VOLUME I

Drug Information for the Health Care Professional

USP DI®

1997

17TH EDITION

By authority of the United States Pharmacopeial Convention. Inc.

QUAZEPAM—See *Benzodiazepines (Systemic)*

QUINACRINE Systemic

INN: Mepacrine

VA CLASSIFICATION (Primary): API09

Note: For a listing of dosage forms and brand names by country availability. see ***Dosage Forms*** section(s). For a listing of brand names for the articles in this monograph, refer to the General Index.

Category
Antiprotozoal.

Indications
Note: Bracketed information in the ***Indicar tions*** section refers to uses that are not included in U.S. product labeling.

Accepted

Giardiasis (treatment)-Quinacrine is indicated as a primary agent in the treatment of giardiasis caused by ***Giard ia lamb lia.***

[pneumothorax (prophylaxis)]'-Quinacnne powder is used as an intrapleural sclerosing agent to prevent recurrence of pneumothorax in patients at high nsk of recurrence, e.g., cystic fibrosis patients.

[Lupus erythematosus. discoid (treatment)]'-Quinacrine is used in the treatment of mild to moderate discotd lupus erythematosus.

[Sterilization, female]'-Quinacrine is used transcervically as a female sterilizing agent.

Unaccepted
Although quinacrine has been used for the treatment of diphyllobothriasis, hymenotepiasis, malaria, and taeniasis, it has been superseded by safer and/or more effective agents (e.g.. niclosamtde, praziquantel. chloroquine. hydroxychloroquine).

'Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics
Physicochemical characteristics
Molecular weight-508.91.

Mechanism of action/Effect
Exact mechanism of antiparasitic action is unknown; however. quinacrine bids to deoxyribonucleic acid (DNA) by intercalation between adjacent base pairs. inhibiting transcription and translation to nbonucleic acid (RNA). It also inhibits succinate oxidation and interferes with electron transport. In addition, it binds to nucleoproteins. which can suppress the lupus erythematous (LE) cell factor, and acts as a strong inhibitor of cholinesterase.

Absorption
Rapidly absorbed from the gastrointestinal tract following oral admintstration. Also rapidly absorbed after intrapleural administration.

Distribution
Widely distributed; concentrates in the liver, spleen, lungs, and adrenal glands. Concentration in the liver may be 20.000 times that in the plasma. Also deposited in skin, fingernails, and hair. Cerebrospinal fluid (CSF) concentrations are 1 to 5% of corresponding plasma level. Lowest concentrations are found in the brain, heart, skeletal muscles, and breast milk.

Protein binding
High (80 to 90%).

Half-life
5 to 14 days,

Time to peak plasma concentration
8 to 12 hours.

Elimination
Renal; fecal-Less than 1% eliminated in the urine daily; acidification of urine increases urinary excretion of quinacrine by up to 14%; excreted slowly, significant amounts being excreted in the urine for 2 months or more after discontinuation of quinacrine.

*Small amounts also excreted in bile, sweat, and saliva.

Precautions to Consider
Pregnancy/Reproduction
Pregnancy-Quinacrine crosses the placenta and reaches the fetal circulation. There is one case of possible renal agenesis and hydrocephalus in an infant, although normal pregnancies have been reported after quinacrine ingestion during the first 4 weeks of gestation. If possible, quinacrine treatment for giardiasis in asymptomatic pregnant women should be postponed until after delivery.

One study in rats showed an increased incidence of fetal death with high doses of quinacrine.

Breast-feeding
A small amount of quinacrine is excreted in breast milk. However, problems in humans have not been documented.

Pediatrics
Quinacrine may cause vomiting in children due to its bitter taste. The tablets may be crushed and mixed with jam, honey, or chocolate syrup or put in empty gelatin capsules to mask the taste.

Children also tolerate quinacrine less well than do adults.

Geriatrics
Appropriate studies on the relationship of age to the effects of quinacrine have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.

