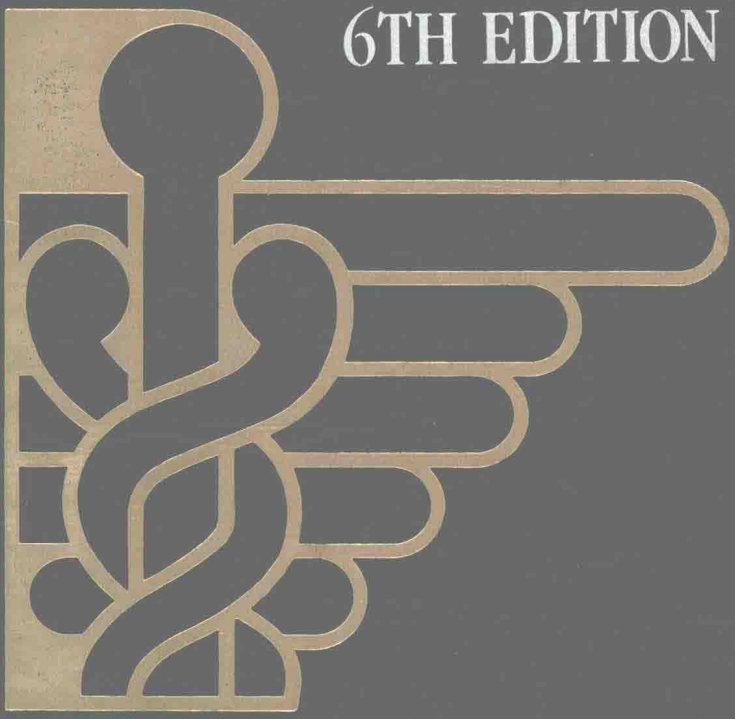
PHYSICIAN'S DRUG HANDBOOK

6TH EDITION



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6TH EDITION

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How to use this book

Physician's Drug Handbook, 6th Edition, provides exhaustively reviewed, completely updated drug information on virtually every drug in current clinical use. It covers all aspects of drug information from fundamental pharmacology to specific management of toxicity and overdose. It also includes several unique features—individual entries that describe major pharmacologic classes, a comprehensive listing of indications that includes clinically approved but unlabeled uses, and specific recommendations for use in renal failure.

Generic drug entries

The individual drug entries provide detailed information on virtually all drugs in current clinical use, all arranged alphabetically by generic name for easy access. Drug entries that describe investigational drugs are clustered in a separate section for easier access. A guide word at the top of each page identifies the generic drug presented on that page. Each generic entry is complete where it falls alphabetically and does not require cross-referencing to other sections of the book.

In each drug entry, the generic name (with alternate generic names following in parentheses) precedes an alphabetically arranged list of current trade names. (An asterisk signals products available only in Canada.) Several drugs available solely as combinations (such as heparin with dihydroergotamine) are listed according to the first generic in the combination.

Next, the pharmacologic and therapeutic classifications identify the drug's pharmacologic or chemical category and its major clinical uses. Listing both classifications helps the reader grasp the multiple, varying, and sometimes overlapping uses of drugs within a single pharmacologic class and among different classes. If appropriate, the next line identifies any drug that the Drug Enforcement Agency (DEA) lists as a controlled substance and specifies the schedule of control as II, III, IV, or V.

The pregnancy risk category identifies the potential risk to the fetus. Categories listed were determined by application of the Food and Drug Administration (FDA) definitions to available clinical data in order to define a drug's potential to cause birth defects or fetal death. These categories, labeled A, B, C, D, and X, are listed below with an explanation of each. Drugs in category A usually are considered safe to use in pregnancy; drugs in category X usually are contraindicated.

A: Adequate studies in pregnant women have failed to show a risk to the fetus in the first trimester of pregnancy—and there is no evidence of risk in later trimesters.

B: Animal studies have not shown an adverse effect on the fetus, but there are no adequate clinical studies in pregnant women.

C: Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans. The drug may be useful in pregnant women despite its potential risks.

D: There is evidence of risk to the human fetus, but the potential benefits of use in pregnant women may be acceptable despite potential risks.

X: Studies in animals or humans show fetal abnormalities, or adverse reaction reports indicate evidence of fetal risk. The risks involved clearly outweigh potential benefits.

Pregnancy risk classifications were assigned for all appropriate generic drugs according to the above criteria.

How supplied lists the preparations available for each drug (for example, tablets, capsules, solution, or injection), specifying available dosage forms and strengths.

Indications, route, and dosage presents all clinically accepted indications for use with general dosage recommendations for adults and children; specific recommendations for infants, elderly patients, or other special patient groups are included when appropriate. A preceding dagger signals clinically accepted but unlabeled uses. Dosage instructions reflect current clinical trends in therapeutics and should not be considered as absolute and universal recommendations. For individual application, dosage must be considered according to the patient's condition.

Pharmacodynamics explains the mechanism and effects of the drug's physiologic action.

Pharmacokinetics describes absorption, distribution, metabolism, and excretion of the drug; it specifies onset and duration of action, peak levels, and half-life as appropriate.

Contraindications and precautions lists conditions that are associated with special risks in patients who receive the drug, and includes the rationale for each warning.

Interactions specifies the clinically significant additive, synergistic, or antagonistic effects that result from combined use of the drug with other drugs.

Effects on diagnostic tests lists significant interference with a diagnostic test or its result by direct effects on the test itself or by systemic drug effects that lead to misleading test results.

