Each film coated tablet contains: Hydroxychloroquine sulfate, USP 200 mg equivalent to 155 mg of base.

For indications and dosage, see package insert.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

PHARMACIST: Children are especially sensitive to this medication. Tablets should be kept out of their reach.

M.L. No.: 16/VSP/AP/2015/F & B/CC

Manufactured for:
Laurus Generics Inc.
400 Connell Drive
Suite 5200
Berkeley Heights, NJ 07922

Manufactured by:
Laurus Labs Limited
Visakhapatnam-531011
India

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

2000277
Each film coated tablet contains: Hydroxychloroquine sulfate, USP 200 mg equivalent to 155 mg of base.

For indications and dosage, see package insert.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

PHARMACIST: Children are especially sensitive to this medication. Tablets should be kept out of their reach.
Hydroxychloroquine Sulfate Tablets, USP

DESCRIPTION
Hydroxychloroquine sulfate is a white or practically white, crystalline powder, freely soluble in water, practically insoluble in alcohol, and is slightly soluble in conc. sulfuric acid. It is slightly hygroscopic and absorbs moisture from the air.

Hydroxychloroquine sulfate tablets contain hydroxychloroquine sulfate 200 mg equivalent to 155 mg of base, and are for oral administration.

Inactive Ingredients: Croscarmellose sodium, lactose monohydrate and magnesium stearate.

Microbiology - Malaria

Mechanism of action: The precise mechanism by which hydroxychloroquine sulfate exerts its antimalarial activity is not entirely known. Hydroxychloroquine, like chloroquine, is a weak base and is highly subject to effect by concentration in the acid vacuole and by inhibiting polymerization of heme. It also can inhibit certain enzymes by its interaction with DNA.

Activity in vitro and in Clinical Trials: Hydroxychloroquine is active against chloroquine-sensitive and chloroquine-resistant strains of Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, and Plasmodium vivax. Patients treated with hydroxychloroquine sulfate are not active against the gametocytes and syncytium forming forms including the hypnozoites (Stage II, III, IV).

Stage I parasites: P. falciparum strain exhibiting reduced sensitivity to chloroquine also showed reduced susceptibility to hydroxychloroquine.

Resistance of Plasmodium parasites to chloroquine is widespread (see INDICATIONS AND USAGE - Malaria).

Patients in whom chloroquine or hydroxychloroquine have failed to prevent or cure clinical malaria or parasitemia, or patients who acquire malaria in a geographic area where chloroquine resistance is known or occurs, should be treated with another form of antimalarial therapy (see INDICATIONS AND USAGE - Malaria and WARNINGS).

Rheumatoid Arthritis and Systemic Lupus Erythematosus

Mechanism of action: The mechanisms underlying the anti-inflammatory and immunomodulatory effects of hydroxychloroquine sulfate are unknown.

INDICATIONS AND USAGE
Malaria
Hydroxychloroquine sulfate tablets are indicated for the treatment of uncomplicated malaria due to P. falciparum, P. malariae, P. ovale, and P. vivax.

Hydroxychloroquine sulfate tablets are indicated for the prophylaxis of malaria in geographic areas where chloroquine resistance is not reported.

LIMITATIONS OF USE IN MALARIA
- Hydroxychloroquine sulfate tablets are not recommended for the treatment of complications of malaria.
- Hydroxychloroquine sulfate tablets are not effective against chloroquine-resistant Plasmodium species (see CLINICAL PHARMACOLOGY - Microbiology).
- Hydroxychloroquine sulfate tablets are not recommended for the treatment of malaria in geographic areas where chloroquine resistance occurs or when the Plasmodium species has not been identified.
- Hydroxychloroquine sulfate tablets are not recommended for malaria prophylaxis in geographic areas where chloroquine resistance occurs.
- Hydroxychloroquine sulfate tablets do not prevent relapses of P. ovale or P. vivax because it is not active against the hypnozoite forms of these parasites. For radical cure of P. vivax and P. ovale infections, concomitant therapy with an 8-aminoquinoline compound is necessary (see CLINICAL PHARMACOLOGY - Microbiology).

Prior to prescribing hydroxychloroquine sulfate tablets for the treatment of malaria, specific advice should be obtained from the Centers for Disease Control and Prevention (CDC) malaria website (http://www.cdc.gov/malaria).

Lupus Erythematosus
Hydroxychloroquine sulfate tablets are indicated for the treatment of chronic discoid lupus erythematosus and systemic lupus erythematosus.

Rheumatoid Arthritis
Hydroxychloroquine sulfate tablets are indicated for the treatment of acute and chronic rheumatoid arthritis in adults.

CONTRAINDICATIONS
Use of hydroxychloroquine sulfate tablets is contraindicated in patients with known hypersensitivity to 4-aminoquinoline compounds.

