CHLOROQUINE PHOSPHATE - chloroquine phosphate tablet
A-S Medication Solutions

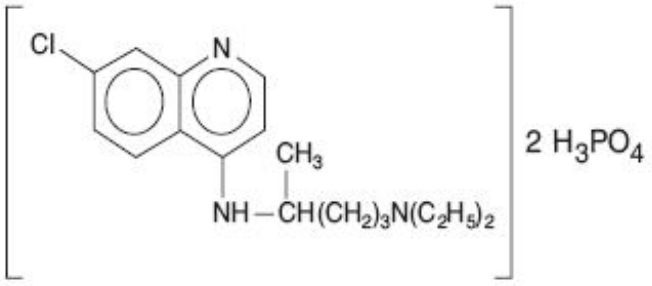
Chloroquine Phosphate Tablet, USP

DESCRIPTION

Chloroquine phosphate tablets 250 mg, chloroquine phosphate, USP, is a 4-aminoquinoline compound for oral administration. It is a white, odorless, bitter tasting, crystalline substance, freely soluble in water.

Chloroquine phosphate is an antimalarial and amebicidal drug.

Chemically, it is 7-chloro-4-[[4- (diethylamino)-1-methylbutyl]amino] quinoline phosphate (1:2) and has the following structural formula:



Each tablet contains 250 mg of chloroquine phosphate USP, equivalent to 150 mg chloroquine base.

Inactive Ingredients: Colloidal silicon dioxide, dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate.

CLINICAL PHARMACOLOGY

Chloroquine is rapidly and almost completely absorbed from the gastrointestinal tract, and only asmall proportion of the administered dose is found in the stools. Approximately 55% of the drug inthe plasma is bound to nondiffusible plasma constituents. Excretion of chloroquine is quite slow,but is increased by acidification of the urine. Chloroquine is deposited in the tissues in considerableamounts. In animals, from 200 to 700 times the plasma concentration may be found in the liver,spleen, kidney, and lung; leukocytes also concentrate the drug. The brain and spinal cord, incontrast, contain only 10 to 30 times the amount present in plasma.

Chloroquine undergoes appreciable degradation in the body. The main metabolite isdesethylchloroquine, which accounts for one fourth of the total material appearing in the urine;bisdesethylchloroquine, a carboxylic acid derivative, and other metabolic products as yetuncharacterized are found in small amounts. Slightly more than half of the urinary drug productscan be accounted for as unchanged chloroquine.

Microbiology

Mechanism of Action: Chloroquine, a 4-aminoquinoline, is an anti-protozoal agent. The

precise mechanism by which chloroquine exhibits activity is not known. Chloroquine, may exert its effect against Plasmodium species by concentrating in the acid vesicles of the parasite and by inhibiting polymerization of heme. It can also inhibit certain enzymes by its interaction with DNA.

Activity *in Vitro* and in Clinical Infections: Chloroquine is active against the erythrocytic forms of susceptible strains of *Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, and Plasmodiumvivax*. Chloroquine is not active against the gametocytes and the exoerythrocytic forms including the hypnozoite stage (*P. vivax and P. ovale*) of the *Plasmodium parasites.*
In vitro studies with Chloroquine demonstrated that it is active against the trophozoites of *Entamoeba histolytica*.

Drug Resistance:

Resistance of Plasmodium parasites to chloroquine is widespread (see INDICATIONS AND USAGE, Limitations of Use in Malaria and WARNINGS).
Plasmodium parasites exhibiting reduced susceptibility to hydroxychloroquine also show reduced susceptibility to chloroquine.
Patients in whom chloroquine or hydroxychloroquine have failed to prevent or cure clinical malaria or parasitemia, or patients who acquired malaria in a geographic area where chloroquine resistance is known to occur should be treated with another form of antimalarial therapy (see WARNINGS and INDICATIONS AND USAGE, Limitations of Use).

INDICATIONS AND USAGE

Chloroquine phosphate is indicated for the:
- Treatment of uncomplicated malaria due to susceptible strains of *P. falciparum, P.malariae, P. ovale, and P.vivax*.
- Prophylaxis of malaria in geographic areas where resistance to chloroquine is not present.
- Treatment of extraintestinal amebiasis.

Chloroquine phosphate tablets do not prevent relapses in patients with vivax or ovale malaria because it is not effective against exoerythrocytic forms of the parasites.
Limitations of Use in Malaria:
- Do not use chloroquine phosphate tablets for the treatment of complicated malaria (high-grade parasitemia and/or complications e.g., cerebral malaria or acute renal failure).
- Do not use chloroquine phosphate tablets for malaria prophylaxis in areas where chloroquine resistance occurs, Resistance to chloroquine phosphate tablets is widespread in *P. falciparum*, and is reported in *P.vivax* (see WARNINGS).
- Concomitant therapy with an 8-aminoquinoline drug is necessary for treatment of the hypnozoite liver stage forms of *P.vivax* and *P.ovale* (see DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS

Use of chloroquine phosphate tablets for indications other than acute malaria is contraindicated in the presence of retinal or visual field changes of any etiology.

