PRIMAQUINE PHOSPHATE TABLETS, USP **Rx Only**

DESCRIPTION

Primaquine phosphate is 8-[(4-Amino-1-methylbutyl)amino]-6-methoxyquinoline phosphate, a synthetic compound with potent antimalarial activity. Each tablet contains 26.3 mg of primaquine phosphate (equivalent to 15 mg of primaquine base). The dosage is customarily expressed in terms of the base.

Inactive Ingredients: Carnauba Wax, Hydroxypropyl Methylcellulose, Lactose, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol 400, Polysorbate 80, Pregelatinized Starch, Red Ferric Oxide, Talc, Titanium Dioxide.

CLINICAL PHARMACOLOGY

Primaquine phosphate is an 8-amino-quinoline compound which eliminates tissue (exo-erythrocytic) infection. Thereby, it prevents the development of the blood (erythrocytic) forms of the parasite which are responsible for relapses in vivax malaria. Primaquine phosphate is also active against gametocytes of *Plasmodium falciparum.*

INDICATIONS AND USAGE

Primaquine phosphate is indicated for the radical cure (prevention of relapse) of vivax malaria.

CONTRAINDICATIONS

Severe glucose-6-phosphate dehydrogenase (G6PD) deficiency (see WARNINGS).

Pregnant women (see WARNINGS, Usage in Pregnancy).

Primaquine phosphate is contraindicated in acutely ill patients suffering from systemic disease manifested by tendency to granulocytopenia, such as rheumatoid arthritis and lupus erythematosus. The drug is also contraindicated in patients receiving concurrently other potentially hemolytic drugs or depressants of myeloid elements of the bone marrow.

Because quinacrine hydrochloride appears to potentiate the toxicity of antimalarial compounds which are structurally related to primaquine, the use of quinacrine in patients receiving primaquine is contraindicated. Similarly, primaquine should not be administered to patients who have received quinacrine recently, as toxicity is increased.

WARNINGS

Hemolytic anemia and G6PD deficiency

Due to the risk of hemolytic anemia in patients with G6PD deficiency, G6PD testing has to be performed before using primaquine. Due to the limitations of G6PD tests, physicians need to be aware of residual risk of hemolysis and adequate medical support and follow-up to manage hemolytic risk should be available.

Primaquine should not be prescribed for patients with severe G6PD deficiency (see CONTRAINDICATIONS).

In case of mild to moderate G6PD deficiency, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of using primaquine. If primaquine administration is considered, baseline hematocrit and hemoglobin must be checked before treatment and close hematological monitoring (e.g. at day 3 and 8) is required. Adequate medical support to manage hemolytic risk should be available.

When the G6PD status is unknown and G6PD testing is not available, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of using primaquine. Risk factors for G6PD deficiency or favism must be assessed. Baseline hematocrit and hemoglobin must be checked before treatment and close hematological monitoring (e.g. at day 3 and 8) is required. Adequate medical support to manage hemolytic risk should be available.

Discontinue the use of primaquine phosphate promptly if signs suggestive of hemolytic anemia occur (darkening of the urine, marked fall of hemoglobin or erythrocytic count).

Hemolytic reactions (moderate to severe) may occur in individuals with G6PD deficiency and in individuals with a family or personal history of favism. Areas of high prevalence of G6PD deficiency are Africa, Southern Europe, Mediterranean region, Middle East, South-East Asia, and Oceania. People from these regions have a greater tendency to develop hemolytic anemia (due to a congenital deficiency of erythrocytic G6PD) while receiving primaquine and related drugs.

Usage in Pregnancy

Safe usage of this preparation in pregnancy has not been established. Primaquine is contraindicated in pregnant women. Even if a pregnant woman is G6PD normal, the fetus may not be (see CONTRAINDICATIONS).