Adverse reactions lists the undesirable effects that may follow use of the drug; these effects are arranged by body systems (CNS, CV, DERM, EENT, GI, GU, HEMA, Hepatic, Metabolic, Respiratory, Local, Systemic, and Other). Local effects occur at the site of drug administration (by application, infusion, or injection); adverse reactions not specific to a single body system (for example, the effects of hypersensitivity) are listed under *Other*. Throughout, life-threatening reactions are italicized. At the end of this section, *Note* signals a list of severe and hazardous reactions that mandate discontinuation of the drug.

Overdose and treatment summarizes the clinical manifestations of drug overdose and recommends specific treatment as appropriate. Usually, this segment recommends emesis or gastric lavage, followed by activated charcoal to reduce the amount of drug absorbed and possibly a cathartic to eliminate the toxin. This section specifies antidotes, drug therapy, and other special care, if known. It also specifies the effects of hemodialysis or peritoneal dialysis for dialyzable drugs.

Special considerations offers detailed recommendations specific to the drug for preparation and administration; for care and teaching of the patient during therapy; and for use in elderly patients, children

and breast-feeding women. This section includes recommendations for monitoring the effects of drug therapy, for preventing and treating adverse reactions, for promoting patient comfort, and for storing the drug. Recommendations that are common to all members of the drug's pharmacologic class are listed only in the relevant *pharmacologic class* entry. Thus, if specific considerations are unknown for geriatric, pediatric, or breast-feeding use of the generic drug, or if known information is listed in the pharmacologic class entry or elsewhere in the generic entry, these headings are omitted. For example, if the *Indications, route and dosage* section lists detailed instructions for use in children and no additional considerations apply, the generic entry omits the heading *Pediatric use*. However, relevant information that applies to all drugs in the drug's pharmacologic class may exist in the pharmacologic class entry. Cross-references to pharmacologic class entries are denoted in italics.

Pharmacologic class entries

Listed alphabetically as a separate section, 61 entries describe the pharmacology, clinical indications and actions, adverse effects, and special implications of drugs that fall into a major pharmacologic group (for example, benzodiazepines, phenothiazines, or thiazide diuretics). This allows the reader to compare the effects and uses of drugs within each class. Pharmacologic class entries list special considerations that are common to all generic members of the class, and include geriatric, pediatric, and breast-feeding use. If specific considerations are unknown, these headings are omitted.

Representative combinations at the end of each class entry lists major combinations of generic drugs in the class with other generics of the same or of another class, followed by trade names of products that contain each combination of generics.

Investigational drugs

Subsections vary within these entries according to the amount of information available. For example, they commonly omit sections on *Pharmacokinetics, Interactions,* and *Effects on diagnostic tests,* because such data have not yet been reported.

Graphic enhancement

Selected charts and tables compare uses, effects, or dosages of drugs within a class.

Appendices

The appendices provide a charted summary of recommended protocols for cancer chemotherapy, a list of designated orphan drugs and biologicals with their trade names and indications, a list of antidotes to poisoning or overdose, and an organized chart about topical drugs. Selected references lists sources of additional information.

Index

The index lists trade names only. Generic drugs, pharmacologic classes, and investigational drugs appear alphabetically within the main text.

ABBREVIATIONS

Abbreviation	Meaning
ALT	serum alanine aminotransferase, formerly SGPT
AST	serum aspartate aminotransferase, formerly SGOT
ATP	adenosine triphosphate
AV	atrioventricular
b.i.d.	twice a day
BUN	blood urea nitrogen
cAMP	cyclic 3', 5' adenosine monophosphate
CHF	congestive heart failure
CNS	central nervous system
CPK	creatine phosphokinase
CPR	cardiopulmonary resuscitation
CSF	cerebrospinal fluid
CV	cardiovascular
CVP	central venous pressure
DNA	deoxyribonucleic acid
ECG	electrocardiogram
EEG	electroencephalogram
FDA	Food and Drug Administration
g	gram
G	gauge
GI	gastrointestinal
GU	genitourinary
h.s.	at bedtime
I.M.	intramuscular
IU	International Unit
I.V.	intravenous
kg	kilogram
L	liter
m^2	square meter
mm^3	cubic millimeter
MAO	monoamine oxidase
mcg or μg	microgram
mEq	milliequivalent
mg	milligram
MI	myocardial infarction
ml	milliliter
ng	nanogram (millimicrogram)
OTC	over-the-counter
P.O.	by mouth
p.r.n.	as needed
q	every
q.i.d.	four times a day
RBC	red blood cell
RNA	ribonucleic acid
SA	sinoatrial
S.C.	subcutaneous
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
t.i.d.	three times a day
WBC	white blood cell

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A

acebutolol
Sectral

- Pharmacologic classification: beta-adrenergic blocking agent
- Therapeutic classification: antihypertensive, antiarrhythmic
- Pregnancy risk category B

How supplied
Available by prescription only
Capsules: 200 mg, 400 mg

Indications, route, and dosage
Hypertension
Adults: 400 mg P.O. either as a single daily dose or divided b.i.d. Patients may receive as much as 1,200 mg daily.
Ventricular arrhythmias
Adults: 400 mg P.O. daily divided b.i.d. Dosage is then increased to provide an adequate clinical response. Usual daily dosage is 600 to 1,200 mg.

Pharmacodynamics
- *Antihypertensive action:* The exact mechanism of acebutolol's antihypertensive effect is unknown. Acebutolol has cardioselective $beta_1$-adrenergic blocking properties and mild intrinsic sympathomimetic activity.
- *Antiarrhythmic action:* Acebutolol decreases heart rate and prevents exercise-induced increases in heart rate; it also decreases myocardial contractility, cardiac output, and sinoatrial (SA) and atrioventricular (AV) nodal conduction velocity.