Drug interactions and/or related problems
The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)-not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Primaquine
(concurrent use with quinacrine may inhibit the metabolism of primaquine or may displace it from ttssue-binding sites, thereby increasing serum concentrations and potential toxicity of primaquine)

Medical considerations/Contraindications
The medical considerations/contraindications included here have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)-not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist:

Hypersensitivity to quinacrine

Porphyria
(quinacrine may exacerbate porphyria)

>> Psoriasis
(quinacrine may precipitate a severe attack of psonasis)

>> Psychosis, history of
(quinacrine may cause transitory psychosis)

Patient monitoring
The following may be especially important in patient monitoring (other tests may be warranted in some patients depending on condition; >> = major clinical significance):

For giardiasis

>> Stool examinations
(3 stool examinations, taken several days apart, beginning 3 to 4 weeks following treatment, are recommended if symptoms persist; however, in some successfully treated patients, the lactose intolerance brought on by the infection may persist for a period of some weeks or months, mimicking the symptoms of giardiasis; in cases of treatment failure, alternative medications may be used)

Side/Adverse Effects

Note: Hepati tis. aplastic anemia. corneal edema. and retmopathy may occur with prolonged and/or high-dose therapy with quinacnne. However, these side/adverse effects occur rarely, if at all. with short-term therapy such as that used in giardiasis.

The followmg side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)-not necessarily inclusive:

Those indicating need for medical attention

Incidence less frequent

Central nervous ***system*** **(CA'S)** ***stimulation*** (hallucinationsIrritabili ty: mood or other mental changes; nervousness; nightmares: psychosis): ***skin rash, redness, itching, or peeling***

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Dizziness; gastrointestinal disturbances (abdominal or stomach cramps; diarrhea; loss of appetite; nausea or vomiting); ***headache***

Those not indicating need for medical attention

incidence more frequent

Yellow ***discoloration of skin and*** urine-due to acndine dye characteristics

Overdose

For specific Information on the agents used in the management of quinacrine overdose, see:

* *Barbiturates (Systemlc)* monograph;
- *Benzodiazepines (Systemic)* monograph: and/or
- *Vasopressors* in *Sympathomimetic Agents-Cardiovasscular Use (Parenteral-Systemlc)* monograph.

For more Information on the management of overdose or unintentional ingestlon, **contact a Poison Control Center (see** *Poison Control Center Listing).*

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)-not necessarily inclusive:

Acute

In order of occurrence-

Seizures; ***hypotension; cardiac arrhythmias; cardiovascular collapse***

Treatment of overdose

Recommended treatment consists of the following:

To decrease absorption-

Evacuating the stomach by gastric lavage or induction of emesis.

Specific treatment-

Controlling seizures with benzodiazepines or ultrashort-act ing barbiturates.

Treating shock by administration of fluids and vasopressors.

Administeringammonium chloride. 8 grams daily in divided doses for adults. to acidify the urine and promote excretion of quinacnne by up to 14%.

Supportive care-

Administering supportive measures such as maintaining an open airway, breathing, and circulation. Closely observing for at least 6 hours those patients who have survived the acute phase and are asymptomatic. Patients in whom intentional overdose is knoun or suspected should be referred for psychiatric consultation.

Patient Consultation

As an aid to patient consultataon. refer to *Advice for the Patient. Quinacrine (Systemic).*

In providing consultation. consider emphasizing the following selected information (>>= major clinical significance):

Before using this medication

» Conditions affecting use, especially:

Hypersensitivity to quinacrine

Pregnancy-Quinacrine crosses the placenta

Breast-feeding-Quinacrine is excreted in breast milk

Use in children-Children tolerate quinacnne less well than do adults

Other medicine, especially primaquine

Other medical problems, especially psoriasis and a history of psychosis

Proper use of this **medication**

Taking after meals wtth a full glass (240mL) of water, tea or fruit juice

Crushing tablets and mixing with Jam. honey. or chocolate syrup or placlng in empty gelatin capsules IO disguise bitter taste for patients unable to swallow tablets or unable to tolerate bitter taste

» Compliance with full course of therapy

» Proper dosing

Missed dose: Taking as soon as possible: not taking if almost time for next dose: not doubling doses

» Proper storage

Precautions **while using this medication**

Periodic visits to physician to check progress after treatment

Checkmg with physician if no improvement within a few days

» Caution if dizziness occurs

Side/adverse effects

Signs of potential side effects especially central nervous system (CNS) stimulatlon and skin rash. redness. Itching. or peeling

Yellow discoloration of skin and urine due to dye-like characteristics of quinacrine. may be alarming to patient although medically msigniticant

General Dosing Information

Quinacrine should preferably be taken after meals with a full glass (240 mL) of water. tea. or fruit juice.