Use of chloroquine phosphate tablets is contraindicated in patients with known hypersensitivity to 4-aminoquinoline compounds.

WARNINGS

Chloroquine-Resistant Malaria

Chloroquine phosphate tablets are not effective against chloroquine-or hydroxychloroquine resistant strains of *Plasmodium* species (see CLINICAL PHARMACOLOGY, Microbiology). Chloroquine resistance is widespread in *P. falciparum* and is reported in *P. vivax*. Before using chloroquine for prophylaxis, it should be ascertained whether chloroquine is appropriate for use in the region to be visited by the traveler. Information regarding the geographic areas where resistance to chloroquine occurs, is available at the Centers for Disease Control and Prevention (www.cdc.gov\malaria).

Patients infected with a resistant strain of plasmodia as shown by the fact that normally adequate doses have failed to prevent or cure clinical malaria or parasitemia should be treated with another form of antimalarial therapy.

Treatment of Exo-Erythocytic Forms of Malaria

Chloroquine does not treat the hypnozoite liver stage forms of Plasmodium and will therefore not prevent relapses of malaria due to *P. vivax* or *P. ovale*. Additional treatment with an anti-malarial agent active against these forms, such as an 8-aminoquinoline, is required for the treatment of infections with *P. vivax* and *P. ovale*.

Cardiac Effects

Cases of cardiomyopathy resulting in cardiac failure, in some cases with fatal outcome, have
been reported in patients treated during long term therapy at high doses with chloroquine (see
ADVERSE REACTIONS and OVERDOSAGE). Monitor for signs and symptoms of cardiomyopathy and discontinue chloroquine if cardiomyopathy develops. Chronic toxicity should be considered when conduction disorders (bundle branch block / atrio-ventricular heart block) are diagnosed. If cardiotoxicity is suspected, prompt discontinuation of chloroquine may prevent life-threatening complications. QT interval prolongation, torsades de pointes, and ventricular arrhythmias have been reported. The risk is greater if chloroquine is administered at high doses. Fatal cases have been reported. Chloroquine should be used with caution in patients with cardiac disease, a history of ventricular arrhythmias, uncorrected hypokalemia and/or hypomagnesemia, or bradycardia (<50 bpm), and during concomitant administration with QT interval prolonging agents due to potential for QT interval prolongation (see WARNINGS, PRECAUTIONS, Drug Interactions, ADVERSE REACTIONS and OVERDOSAGE)

Hypoglycemia

Chloroquine has been shown to cause severe hypoglycemia including loss of consciousness
that could be life-threatening in patients treated with or without antidiabetic medications (see
PRECAUTIONS, Drug Interactions). Patients treated with chloroquine phosphate tablets should be warned about the risk of hypoglycemia and the associated clinical signs and symptoms. Patients presenting with clinical symptoms suggestive of hypoglycemia during treatment with chloroquine should have their blood glucose level checked and treatment reviewed as necessary.

Retinopathy[1]

Irreversible retinal damage has been observed in some patients who had received chloroquine. Significant risk factors for retinal damage include daily doses of chloroquine phosphate greater than 2.3 mg/kg of actual body weight, durations of use greater than five years, subnormal glomerular filtration, use of some concomitant drug products such as tamoxifen citrate (see PRECAUTIONS), and concurrent macular disease.
A baseline ophthalmological examination should be performed within the first year of starting
chloroquine phosphate tablets. The baseline exam should include: best corrected distance visual acuity (BCVA), an automated threshold visual field (VF) of the central 10 degrees (with retesting if an abnormality is noted), and spectral domain optical coherence tomography (SD-OCT). For individuals with significant risk factors (daily dose of chloroquine phosphate greater than 2.3 mg/kg of actual body weight, subnormal glomerular filtration, use of tamoxifen citrate or concurrent macular disease) monitoring should include annual examinations which include BCVA, VF and SDOCT.
For individuals without significant risk factors, annual exams (including BCVA, VF and SD-OCT) can usually be deferred until five years of treatment.
In individuals of Asian descent, retinal toxicity may first be noticed outside the macula. In patients of Asian descent, it is recommended that visual field testing be performed in the central 24 degrees instead of the central 10 degrees.
It is recommended that chloroquine be discontinued if ocular toxicity is suspected and the patient should be closely observed given that retinal changes (and visual disturbances) may progress even after cessation of therapy.