Pharmacokinetics
- *Absorption:* Acebutolol is absorbed well after oral administration. Peak plasma levels occur at about 2½ hours.
- *Distribution:* Acebutolol is about 26% protein-bound; minimal quantities are detected in CSF.
- *Metabolism:* Acebutolol undergoes extensive first-pass metabolism in the liver; peak levels of its major active metabolite, diacetolol, occur at about 3½ hours.
- *Excretion:* From 30% to 40% of a given dose of acebutolol is excreted in urine; remainder is excreted in feces and bile. Half-life of acebutolol is about 3 to 4 hours; half-life of diacetolol is 8 to 13 hours.

Contraindications and precautions
Acebutolol is contraindicated in patients with known hypersensitivity to the drug; in patients with persistent severe bradycardia or overt cardiac failure because drug may worsen these conditions; and in patients with second- or third-degree AV block or cardiogenic shock.

Acebutolol should be used cautiously in patients with impaired hepatic or renal function (decrease dosage if creatinine clearance falls below 50 ml/minute); in patients with coronary insufficiency because beta-adrenergic blockade may precipitate congestive heart failure (CHF); in patients with diabetes mellitus or hyperthyroidism because acebutolol may mask tachycardia (but not dizziness or sweating) caused by hypoglycemia or hyperthyroidism; and in patients with bronchospastic diseases, such as asthma or emphysema, because higher doses of the drug may inhibit bronchodilating effects of endogenous catecholamines.

Interactions
Acebutolol may potentiate hypotensive effects of other antihypertensive agents; it also may alter insulin or oral hypoglycemic dosage requirements in stable diabetic patients. Hypotensive effects of acebutolol may be antagonized by indomethacin, nonsteroidal anti-inflammatory agents, and alpha-adrenergic stimulants, such as those contained in nonprescription cold remedies.

Effects on diagnostic tests
Acebutolol may cause positive antinuclear antibody titers.

Adverse reactions
- CNS: fatigue, headache, dizziness, insomnia.
- CV: chest pain, edema, bradycardia, CHF, hypotension.
- DERM: rash.
- EENT: dry eye, eye pain, abnormal vision, conjunctivitis.
- GI: nausea, constipation, diarrhea, dyspepsia.
- GU: impotence.
- Metabolic: hypoglycemia without tachycardia.
- Other: fever, wheezing, dyspnea, cough.

Note: Drug should be discontinued if patient develops signs of CHF.

Overdose and treatment
Clinical signs of overdose include severe hypotension, bradycardia, heart failure, and bronchospasm.

After acute ingestion, empty stomach by emesis or gastric lavage; follow with activated charcoal to reduce absorption. Thereafter, treat symptomatically and supportively.

▶ Special considerations
Besides those relevant to all *beta-adrenergic blockers*, consider the following recommendation.
- Do not discontinue acebutolol abruptly.

Information for the patient
Advise patient to report wheezing promptly.

Geriatric use
Elderly patients may require lower maintenance dosages of acebutolol because of increased bioavailability. Do not exceed 800 mg/day.

Pediatric use
Safety and efficacy of acebutolol in pediatric patients have not been established; use only if potential benefit outweighs risk.

Breast-feeding
Both acebutolol and its metabolite, diacetolol, are distributed into breast milk; breast-feeding is not recommended for women receiving this drug.

acetaminophen
Acephen, Anacin-3, Bromo-Seltzer, Datril, Datril-500, Tempra, Tylenol, Valadol, Valorin

- Pharmacologic classification: para-aminophenol derivative
- Therapeutic classification: nonnarcotic analgesic, antipyretic
- Pregnancy risk category B

How supplied
Available without prescription
Tablets: 160 mg, 325 mg, 500 mg, 650 mg
Tablets (chewable): 80 mg, 160 mg
Capsules: 325 mg, 500 mg
Suppositories: 120 mg, 125 mg, 135 mg, 325 mg, 650 mg
Solution: 100 mg/ml
Elixir: 120 mg/5 ml, 160 mg/5 ml, 320 mg/5 ml
Liquid: 160 mg/5 ml; 500 mg/15 ml
Effervescent granules: 325 mg/capful
Granules: 80 mg/packet

Indications, route, and dosage
Mild pain or fever
Adults and children over age 12: 325 to 650 mg P.O. or rectally q 4 hours, p.r.n. Maximum dose should not exceed 4 g daily. Dosage for long-term therapy should not exceed 2.6 g daily.
Children under age 12: 1.5g/m² P.O. daily in divided doses or as shown below.
Children age 11 to 12: 480 mg/dose q 4 to 6 hours.
Children age 9 to 10: 400 mg/dose q 4 to 6 hours.
Children age 6 to 8: 320 mg/dose q 4 to 6 hours.
Children age 4 to 5: 240 mg/dose q 4 to 6 hours.
Children age 2 to 3: 160 mg/dose q 4 to 6 hours.
Children age 12 to 23 months: 120 mg/dose q 4 to 6 hours.
Children age 4 to 11 months: 80 mg/dose q 4 to 6 hours.
Children age 3 months or younger: 40 mg/dose q 4 to 6 hours.

Pharmacodynamics
The mechanism and site of action is unclear and may be related to inhibition of prostaglandin synthesis in the CNS.
- *Antipyretic action:* Acetaminophen is believed to exert its antipyretic effect by direct action on the hypothalamic heat-regulating center to block the effects of endogenous pyrogen. This results in increased heat dissipation through sweating and vasodilation.
- *Analgesic action:* Its analgesic effect may be related to an elevation of the pain threshold.