For patients unable to swallow tablets or unable to tolerate bitter taste, quinacrine tablets may be crushed and mlxed with jam. honey, or chocolate syrup or placed in empty gelatin capsules to disguise the bitter taste. Quinacrine is not stable in solution for any length of time. it is convened to an insoluble precipitate.

Oral Dosage Forms

QUINACRINE HYDROCHLORIDE TABLETS USP

Usual adult and adolescent dose

Giardiasis-

Oral, 100 mg three times a day for live to seven days.

Usual pediatric dose

Giardiasis-

Oral. 2 mg per kg of body weight three times a day for five to seven days.

Note: The maximum dose in children is *300* mg daily.

Strength(s) usually available

IJ.S.-

100 mg (Rx) *[Atabrine].*

Canada-

100 mg (Rx) *[Atabrine* (scored)].

Packaging and storage

Store below JO °C (I04 °F), preferably between 15 and 30°C (59 and 86 °F) in a light-resistant contamer. unless otherwise specified by manufacturer Store in a tight contamer.

Preparation of dosage form

For patients who cannot take oral solids-Tablets may be crushed and mixed with jam. honey, or chocolate syrup or placed in empty gelatin capsules to disguise the bitter taste. Quinacrine is not stable in solution for any length of time: it is converted to an insoluble precipitate

Auxiliary labeling

- Take after meals with liquids.
- May cause dizziness.
- Continue medicine for full time of treatment.

Revised: 02/01/93

QUINAPRIL—See *Angiotensin-converting Enzyme (ACE) Inhibitors (Systemic)*

QUINESTROL—See *Estrogens (Systemic)*

QUINETHAZONE-See *Diuretics.Thiazide(Systemic)*

Foreword

THE NATIONAL CONSENSUS

A generation before American physicians joined together to form a national organization to promote and protect medicine as a profession, they joined together to create a national pharmacopeia to promote and protect the public health.

A generation before pharmacists joined together to form a national organization to promote and protect pharmacy as a profession, they joined the physicians in the work of the Pharmacopeia.

This magnificent record of public service of the health professions results now in the establishment of legally recognized national standards of quality for drugs and this national consensus on the clinically relevant drug use information needed by the patient and needed by those practitioners caring for the patient who is taking the medicine.

The national consensus. A proud claim. It is based on the comprehensiveness of the involvement of all interested parties, the unbiased structure of the system, and the constant public access to the system.

- An extensive expert advisory panel system reaching across the entire health field; a cross-fertilized matrix of:
  - -medical specialty panels, which consider drug use information from the standpoint of its scientific accuracy and clinical relevance in each of the therapeutic or medical specialty areas;
  - -practice oriented panels, which review drug use information from the standpoint of its utility in each of the professions that care for patients who use the drug;
  - -a panel of consumers who watch over language, format, and general approach;
  - -and an international health advisory panel to reflect drug information needs and use in other countries and to enrich the database with the experience of those countries.
- The system is designed to secure an evidence-based, unbiased consensus or, more properly, to secure a balance of biases, because no human or human endeavor is ever totally unbiased:
  - -USP Committee of Revision members are elected for their individual expertise, regardless of their current place of employment or organizational memberships;
  - -electors in this nationwide election procedure include members of the U.S. Pharmacopeial Convention (USP) from each college and state association in medicine and pharmacy; national scientific, professional, and trade associations and agencies of the federal government that are concerned with drugs; consumer organizations; international organizations and foreign government; and members at large;
  - -panelists, all of whom are volunteers, are selected by the USP Committee of Revision member who has been elected to represent that particular area or specialty, and consented to by the USP Nominating Committee;
  - -freedom from influence resulting from financial interests in organizations that manufacture and market drugs is guaranteed by a conflict-of-interest program that protects the integrity of the consensus process.
- Opportunity for input from all interested parties and public review of the text that is proposed by the Panels for adoption by the Committee of Revision:
  - -several hundred reviewers are designated by colleges, associations, and government agencies, including the U.S. Food and Drug Administration and Canada's Drugs Directorate;
  - -researchers and manufacturers involved with the individual drug provide review;
  - -review and comment by any interested member of the public of draft text for USP DI monographs as listed in ***USP DI Review,*** a special section of the monthly ***USP DI Update,*** is encouraged;
  - -meetings of all advisory panels are open to the public;
  - -review and revision are continuous, with the electronic database updated daily and representing the most current information and print publications representing the official text at the time of publication.

