial matters, may disagree with opinions from other sources. Statements are based on the convergent trend of information available from the scientific literature, unpublished data, the advice of consultants, and the opinions of reviewers from the ASCPT.

Scope and Organization of AMA-DE: As have previous editions of AMA-DE, the fifth edition has been organized into sections and chapters that are based, insofar as possible, on therapeutic classifications. The first three chapters differ from the others in that they contain *general information* on therapeutic principles or prescribing practices (ie, prescription practices and regulatory agencies, drug interactions and adverse drug reactions, drug response variation and dosing information).

In most of the remaining chapters, drugs within a therapeutic category are reviewed in the chapter introduction. When possible, drugs are compared and drugs of choice are recommended within a therapeutic or pharmacologic class. Discussions on the comparative merits of drugs have been expanded considerably for many of the chapters, and the number of tables has increased by 50%.

Information on investigational drugs and uses not approved by the Food and Drug Administration is included to alert physicians to the state of the art in a particular area of therapeutics or to anticipated or ongoing investigational studies that could be of potential benefit to their patients. Such information usually appears in the introductory section of the chapter; however, if an investigational drug's approval is deemed likely in the near future, an evaluation of the agent may appear.

Seventy-eight investigational agents are included in AMA-DE 5; these drugs are listed alphabetically just prior to Chapter 1 and are so designated in the text.

The introductory section of each chapter is followed by evaluations of individual drugs. Evaluations of 69 new drugs marketed since the fourth edition of AMA-DE have been added, and these drugs are listed alphabetically following the Acknowledgement Section.

More headings have been used in AMA-DE 5 for easier accessibility to information. Generally, titled headings in the evaluations include *Actions and Uses; Pharmacokinetics; Adverse Reactions and Precautions; and Route(s), Usual Dosage, and Preparations.*

Discussion of drug *action* is limited to the extent deemed necessary to facilitate drug use in patients.

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 for individual patients; therefore, because indications approved for labeling by the FDA may lag behind both the world literature and good medical practice, AMA-DE describes scientific, recognized uses of drugs regardless of their status in approved labeling.

Pharmacokinetic information, especially that contained in individual drug evaluations, has been expanded considerably. Information on bioavailability, absorption, distribution (including protein binding and apparent volume of distribution), biotransformation (if any), and elimination has been included when available. Therapeutic drug blood concentrations are included when there is a documented correlation to the therapeutic effect.

Information on *adverse reactions* and *precautions* usually has been condensed and represents that considered most essential to

the physician's use of the drugs. Accordingly, rare, minor, or unconfirmed reactions or precautions that relate to obvious or remote situations are sometimes omitted. For other information, for basic data, and even for varying points of view, the physician is encouraged to consult and compare statements made in this text with those appearing in the many other sources of information on drugs.

The *usual dosage* information cited in AMA-DE falls within the ranges suggested by manufacturers and the FDA or those 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 could not be expected to provide full therapeutic effects for most patients. In some evaluations, a collateral statement may make it clear that, on the basis of the evaluation, no dosage is suggested for that drug.

The *preparations* listed for each drug, including those available generically, appear at the end of each evaluation. However, published reports of clinical experience often are limited to the 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.

The number of *cited* and/or *selected* references at the end of each chapter has at least doubled in the fifth edition of AMA-DE. Most often, specific statements in the evaluations are cited; however, some general references also have been selected to provide sources of additional information that the reader may wish to consult or to provide initial access to a more extensive bibliography of that literature.

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.

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

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New Drugs Evaluated for Fifth Edition

Drug	Indication/Classification
Acyclovir [Zovirax]	Antiviral agent
Albuterol [Proventil, Ventolin]	Bronchodilator
Alprazolam [Xanax]	Antianxiety agent
Alprostadil [Prostin VR Pediatric]	Prostaglandin (maintain patency of ductus arteriosus in neonates)
Amcinonide Hydrochloride [Cyclocort]	Corticosteroid, topical
Amiloride [Midamor]	Diuretic/Antihypertensive
Aminoglutethimide [Cytadren]	Suppressant of adrenal function
Amoxapine [Asendin]	Antidepressant
Anti-Inhibitor Coagulant Complex [Autoplex]	Hemorrhagic agent
Atenolol [Tenormin]	Antihypertensive agent
Azlocillin [Azlin]	Penicillin
Bacampicillin Hydrochloride [Spectrobid]	Penicillin
Calcifediol [Calderol]	Vitamin D metabolite
Captopril [Capoten]	Antihypertensive agent
Cefoperazone Sodium [Cefobid]	Cephalosporin
Cefotaxime Sodium [Claforan]	Cephalosporin
Cephradine Dihydrate [Velosef]	Cephalosporin
Cinoxacin [Cinobac]	Urinary tract antiseptic
Clidinium Bromide [Quarzan]	Anticholinergic antispasmodic
Clocortolone Pivalate [Cloderm]	Corticosteroid, topical
Cyclacillin [Cyclapen]	Penicillin
Daunorubicin Hydrochloride [Cerubidine]	Antineoplastic agent
Diflunisal [Dolobid]	Antiarthritic agent
Diltiazem [Cardizem]	Antianginal agent
Dipivefrin Hydrochloride [Propine]	Glaucoma
Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl [Pediazole]	Antibacterial preparation
Estramustine Phosphate Sodium [Emcyt]	Antineoplastic agent
Flunisolide [Nasalide]	Corticosteroid, nasal
Gemfibrozil [Lopid]	Hyperlipidemia
Guanabenz Acetate [Wytensin]	Antihypertensive agent