Pharmacokinetics
- *Absorption:* Acetaminophen is absorbed rapidly and completely via the GI tract. Peak plasma concentrations occur in ½ to 2 hours, slightly faster for liquid preparations.
- *Distribution:* The drug is 25% protein-bound. Plasma concentrations do not correlate well with analgesic effect, but do correlate with toxicity.
- *Metabolism:* Approximately 90% to 95% is metabolized in the liver.
- *Excretion:* Acetaminophen is excreted in urine. The average elimination half-life ranges from 1 to 4 hours. In acute overdose, prolongation of elimination half-life is correlated with toxic effects. Half-life greater than 4 hours is associated with hepatic necrosis; greater than 12 hours is associated with coma.

Contraindications and precautions
Acetaminophen is contraindicated in patients with known hypersensitivity to this compound. Administer drug cautiously to patients with anemia or hepatic or renal disease because it has been known to induce these disorders; and to patients with a history of GI disease, increased risk of GI bleeding, or decreased renal function. Acetaminophen may mask the signs and symptoms of acute infection (fever, myalgia, erythema); patients with high infection risk (such as those with diabetes) should be carefully evaluated.

Interactions
Concomitant use of acetaminophen may potentiate the effects of anticoagulants and thrombolytic drugs, but this effect appears to be clinically insignificant. Antacids and food delay and decrease the absorption of acetaminophen. Combined caffeine and acetaminophen may enhance the therapeutic effect of acetaminophen. Concomitant use of phenothiazines and acetaminophen in large doses may result in hypothermia.

Effects on diagnostic tests
Acetaminophen may cause a false-positive test result for urinary 5-hydroxyindoleacetic acid (5-HIAA).

Adverse reactions
- CNS: mental changes, stupor, confusion, agitation (with toxic doses), weakness.
- DERM: rash, urticaria, itching, unusual bruising, erythema.
- EENT: unexplained sore throat.
- GI: nausea, vomiting, diarrhea, abdominal cramps, abdominal pain, loss of appetite.
- GU: bloody or cloudy urine, difficult or painful urination, sudden decrease in amount of urine.
- HEMA: unusual bleeding, tiredness or weakness, *hemolytic anemia,* neutropenia, leukopenia, pancytopenia, thrombocytopenia, methemoglobinemia.
- Hepatic: *severe liver damage* (toxic doses).
- Other: hypoglycemia, jaundice, unexplained fever.

Note: Drug should be discontinued if hypersensitivity or signs and symptoms of hepatic toxicity occur.

Overdose and treatment
In acute overdose, plasma levels of 300 mcg/ml 4 hours postinjection or 50 mcg/ml 12 hours postinjection are associated with hepatotoxicity. Clinical manifestations of overdose include cyanosis, anemia, jaundice, skin eruptions, fever, emesis, CNS stimulation, delirium, methemoglobinemia progressing to depression, coma, vascular collapse, convulsions, and death. Acetaminophen poisoning develops in stages:
Stage 1 (12 to 24 hours after ingestion): nausea, vomiting, diaphoresis, anorexia.
Stage 2 (24 to 48 hours after ingestion): clinically improved but elevated liver function tests.

Stage 3 (72 to 96 hours after ingestion): peak hepatotoxicity.
Stage 4 (7 to 8 days after ingestion): recovery.

To treat toxic overdose of acetaminophen, empty stomach immediately by inducing emesis with ipecac syrup if patient is conscious, or by gastric lavage. Administer activated charcoal via nasogastric tube. Oral acetylcysteine (Mucomyst) is a specific antidote for acetaminophen poisoning and is most effective if started within 10 to 12 hours after ingestion, but can help if started within 24 hours after ingestion. Administer a Mucomyst loading dose of 140 mg/kg P.O., followed by maintenance doses of 70 mg/kg P.O. every 4 hours for an additional 17 doses. Doses vomited within 1 hour of administration must be repeated. Remove charcoal before administering acetylcysteine because it may interfere with this antidote's absorption.

Acetylcysteine minimizes hepatic injury by supplying sulphydryl groups that bind with acetaminophen metabolites. Hemodialysis may be helpful to remove acetaminophen from the body. Monitor laboratory parameters and vital signs closely. Cimetidine has been used investigationally to block acetaminophen's metabolism to toxic intermediates. Provide symptomatic and supportive measures (respiratory support, correction of fluid and electrolyte imbalances). Determine plasma acetaminophen levels at least 4 hours after overdose. If plasma acetaminophen levels indicate hepatotoxicity, perform liver function tests every 24 hours for at least 96 hours.

▶ Special considerations

- Acetaminophen has no significant anti-inflammatory effect. In spite of this, studies have shown substantial benefit in patients with osteoarthritis of the knee. Therapeutic benefits may stem from the drug's analgesic effects.
- Many nonprescription products contain acetaminophen. Be aware of this when calculating total daily dose.
- Patients unable to tolerate aspirin may be able to tolerate acetaminophen.
- Use this medication cautiously in the presence of alcoholism, hepatic disease, viral infection, renal function impairment, or cardiovascular disease.
- Monitor vital signs, especially temperature, to evaluate drug's effectiveness.
- Assess patient's level of pain and response before and after administration of acetaminophen.
- Store suppository form in refrigerator.