The national consensus. Why is such an extensive and costly system needed? Because practitioners and patients need ***up-to-date*** information about ***all*** drugs; because patients need consistency and reinforcement in the information given to them; because the health professions and the public need confidence in the authoritativeness of the information they give and get; and because the provision

of patient information about prescription drugs breaks and bends a number of outdated legal and professional boundaries.

- Confidence in the ***authoritativeness*** of the information requires that USP DI information is accurate and can be relied upon by health care practitioners and patients.
- Confidence in the ***credibility*** of the process by which USP DI is assembled requires confidence in the ***integrity*** of the people who operate it.
- Consistency and reinforcement are accepted principles of education. It is important, therefore, that the patient receive essentially the same information from both the prescriber and the dispenser.
- Confidence by the professions is exemplified by USP's strategic alliance with the American Medical Association (AMA) whereby USP has taken over repsonsibility for the AMA Drug Evaluations (AMA DE) database, in the acceptance of ***USP DI*** as a practice parameter by the AMA/Specialty Society Practice Parameter Forum, and in the use of ***USP DI*** information by numerous pharmacy associations and practice sites.
- Confidence by the Federal government is shown in the recognition of ***USP DI*** in the 1990 and 1993 federal Omnibus Budget Reconciliation Acts (OBRA '90 and '93) as an "official" compendium for use by state Medicaid agencies for drug utilization review (DUR) and patient counseling, and information on medically accepted unlabeled uses of medications, and recognized under the Medicare provisions of OBRA '93 as a source of medically accepted indications or "off label" uses of anticancer drugs.
- Legal barriers and legal threats based on decades of non-information and misinformation are shifting before the increasing demand for patient drug use information:

  -pharmacists, who in some states previously were prohibited from discussing a prescription drug with the patient, are now legally required to offer counseling and to give patient information for certain drugs and are proclaimed by leaders in pharmacy as the source of patient information on any drug;
  -physicians, who have been the gate-keepers of prescription drugs, are being urged by leaders in medicine to open the gates wider and provide more information to patients about the medicines they are prescribing;
  -and pharmaceutical manufacturers, who have fulfilled their legal obligation by providing information only to the prescriber (the government generally did not allow them to do more), are now being encouraged by the government voluntarily to provide information to patients. The issue at hand is how to do it in a way that balances patients' needs for accurate, understandable information within the legal requirements.

The shifting of these legal barriers and regulatory requirements should be less litigious with the presence of this USP-developed, strong national consensus on what generally is the appropriate content of information for today's patient. Of course, the shift can work both ways. The practitioner who ignores it, or who continues the tradition of providing no information, is at increasing risk. The practitioner who bases his or her information on the national consensus and then individualizes it for the patient will have a better defense.

Jerome A. Halperin
Executive Vice President

Rockville, Maryland
January 2, 1997

Preface

Since 1820, the United States Pharmacopeia has set standards for the medications used by the American public. In establishing the Pharmacopeia, the founders were reacting to an unmet need of the professions and their patients-that is, the need for generally accepted procedures for the preparation of medications which would allow for confidence in their use.