Halazepam [Paxipam]	Antianxiety agent
Insulin Human [Humulin]	Insulin preparation
Hepatitis B Vaccine [Heptavax-B]	Immunologic agent
Human Diploid Cell Rabies Vaccine	Immunologic agent
Immune Globulin Intravenous	Immunologic agent
Isoflurane [Forane]	General anesthetic
Isotretinoin [Accutane]	Acne preparation
Ketoconazole [Nizoral]	Antifungal agent
Lymphocyte immune globulin [Atgam]	Agent to prevent kidney transplant rejection
Malathion [Prioderm]	Pediculicide
Maprotiline Hydrochloride [Ludiomil]	Antidepressant
Meclocycline Sulfosalicylate [Meclan]	Tetracycline (acne)
Meclofenamate Sodium Monohydrate [Meclomen]	Antiarthritic agent
Metyrosine [Demser]	Pheochromocytoma
Mezlocillin Sodium Monohydrate [Mezlin]	Penicillin
Moxalactam Disodium [Moxam]	Antibacterial agent
Nadolol [Corgard]	Beta-blocker (cardiovascular)
Niclosamide [Niclocide]	Anthelmintic
Nifedipine [Procardia]	Antianginal agent
Oxamniquine [Vansil]	Schistosomiasis
Pindolol [Visken]	Beta-blocker (cardiovascular)
Piperacillin [Pipracil]	Penicillin
Piroxicam [Feldene]	Antiarthritic agent
Pyrimethamine and Sulfadoxine [Fansidar]	Antimalarial preparation
Quinestrol [Estrovis]	Estrogen
Ritodrine Hydrochloride [Yutopar]	Preterm labor
Saralasin [Sarenin]	Renovascular hypertension (diagnosis)
Sisomicin Sulfate [Siseptin]	Aminoglycoside
Streptozocin [Zanosar]	Antineoplastic agent
Sucralfate [Carafate]	Ulcer therapy
Temazepam [Restoril]	Hypnotic
Trazodone Hydrochloride [Desyrel]	Antidepressant
Triazolam [Halcion]	Hypnotic
Trifluridine [Viroptic]	Antiviral agent (eye)
Trimethoprim [Proloprim, Trimpex]	Antimicrobial agent
Vaccinia Immune Globulin	Immunologic agent
Verapamil Hydrochloride [Isoptin, Calan]	Antiarrhythmic antianginal agent
Zomepirac Sodium [Zomax]	Analgesic/Antiarthritic

Investigational Drugs and Uses in Fifth Edition

Drug	Indication/Classification
Acecainide (NAPA)	Antiarrhythmic agent
Amiodarone [Cordarone]	Antiarrhythmic agent
Amrinone [Inocor]	Congestive heart failure
Amsacrine [m-Amsa]	Antineoplastic agent
Aprindine Acetate, Aprindine Hydrochloride [Fibocil]	Antiarrhythmic agent
Atracurium	Nondepolarizing muscle relaxant
Auranofin [Ridaura]	Antiarthritic agent
Azacitidine	Antineoplastic agent
BCG Vaccine	Immunomodulator
Bumetanide [Bumex]	Diuretic
Buprenorphine Hydrochloride [Buprenex]	Analgesic
Bupropion Hydrochloride [Wellbatrin]	Antidepressant
Chenodiol (Chenodeoxycholic Acid) [Chenix]	Gallstone dissolution
Clofazimine [Lamprene]	Leprosy
Corynebacterium Parvum (CP)	Immunomodulator
Cromolyn (Ophthalmic)	Atopic ophthalmic disorders
Cyclosporin A	Immunomodulator
Delta-9-Tetrahydrocannabinol Hydrochloride (THC)	Antiemetic
Deprenyl	Antidepressant/Antiparkinsonism agent
Domperidone	Antiemetic
Encainide	Antiarrhythmic agent
Etomidate [Amidate, Hypnomidate]	Induction of general anesthesia
Etoposide (VP-16, VP-16213)	Antineoplastic agent
Flecainide Acetate [Tambocor]	Antiarrhythmic agent
Flunitrazepam [Rohypnol]	Induction of general anesthesia
Glipizide [Glucotrol]	Oral hypoglycemic agent
Glyburide [Diabeta, Micronase]	Oral hypoglycemic agent
Guanadrel [HYLOREL]	Antihypertensive agent
Guanfacine	Antihypertensive agent
Haemophilus Influenzae Type B Vaccine	Immunologic agent
Haloperidol Decanoate	Antipsychotic agent