Information for the patient

- Instruct patient in proper administration of prescribed form.
- Advise the patient on chronic high-dose acetaminophen therapy to arrange for monitoring of laboratory parameters, especially BUN, serum creatinine, liver function tests, and CBC.
- Warn the patient with current or history of rectal bleeding to avoid using rectal acetaminophen suppositories. If they are used, they must be retained in the rectum for at least 1 hour.
- Warn patient that high doses or unsupervised chronic use of acetaminophen can cause liver damage. Use of alcoholic beverages increases the risk of liver toxicity.
- Tell the patient to avoid use for self-medication of a fever above 103.1° F. (39.5° C.), a fever persisting longer than 3 days, or a recurrent fever.
- When prescribing buffered acetaminophen effervescent granules, consider sodium content for sodium-restricted patients.
- Tell the patient not to take nonsteroidal anti-inflammatory drugs together with acetaminophen on a regular basis.
- Warn the patient to avoid taking tetracycline antibiotics within 1 hour after taking buffered acetaminophen effervescent granules.
- Tell the patient not to use this medication for arthritic or rheumatic conditions without medical approval. This medication may relieve pain but not other symptoms.
- Tell the adult patient not to take this medication more than 10 days without medical approval.
- Tell the patient to call if symptoms do not improve or if fever lasts more than 3 days.
- Tell the patient on high-dose or long-term therapy that regular follow-up visits are essential.

Geriatric use

Elderly patients are more sensitive to this drug. Use with caution.

Pediatric use

Children should not take more than five doses per day or take the drug for more than 5 days unless specifically prescribed.

Breast-feeding

Excreted into breast milk in low concentrations. No adverse effects have been reported.

acetazolamide
acetazolamide sodium

Ak-Zol, Diamox, Diamox Sequels

- Pharmacologic classification: carbonic anhydrase inhibitor
- Therapeutic classification: adjunctive treatment for open-angle glaucoma and perioperative treatment for acute angle-closure glaucoma, anticonvulsant, management of edema, prevention and treatment of acute high-altitude sickness
- Pregnancy risk category C

How supplied

Available by prescription only
Tablets: 125 mg, 250 mg
Capsules (extended-release): 500 mg
Injection: 500 mg

Indications, route, and dosage

Perioperative management of acute angle-closure glaucoma

Adults: 250 mg P.O. q 4 hours; or 250 mg b.i.d. P.O., I.M., or I.V. for short-term therapy. I.M. injection is very painful and may cause sterile abscesses from alkalinity of drug; I.V. administration (100 to 500 mg/minute) is preferred.

Edema, in congestive heart failure

Adults: 250 to 375 mg P.O., I.M., or I.V. daily in a.m.
Children: 5 mg/kg P.O., I.M., or I.V. daily in a.m.

Open-angle glaucoma

Adults: 250 mg to 1 g P.O., I.M., or I.V. daily, divided q.i.d.

Prevention or amelioration of acute mountain sickness

Adults: 250 mg P.O. q 8 to 12 hours or 500 mg extended-release capsules q 12 to 24 hours.

Myoclonic seizures, refractory generalized tonic-clonic (grand mal) or absence (petit mal) seizures, mixed seizures

Adults: 375 mg P.O., I.M., or I.V. daily up to 250 mg q.i.d. Or, Diamox Sequels 250 to 500 mg daily or b.i.d. Initial dosage when used with other anticonvulsants usually is 250 mg daily.

Children: 8 to 30 mg/kg P.O., I.M., or I.V. daily, divided t.i.d. or q.i.d. Maximum dosage is 1.5 g daily, or 300 to 900 mg/m² daily.

†Diuresis and alkalization of urine in the treatment of toxicity associated with weakly acidic drugs

Adults: 5 mg/kg I.V. p.r.n.

Children: 5 mg/kg I.V. or 150 mg/m² I.V. for 1 to 2 days (in the a.m.).

†Prevention of cystine or uric acid nephrolithiasis

Adults: 250 mg P.O. h.s.

Pharmacodynamics

● *Diuretic action:* Acetazolamide and acetazolamide sodium act by noncompetitive reversible inhibition of the enzyme carbonic anhydrase, which is responsible for formation of hydrogen and bicarbonate ions from carbon dioxide and water. This inhibition results in decreased hydrogen concentration in the renal tubules, promoting excretion of bicarbonate, sodium, potassium, and water; because carbon dioxide is not eliminated as rapidly, systemic acidosis may occur.

● *Antiglaucoma action:* In open-angle glaucoma and perioperatively for acute angle-closure glaucoma, acetazolamide and acetazolamide sodium decrease the formation of aqueous humor, lowering intraocular pressure.

● *Anticonvulsant action:* The mechanism is unknown. Other actions: Acetazolamide is used with other anticonvulsants in various types of epilepsy, particularly petit mal.

● Acetazolamide shortens the period of high-altitude acclimatization; by inhibiting conversion of carbon dioxide to bicarbonate, it may increase carbon dioxide tension in tissues and decrease it in the lungs. The resultant metabolic acidosis may also increase oxygenation during hypoxia.

Pharmacokinetics

● *Absorption:* Acetazolamide is well absorbed from the GI tract after oral administration.

● *Distribution:* Acetazolamide is distributed throughout body tissues.

● *Metabolism:* None.

● *Excretion:* Acetazolamide is excreted primarily in urine via tubular secretion and passive reabsorption.

Contraindications and precautions

Acetazolamide is contraindicated in patients with hepatic insufficiency because the drug may precipitate hepatic coma; in patients with low potassium or sodium concentration level or hyperchloremic acidosis because it may worsen electrolyte imbalance; and in patients with severe renal impairment because nephrotoxicity has been reported.

Acetazolamide should be used cautiously in patients with respiratory acidosis or other severe respiratory problems because the drug may produce acidosis; in patients with diabetes because it may cause hyperglycemia and glycosuria; in patients taking cardiac glycosides because they are more susceptible to digitalis toxicity from acetazolamide-induced hypokalemia; and in patients taking diuretics.