WARNINGS
Resistant strains of malaria: Hydroxychloroquine sulfate is not effective against chloroquine-resistant P. falciparum (see CLINICAL PHARMACOLOGY - Microbiology).

Doser: Irreversible retinal damage has been observed in some patients who have taken hydroxychloroquine sulfate greater than 6 mg/kg (5 mg/kg of base) of actual body weight, durations of use greater than five years, subnormal glomerular filtration, use of some concomitant products such as tamsulosine and concurrent molecular disease.

A baseline ophthalmic examination is recommended within the first year of starting hydroxychloroquine sulfate. The baseline exam should include best corrected distance visual acuity (BCVA), full-field (FF) visual field testing, and pertinent ophthalmologic information. Examinations should be repeated annually (see CLINICAL PHARMACOLOGY - Ophthalmic).

For individuals with significant risk factors (daily dose of hydroxychloroquine sulfate greater than 5 mg/kg of actual body weight, subnormal glomerular filtration, use of factors that increase risk for macular disease) monitoring should include annual examinations which include BCVA, VF, and OCT (see INDICATIONS AND USAGE - Malaria and WARNINGS).

Hematomas: Hematomas have been reported in patients with hemolytic disease (e.g., G6PD deficiency). Hydroxychloroquine sulfate should be administered with caution in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Drug Interactions
Cyclophosphamide: Concurrent hydroxychloroquine sulfate and cyclophosphamide therapy may result in increased serum creatinine levels; urinalysis tests should be closely monitored in patients receiving combined therapy.

Insulin or Antidiabetic Drugs: As hydroxychloroquine sulfate may enhance the effects of insulin and oral antidiabetic drugs, patients treated with these agents should be observed carefully for hypoglycemia.

Drugs that prolong QT interval and other arrhythmogenic drugs: Hydroxychloroquine sulfate prolongs the QT interval and should not be administered with other drugs that have the potential to increase the QT interval (see DRUG INTERACTIONS).

Warfarin: Concurrent use of warfarin and hydroxychloroquine sulfate may increase the risk of bleeding. Monitoring of prothrombin times is recommended in patients receiving combined therapy (see CLINICAL PHARMACOLOGY - Microbiology).

Prior to prescribing hydroxychloroquine sulfate tablets for the treatment of lupus erythematosus, specific advice should be obtained from the Centers for Disease Control and Prevention (CDC) lupus website (http://www.cdc.gov/lupus).

Lupus Erythematosus
Hydroxychloroquine sulfate tablets are indicated for the treatment of chronic discoid lupus erythematosus and systemic lupus erythematosus.

Rheumatoid Arthritis
Hydroxychloroquine sulfate tablets are indicated for the treatment of acute and chronic rheumatoid arthritis in adults.
Information for Patients: Patients recommended in some patients. Patients Carcinogenesis, mutagenesis, impairment of ONA extremely sensitive to the toxic effects of especially CVclosone in: defects has been demonstrated. Embryonic death and signs and symptoms of toxicity such as rash or

Teratogenic Effects: Human pregnancies to drug exposure. This drug is known to be

whether they respond differently from younger subjects. However, this drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be necessary to monitor renal function.

Adverse Reactions

The following adverse reactions have been identified during post-approval use of hydroxychloroquine sulfate or other 4-aminoquinoline compounds. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Bleed and lymphatic system disorders: Bone marrow failure, anemia, aplastic anemia, agranulocytosis, neutropenia, and thrombocytopenia. Drug-induced leukopenia with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency.

Cardiac disorders: Conduction abnormalities which result in cardiac failure and in some cases a total oucome (see WARNINGS and USAGE). Hydroxychloroquine sulfate prolongs the QT interval. Ventricular arrhythmias and torsades de pointes have been reported in patients taking hydroxychloroquine sulfate (see OVERDOSAGE and DRUG INTERACTIONS).

Ear and labyrinth disorders: Vertigo, tinnitus, hypacusis, deafness, dizziness.

Eye disorders: Irreversible retinopathy with external retinal changes (half's eye appearance), visual field defects (peripheral scotomas) and visual disturbances (visual acuity, maculopapular (macular degeneration), decreased dark adaptation, color vision abnormalities, central scotomas, and peripheral visual field involvement) and impaired visual accommodation (halo around lights, photophobia, blurred vision).

Gastrointestinal disorders: Nausea, vomiting, diarrhea, and abdominal pain.

General disorders and administration site conditions: Fatigue.

Hepatobiliary disorders: Liver function tests abnormal, hepatic failure acute.

Immune system disorders: Urticaria, angioedema, bronchospasm.

Metabolism and nutrition disorders: Decreased appetite, hypoalbuminemia, polyphagia, weight decreased.

Musculoskeletal and connective tissue disorders: Musculoskeletal pain, pain on movement or masticatory pain, soft tissue disorders and dermatological symptoms.