The need for quality standards remains, and the work of USP in establishing those standards continues. However, additional needs regarding the use of medications have arisen, within both the health care provider and health care recipient populations. Some of these newly recognized needs relate to information sources. USP ***Dt*** is one reaction to these previously unmet needs.

At the 1970 meeting of the Pharmacopeial Convention, a resolution to increase in the Pharmacopeia or in a companion volume the amount of information that would be useful to pharmacists and otheis was adopted. In response to this, the l970-1975 Subcommittee on Posology and Related Information, under the chairmanship of John A. Owen, Jr., M.D., expanded the category and dose information and introduced in the ***USP XIX*** monographs of many dosage forms a section entitled Dispensing Information. This information served as a basic reminder or general guide to the pharmacist, who could vary or omit it in accordance with the best interests of the patient or the particular circumstances involved.

Continuing this development, the 1975-I 980 Subcommittee, under the chairmanship of Harry C. Shirkey, R.Ph., .M.D., greatly expanded the amount and kinds of information in the USP DI database, focusing on that believed to enhance the safe and effective use of a medication once it was prescribed. This included drug use information relating to dispensing, administration, monitoring, and/or patient consultation. The work of the Subcommittee resulted in the first edition (1980) of ***USP DI.*** From one book in 1980, it grew to two volumes in 1983, and three volumes in 1989.

USP DI is, and it always will be, a work in progress. The information is under constant revision. This seventeenth edition incorporates the experiences and comments generated by previous editions. New drug monographs and information have been added. and the existing text has been reviewed for changes and revised accordingly.

USP DI is an ongoing publication. The main **volumes** are supplemented by publication of an update every month. ***USP DI Update*** presents monographs on selected, newly marketed drugs as well as selected changes in the information base of drugs already in the data base. Not all new drugs and not all new information on drugs already in ***USP DI*** will appear in ***USP DI Update. Updates.*** therefore, are only an interim partial supplement to the most recent ***USP DI*** annual volumes.

Development of *USP DI*

The ***USP DI*** is a comprehensive collection of clinically relevant, established information about each drug. However, it is far more than that. It is a continuous collection of the current judgments of experts in the use of drugs. The information included is the result of a planned, organized, nationwide consensus-generating system (with worldwide input). This system has been designed to involve not only the experts but all interested parties through open public review and comment.

Using the parameters established by the USP Division of Information Development Executive Committee, staff develops draft monographs for each drug selected for inclusion in ***USP DI.*** These initial drafts are reviewed by the appropriate Advisory Panel(s) and other designated reviewers and are revised accordingly. Re-drafted text may again be reviewed by Advisory Panel(s) as many times as necessary to achieve an initial consensus. Proposed monographs are then made available for general public review and comment. Announcement of availability is made in the ***USP DI Review*** listing as published in the monthly ***USP DI Update.***

The comments generated by the public review process are fed back into the USP Advisory Panel system. If substantive changes result, the monograph is again listed in ***USP DI Review*** announcing additional proposed changes. The process is repeated as required to develop final consensus.

Of course, the consensus can change from one edition to the next, and users of ***USP DI*** are encouraged to submit comments at any time to:

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Organization of *USP DZ*

USP DI comprises three distinct sections. The first volume, ***Drug Information for the Health Care Professional,*** includes the DI monographs arranged in alphabetic order. The Volume 1 general index includes established names, cross-references by brand names (both U.S. and Canadian), and older nonproprietary names. In addition, an indications index and appendixes presenting categories of use and other useful information are included. The second volume, ***Advice for the Patient,*** includes the lay language versions of the patient consultation guidelines found in Volume I. These lay language versions are intended to be used at the discretion of the health care provider as an aid to patient consultation if written information would be of benefit or if it is requested by the prescriber. Brand and generic names are cross-referenced in the index of ***Advice for the Patient.*** The third volume, ***Approved Drug Products and Legal Requirements,*** reproduces information from the Food and Drug Administration on therapeutic equivalence and other requirements relating to drug product selection. It includes USP and NF legal requirements for labeling, storage, packaging, and quality for drugs. It also contains those portions of the federal Controlled Substances Act Regulations, the Poison Prevention