Lactation

It is not known whether primaquine is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from primaquine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PRECAUTIONS

Blood Monitoring

Since anemia, methemoglobinemia, and leukopenia have been observed following administration of large doses of primaquine, the adult dosage of 1 tablet (= 15 mg base) daily for fourteen days should not be exceeded. In G6PD normal patients it is also advisable to perform routine blood examinations (particularly blood cell counts and hemoglobin determinations) during therapy.

If primaquine phosphate is prescribed for an individual who has shown a previous idiosyncratic reaction to primaquine phosphate as manifested by hemolytic anemia, methemoglobinemia, or leukopenia; an individual with a family or personal history of hemolytic anemia or nicotinamide adenine dinucleotide (NADH) methemoglobin reductase deficiency, the person should be observed closely. In all patients, the drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or leukocyte count occurs.

Potential Prolongation of QT Interval

Due to potential for QT interval prolongation, monitor ECG when using primaquine in patients with cardiac disease, long QT syndrome, a history of ventricular arrhythmias, uncorrected hypokalemia and/or hypomagnesemia, or bradycardia (<50 bpm), and during concomitant administration with QT interval prolonging agents (see PRECAUTIONS, Drug Interactions, ADVERSE REACTIONS, and OVERDOSAGE).

Drug Interactions

Caution is advised if primaquine is used concomitantly with other drugs that prolong the QT interval (see PRECAUTIONS, ADVERSE REACTIONS, and OVERDOSAGE).

Geriatric Use

Clinical studies of primaquine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

Gastrointestinal: Nausea, vomiting, epigastric distress, and abdominal cramps.

Hematologic: Leukopenia, hemolytic anemia in G6PD deficient individuals, and methemoglobinemia in nicotinamide adenine dinucleotide (NADH) methemoglobin reductase deficient individuals.

Cardiac: Cardiac arrhythmia and QT interval prolongation (see PRECAUTIONS, OVERDOSAGE).

Nervous System: Dizziness.

Skin and Soft Tissue: Rash, pruritus.

OVERDOSAGE

Symptoms of overdosage of primaquine phosphate include abdominal cramps, vomiting, burning epigastric distress, central nervous system and cardiovascular disturbances, including cardiac arrhythmia and QT interval prolongation, cyanosis, methemoglobinemia, moderate leukocytosis or leukopenia, and anemia. The most striking symptoms are granulocytopenia and acute hemolytic anemia in G6PD deficient patients. Acute hemolysis occurs, but patients recover completely if the dosage is discontinued.

DOSAGE AND ADMINISTRATION

Primaquine phosphate is recommended only for the radical cure of vivax malaria, the prevention of relapse in vivax malaria, or following the termination of chloroquine phosphate suppressive therapy in an area where vivax malaria is endemic. Patients suffering from an attack of vivax malaria or having parasitized red blood cells should receive a course of chloroquine phosphate, which quickly destroys the erythrocytic parasites and terminates the paroxysm. Primaquine phosphate should be administered concurrently in order to eradicate the exoerythrocytic parasites in a dosage of 1 tablet (equivalent to 15 mg base) daily for 14 days.

HOW SUPPLIED

Primaquine phosphate is supplied as pink, convex, discoid, film-coated tablets of 26.3 mg (= 15 mg base), printed with a ″W″ and ″P97″ on one side.

Available in bottles of 100. (NDC 0024-1596-01)

Store at 25° C (77° F); excursions permitted to 15° C – 30° C (59° F – 86° F) [see USP Controlled Room Temperature]

Dispense in tight, light-resistant container as defined in the USP/NF.

CLINICAL STUDIES

Persons with acute attacks of vivax malaria, provoked by the release of erythrocytic forms of the parasite, respond readily to therapy, particularly to chloroquine phosphate. Primaquine eliminates tissue (exoerythrocytic) infection and prevents relapses in experimentally induced vivax malaria in human volunteers and in persons with naturally occurring infections and is a valuable adjunct to conventional therapy in vivax malaria.

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Manufactured for:
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