Interactions

Acetazolamide alkalizes urine and thus may decrease excretion of amphetamines, procainamide, quinidine, and flecainide. Acetazolamide may increase excretion of salicylates, phenobarbital, and lithium, lowering plasma levels of these drugs and possibly necessitating dosage adjustments.

Effects on diagnostic tests

Because it alkalinizes urine, acetazolamide may cause false-positive proteinuria in Albustix or Albutest. Acetazolamide may also decrease thyroid iodine uptake.

Adverse reactions

● CNS: drowsiness, paresthesias, confusion.

● DERM: rash.

● EENT: transient myopia.

● GI: nausea, vomiting, anorexia.

● GU: crystalluria, renal calculi, hematuria.

● HEMA: *aplastic anemia,* hemolytic anemia, leukopenia.

● Metabolic: *hyperchloremic acidosis,* hypokalemia, asymptomatic hyperuricemia.

● Local: pain at injection site, sterile abscesses.

Note: Drug should be discontinued if blood pH is below 7.2.

Overdose and treatment

Specific recommendations are unavailable. Treatment is supportive and symptomatic. Acetazolamide increases bicarbonate excretion and may cause hypokalemia and hyperchloremic acidosis. Induce emesis or perform gastric lavage. Do not induce catharsis because this may exacerbate electrolyte disturbances. Monitor fluid and electrolyte levels.

▶ Special considerations

Besides those relevant to all *carbonic anhydrase inhibitors,* consider the following recommendations.

● For patients who have difficulty swallowing tablets, a single dose may be prepared by softening 1 tablet in 2 teaspoons of warm water and adding 2 teaspoonfuls of honey or syrup (chocolate, cherry) and then taken immediately.

● Suspensions containing 250 mg/5 ml of syrup are the most palatable and can be made by a pharmacist. These will remain stable for about 1 week. Tablets will not dissolve in fruit juice.

● Reconstitute powder by adding at least 5 ml sterile water for injection.

● I.M. injection is painful because of alkalinity of solution. Direct I.V. administration is preferred if drug must be given parenterally.

● Acetazolamide has been used for periodic paralysis in dosages up to 1.5 g daily in divided doses b.i.d. or t.i.d.

Geriatric use

Elderly and debilitated patients require close observation, as they are more susceptible to drug-induced diuresis. Excessive diuresis promotes rapid dehydration, leading to hypovolemia, hypokalemia, and hypo-

natremia, and may cause circulatory collapse. Reduced dosages may be indicated.

Breast-feeding
Safety of acetazolamide in breast-feeding women has not been established.

acetic acid
Domeboro Otic, VōSol Otic Solution

- Pharmacologic classification: acid
- Therapeutic classification: antibacterial, antifungal
- Pregnancy risk category C

How supplied
Available by prescription only
Otic solution: 2% in aluminum acetate, 2% in propylene glycol, 3%

Indications, route, and dosage
External ear canal infection
Adults and children: 4 to 6 drops into ear canal t.i.d. or q.i.d.; or insert saturated wick for first 24 hours, then continue with instillations.
Prophylaxis of swimmer's ear
Adults and children: 2 drops in each ear b.i.d.

Pharmacodynamics
Antibacterial and antifungal action: Inhibits or destroys bacteria and fungi in the ear canal by increasing acidity of normal skin, creating an undesirable environment for the growth of these organisms, particularly *Pseudomonas.* Can be used as both an otic and topical anti-infective.

Pharmacokinetics
Unknown.

Contraindications and precautions
Acetic acid is contraindicated in patients with hypersensitivity to any component of the preparation. Otic preparations should be used with caution in the presence of perforated eardrum.

Interactions
None reported.

Effects on diagnostic tests
None significant.

Adverse reactions
- DERM: urticaria.
- Ear: irritation or itching.
- Other: overgrowth of nonsusceptible organisms.

Note: Drug should be discontinued if severe irritation or sensitivity develops.

Overdose and treatment
To treat accidental ingestion, dilute drug but do not induce vomiting, and evaluate for burns. Treat accidental ocular exposure by flushing the eye with warm water for at least 15 minutes. Treat accidental dermal exposure by washing affected area twice with soap and water.

▶ Special considerations
- Reculture persistent otic drainage.
- Avoid contact with eyes and mucous membranes.
- Apply to freshly cleansed area free of other medications.
- Topical application is especially useful for treating superficial gram-negative infections.
- Use aseptic technique to prevent infection.
- To administer eardrops to adults, pull the earlobe up and back.

Information for the patient
Teach patient correct and safe procedures for using acetic acid and administering eardrops.

Pediatric use
To administer eardrops to children, pull the earlobe down and back.

acetohexamide
Dymelor

- Pharmacologic classification: sulfonylurea
- Therapeutic classification: antidiabetic agent
- Pregnancy risk category D

How supplied
Available by prescription only
Tablets: 250 mg, 500 mg

Indications, route, and dosage
Adjunct to diet to lower blood glucose levels in patients with non-insulin-dependent diabetes mellitus (type II)
Adults: Initially, 250 mg P.O. daily before breakfast; may increase dose q 5 to 7 days (by 250 to 500 mg) as needed to a maximum of 1.5 g daily, divided b.i.d. or t.i.d. before meals.
To replace insulin therapy
Adults: If insulin dosage is less than 20 units daily, insulin may be stopped and oral therapy started with 250 mg P.O. daily before breakfast, increased as above, if needed. If insulin dosage is 20 or more units daily, start oral therapy with 250 mg P.O. daily before breakfast, while reducing the insulin dosage 25% to 30% daily or every other day, depending on response to oral therapy.