Neurological disorders: Headache, dizziness, seizures, ataxia and extrapyramidal disorders such as dyskinesia, dyskinesia, and tetanus have been reported with this class of drugs.

Psychiatric disorders: Affective/mood liability, nervousness, irritability, anxiety, depression.

Skin and subcutaneous tissue disorders: Rash, purpura, alopecia, erythematous, maculopapular eruptions including pityriasis amiantacea, Stevens-Johnson syndrome, and toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), photosensitivity, desquamative, and toxic generalized exanthematous pustulosis (TIGEP). ANCA has been distinguished from pleuritis, although hydroxychloroquine sulfate may precipitate attacks of pleuritis. It may be associated with pyrexia and/or hyperleukocytosis.

To report SUSPECTED ADVERSE REACTIONS, contact Merck & Co., Inc., Kenilworth, NJ 07033, 1-800-638-9059, or FDA at 1-888-4-FDA-0888 (1-888-4-FDA-0888) or 1-800-332-1088 (1-800-332-1088) for (DRESS).

OVERDOSAGE

The 4-aminoquinoline compounds are very rapidly and completely absorbed after ingestion, and in accidental overdosage, or with lower doses in hypersensitive patients, toxic symptoms may occur within 50 minutes. The symptoms of overdose may include headache, dizziness, visual disturbances, cardiovascular collapse, convulsions, hypoglycemia, hypocalcemia, hypomagnesemia and cardiac arrest. Treatment is symptomatic and must be prompt. Immediate gastric lavage until the stomach is completely emptied is indicated. After lavage, activated charcoal is introduced by the stomach tube within 30 minutes of ingestion of the drug may inhibit further intestinal absorption. If the drug has been effective, the dose of activated charcoal should be at least five times the estimated dose of hydroxychloroquine ingested.

Consideration should be given to administering diazepam parenterally since studies suggest that it may be beneficial in reversing chloroquine and hydroxychloroquine cardiovascular effects. Respiratory support and shock management should be instituted as necessary. Excitation exchanges are used to reduce the level of 4-aminoquinoline drugs in the blood.

A patient who survives the acute phase and is asymptomatic should be carefully observed for at least six hours. Fluids may be forced and sodium bicarbonate (6 g daily in divided doses for adults) may be administered for a few days to aid the urine. This may prevent urination excretion in cases of both overdose and sensitivity. However, caution must be exercised in patients with impaired renal function and/or metabolic acidosis.

DOSAGE AND ADMINISTRATION

One hydroxychloroquine sulfate tablet contains 200 mg of hydroxychloroquine sulfate, which is equivalent to 155 mg base. Take hydroxychloroquine sulfate tablet with a meal or a glass of milk.

Preparations

Tablet

Adults: 400 mg (310 mg base) once daily for the first 2 weeks prior to exposure, and continued for 4 weeks after leaving the endemic area.

Weight-based dosage in adults and adolescents: 6.5 mg/kg (6 mg/kg base) once daily for the first 2 weeks prior to exposure, and continued for 4 weeks after leaving the endemic area.

Treatment of Uncomplicated Malaria

Adults: 800 mg (600 mg base) followed by 400 mg (310 mg base) at 6 hours, 24 hours and 48 hours after the initial dose (total 2000 mg hydroxychloroquine sulfate or 1550 mg base).

Weight-based dosage in adults and adolescents: 10 mg/kg (9 mg/kg base) once daily for the first 2 weeks prior to exposure, and continued for 4 weeks after leaving the endemic area.

Weight-based dosage in adults and adolescents: 10 mg/kg (9 mg/kg base) once daily for the first 2 weeks prior to exposure, and continued for 4 weeks after leaving the endemic area. Hydroxychloroquine sulfate film-coated tablets cannot be crushed, therefore they should not be used to treat patients who weigh less than 31 kg.

For radical cure of P. vivax and P. malariae infections, concomitant therapy with an 8-aminoquinoline compound is necessary.

Luoos' Chloroquine

The recommended adult dosage is 290 to 400 mg (105 to 130 mg base) daily, administered as a single daily dose or in two divided doses, at least 4 hours apart. Above 400 mg a day are not recommended.

The incidence of retinopathy has been reported to be higher when this maintenance dose is exceeded.

Rheumatoid Arthritis

The action of hydroxychloroquine is cumulative and may require several months to achieve the maximum therapeutic effect (see CLINICAL PHARMACOLOGY).

Initial adult dosage: 400 mg to 600 mg (310 to 465 mg base) daily, administered as a single daily dose or in two divided doses. In a small percentage of patients, side effects may require temporary reduction of the initial dosage.

Maintenance adult dosage: When a good response is obtained, the dosage may be reduced by 50 percent and continued at a maintenance level of 400 mg to 600 mg (310 to 465 mg base) daily, administered as a single daily dose or in two divided doses.