Pharmacodynamics
Antidiabetic action: Acetohexamide lowers blood glucose levels by stimulating insulin release from functioning beta cells in the pancreas. After prolonged administration, the drug's hypoglycemic effects appear to reflect extrapancreatic effects, possibly including reduction of basal hepatic glucose production and enhanced peripheral sensitivity to insulin. The latter may result either from an increase in the number of insulin receptors or from changes in events subsequent to insulin binding. Acetohexamide has a moderate uricosuric effect.

Pharmacokinetics
- *Absorption:* Acetohexamide is absorbed rapidly from the GI tract. Onset of action occurs within 1 hour, with

a maximum decrease in serum glucose levels within 2 hours.

- *Distribution:* Acetohexamide's distribution is not fully understood, but probably is similar to that of the other sulfonylureas; it is highly protein-bound.
- *Metabolism:* Acetohexamide is metabolized in the liver, primarily to a potent active metabolite.
- *Excretion:* Acetohexamide and its metabolites are excreted primarily (80%) in urine. The duration of action is 12 to 24 hours. Half-life of acetohexamide and its metabolite is approximately 6 hours.

Contraindications and precautions

Acetohexamide is contraindicated in patients with known hypersensitivity to sulfonylureas or thiazides; in patients with burns, acidosis, diabetic coma, severe infection, ketosis, severe trauma, or major surgery because such conditions of severe physiologic stress require insulin for adequate control of serum glucose levels; and in patients with nonfunctioning beta cells.

This drug should be used with caution in patients with hepatic or renal insufficiency because it is metabolized in the liver and excreted in urine; and in those with adrenal, pituitary, or thyroid dysfunction.

Interactions

Concomitant use of acetohexamide with alcohol may produce a disulfiram-like reaction consisting of nausea, vomiting, abdominal cramps, and headaches. Concomitant use with anticoagulants may produce an increase in plasma levels of both drugs and, after continued therapy, reduced plasma levels and anticoagulant effects. Concomitant use with chloramphenicol, guanethidine, insulin, monoamine oxidase inhibitors, oxyphenbutazone, phenylbutazone, probenecid, salicylates, or sulfonamides may enhance the hypoglycemic effect by displacing acetohexamide from its protein-binding sites.

Concomitant use of acetohexamide with beta-adrenergic blocking agents (including ophthalmics) may increase the risk of hypoglycemia by masking symptoms of developing hypoglycemia, such as rising pulse rate and blood pressure, and by blocking gluconeogenesis, thereby prolonging hypoglycemia. Use with drugs that may increase blood glucose levels (adrenocorticoids, glucocorticoids, amphetamines, baclofen, corticotropin, epinephrine, ethacrynic acid, furosemide, oral contraceptives, phenothiazines, phenytoin, thiazide diuretics, triamterene, or thyroid hormones) may require dosage adjustments for either or both drugs.

Concomitant use of acetohexamide may increase the hypoglycemic effects of anabolic steroids, cimetidine, clofibrate, NSAIDs, and miconazole; and may decrease the hypoglycemic effects of isoniazid, nicotinic acid, calcium channel blockers, and rifampin.

Because smoking increases corticosteroid release, patients who smoke may require a higher dosage of acetohexamide.

Effects on diagnostic tests

Acetohexamide therapy alters serum uric acid concentration, cholesterol, alkaline phosphatase, bilirubin, and blood urea nitrogen levels.

Adverse reactions

- CNS: weakness, paresthesia.
- DERM: eczema, pruritus, facial flushing, erythema, urticaria, morbilliform or maculopapular eruptions, photosensitivity.
- GI: cholestatic jaundice, nausea, vomiting, epigastric fullness, heartburn.
- HEMA: leukopenia, thrombocytopenia, mild anemia, *agranulocytosis.*
- Metabolic: sodium loss, hypoglycemia.
- Other: *hypersensitivity reactions.*

Note: Drug should be discontinued if signs or symptoms of hypersensitivity, including jaundice, skin eruptions, blood dyscrasias, and severe diarrhea, occur, or if serial and progressive increases in serum alkaline phosphatase levels occur.

Overdose and treatment

Clinical manifestations of overdose include low blood glucose levels, tingling of lips and tongue, hunger, nausea, decreased cerebral function (lethargy, yawning, confusion, agitation, and nervousness), increased sympathetic activity (tachycardia, sweating, and tremor), and ultimately convulsions, stupor, and coma.

Mild hypoglycemia (without loss of consciousness or neurologic findings) can be treated with oral glucose and dosage adjustments. In severe hypoglycemia, the patient should be hospitalized immediately. If patient loses consciousness or experiences neurologic symptoms, patient should receive rapid injection of dextrose 50%, followed by a continuous infusion of dextrose 10% at a rate to maintain blood glucose levels greater than 100 mg/dl. Monitor for 24 to 48 hours.

▶ Special considerations

Besides those relevant to all *sulfonylureas*, consider the following recommendations.

- To avoid GI intolerance in patients taking dosages of 1 g/day or more and to improve control of hyperglycemia, divided doses are recommended. These are given before the morning and evening meals.
- Patients switching from chlorpropamide to acetohexamide should be monitored closely for 1 week because of chlorpropamide's prolonged retention in the body.
- Elderly, debilitated, or malnourished patients and those with impaired renal or hepatic function usually require a lower initial dosage.
- The manufacturer recommends against using acetohexamide in pregnancy complicated by diabetes.
- Oral hypoglycemic agents have been associated with an increased risk of cardiovascular mortality as compared to diet or diet and insulin treatments.

Information for the patient

- Emphasize the importance of following prescribed diet, exercise, and medical regimen.
- Tell patient to take medication at the same time each day. If a dose is missed, it should be taken immediately, unless it's almost time for the next dose. Patient should never take double doses.
- Advise patient to avoid alcohol; disulfiram-like reaction is possible with moderate to large intake.
- Advise patient to wear a Medic Alert bracelet or necklace.
- Tell patient to take acetohexamide with food if the drug causes GI upset.
- Teach patient to recognize signs and symptoms of hypoglycemia and hyperglycemia and what to do if they occur.
- Teach patient to monitor blood glucose, urine glucose, or ketone levels, as prescribed.

iron intake may interfere with absorption of drug because of chelate formation.
• Do not administer to fertile female until pregnancy has been ruled out and appropriate contraception is in effect.

Information for the patient
• Advise patient to avoid alcohol, which can cause a skin rash in patients who are taking acetohydroxamic acid.
• Warn patient to avoid pregnancy during treatment because drug is teratogenic.
• Warn patient to avoid oral iron supplements and all other oral preparations containing iron because drug can chelate iron and decrease absorption.

Geriatric use
Lower doses may be required for elderly patients with decreased renal function.

Pediatric use
Safe use has not been established in children under age 8. If the drug is used in a child, the patient should be closely monitored.

Breast-feeding
It is not known whether acetohydroxamic acid enters breast milk, but use should be avoided in breast-feeding women.

acetophenazine maleate
Tindal

• Pharmacologic classification: phenothiazine (piperazine derivative)
• Therapeutic classification: antipsychotic
• Pregnancy risk category C

How supplied
Available by prescription only
Tablets: 20 mg

Indications, route, and dosage
Psychotic disorders
Adults: Initially, 20 mg P.O. t.i.d. or q.i.d. Daily dosage ranges from 40 to 80 mg in outpatients or 80 to 120 mg in hospitalized patients; however, in severe psychotic states, up to 600 mg daily has been administered safely. Smallest effective dose should be used at all times.

Pharmacodynamics
Antipsychotic action: Acetophenazine is thought to exert its antipsychotic effects by postsynaptic blockade of CNS dopamine receptors, thereby inhibiting dopamine-mediated effects.

Acetophenazine has many other central and peripheral effects: it produces alpha and ganglionic blockade and counteracts histamine- and serotonin-mediated activity. Its most prominent adverse reactions are extrapyramidal.

Pharmacokinetics
• *Absorption:* Oral tablet absorption is erratic and variable, with onset of action ranging from ½ to 1 hour.
• *Distribution:* Acetophenazine is distributed widely into the body, including breast milk. CNS concentrations are higher than plasma concentrations. Drug is 91% to 99% protein-bound. Peak effect occurs at 2 to 4 hours; steady-state serum levels are achieved within 4 to 7 days.
• *Metabolism:* Acetophenazine is metabolized extensively by the liver, but no active metabolites are formed; duration of action is about 4 to 6 hours.
• *Excretion:* Most of the drug is excreted in urine as inactive metabolites; some is excreted in feces via the biliary tract.

Contraindications and precautions
Acetophenazine is contraindicated in patients with known hypersensitivity to phenothiazines and related compounds, including allergic reactions involving hepatic function; in patients with blood dyscrasias and bone marrow depression because it may cause agranulocytosis; in patients in coma or with brain damage, CNS depression, circulatory collapse, or cerebrovascular disease because of its hypotensive effects; and in patients with adrenergic blocking agents or spinal or epidural anesthetics because of the potential for additive adrenergic blocking effects.

Acetophenazine should be used cautiously in patients with cardiac disease (arrhythmias, congestive heart failure, angina pectoris, valvular disease, or heart block), encephalitis, Reye's syndrome, head injury, respiratory disease, epilepsy and other seizure disorders, glaucoma, prostatic hypertrophy, urinary retention, hepatic or renal dysfunction, Parkinson's disease, pheochromocytoma, or hypocalcemia.

Interactions
Concomitant use of acetophenazine with sympathomimetics, including epinephrine, phenylephrine, phenylpropanolamine, and ephedrine (often found in nasal sprays), and appetite suppressants may decrease their stimulatory and pressor effects. Concomitant use of epinephrine as a pressor agent may cause epinephrine reversal because of its alpha-adrenergic blocking effects.

Acetophenazine may inhibit blood pressure response to centrally acting antihypertensive drugs such as guanethidine, guanabenz, guanadrel, clonidine, methyldopa, and reserpine. Additive effects are likely after concomitant use of acetophenazine with CNS depressants (including alcohol, analgesics, barbiturates, narcotics, tranquilizers, and general, spinal, or epidural anesthetics) and parenteral magnesium sulfate (oversedation, respiratory depression, and hypotension); antiarrhythmic agents, quinidine, disopyramide, or procainamide (increased incidence of cardiac dysrhythmias and conduction defects); atropine and other anticholinergic drugs (including antidepressants, monoamine oxidase inhibitors, phenothiazines, antihistamines, meperidine, and antiparkinsonian agents [oversedation, paralytic ileus, visual changes, and severe constipation]); nitrates (hypotension); or metrizamide (increased risk of convulsions).

Beta-blocking agents may inhibit acetophenazine metabolism, increasing plasma levels and toxicity.

Concomitant use with propylthiouracil increases risk of agranulocytosis; concomitant use with lithium may result in severe neurologic toxicity with an encephalitis-like syndrome, and a decreased therapeutic response to acetophenazine.

Pharmacokinetic alterations and subsequent decreased therapeutic response to acetophenazine may

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