Central Nervous System Effects

Acute extrapyramidal disorders may occur with chloroquine (see PRECAUTIONS, ADVERSE
REACTIONS and OVERDOSAGE). These adverse reactions usually resolve after treatment
discontinuation and/or symptomatic treatment.

Muscular Weakness

All patients on long-term therapy with chloroquine should be questioned and examined periodically, including testing knee and ankle reflexes, to detect any evidence of muscular weakness. If weakness occurs, discontinue the drug.

Pediatric Accidental Ingestion

A number of fatalities have been reported following the accidental ingestion of chloroquine,
sometimes in relatively small doses (0.75 g or 1 g chloroquine phosphate in one 3-year-old child). Patients should be strongly warned to keep chloroquine phosphate tablets out of the reach of children because they are especially sensitive to the 4-aminoquinoline compounds (see OVERDOSAGE and ADVERSE REACTIONS).

Worsening of Psoriasis and Porphyria

Use of chloroquine phosphate tablets in patients with psoriasis may precipitate a severe attack of psoriasis. When used in patients with porphyria the condition may be exacerbated. Chloroquine phosphate tablets should not be used in these conditions unless the benefit to the patient outweighs the potential risks.

Usage in Pregnancy

Usage of chloroquine during pregnancy should be avoided except in the prophylaxis or treatment of malaria when the benefit outweighs the potential risk to the fetus.
Radioactively tagged chloroquine administered intravenously to pregnant pigmented CBA mice passed rapidly across the placenta and accumulated selectively in the melanin

structures of the fetal eyes. It was retained in the ocular tissues for five months after the drug had been eliminated from the rest of the body[2]. There are no adequate and well-controlled studies evaluating the safety and efficacy of chloroquine in pregnant women.

PRECAUTIONS

Hematological Effects/Laboratory Tests

Complete blood cell counts should be checked periodically if patients are given prolonged therapy
(see ADVERSE REACTIONS).
Chloroquine may cause hemolysis in glucose-6 phosphate dehydrogenase (G-6-PD) deficiency. Blood monitoring may be needed as hemolytic anemia may occur, in particular in association with
other drugs that cause hemolysis (see ADVERSE REACTIONS).

Auditory Effects

In patients with preexisting auditory damage, chloroquine should be administered with caution. In case of any defects in hearing, chloroquine should be immediately discontinued, and the patient closely observed (see ADVERSE REACTIONS).

Use in Patients with Hepatic Impairment

Since chloroquine phosphate tablets are known to concentrate in the liver, it should be used with
caution in patients with hepatic disease or alcoholism or in conjunction with known hepatotoxic
drugs.

Central Nervous System Effects

Chloroquine may increase the risk of convulsions in patients with a history of epilepsy.

Drug Interactions

Antacids and kaolin: Antacids and kaolin can reduce absorption of chloroquine; an interval of at least4 hours between intake of these agents and chloroquine should be observed.

Cimetidine: Cimetidine can inhibit the metabolism of chloroquine, increasing its plasma level. Concomitant use of cimetidine should be avoided.
Insulin and other antidiabetic drugs: As chloroquine may enhance the effects of a hypoglycemic
treatment, a decrease in doses of insulin or other antidiabetic drugs may be required.
Arrhythmogenic drugs: There may be an increased risk of inducing ventricular arrhythmias if
chloroquine is used concomitantly with other arrhythmogenic drugs, such as amiodarone or
moxifloxacin.

Ampicillin: In a study of healthy volunteers, chloroquine significantly reduced the bioavailability of ampicillin. An interval of at least two hours between intake of ampicillin and chloroquine should be observed.

Cyclosporine: After introduction of chloroquine (oral form), a sudden increase in serum cyclosporine level has been reported. Therefore, close monitoring of serum cyclosporine level is recommended and, if necessary, chloroquine should be discontinued.

Mefloquine: Co-administration of chloroquine and mefloquine may increase the risk of convulsions.

The blood concentrations of chloroquine and desethylchloroquine (the major metabolite of chloroquine, which also has antimalarial properties) were negatively associated with log antibody titers. Chloroquine taken in the dose recommended for malaria prophylaxis can reduce the antibody response to primary immunization with intradermal human diploid-cell rabies vaccine.
Praziquantel: In a single-dose interaction study, chloroquine has been reported to reduce the
bioavailability of praziquantel.
Tamoxifen: Concomitant use of chloroquine with drugs known to induce retinal toxicity such as
tamoxifen is not recommended (see WARNINGS).

Pregnancy

See WARNINGS,Usage in Pregnancy.

Nursing Mothers

Because of the potential for serious adverse reactions in nursing infants from chloroquine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the potential clinical benefit of the drug to the mother.

The excretion of chloroquine and the major metabolite, desethylchloroquine, in breast milk wasinvestigated in eleven lactating mothers following a single oral dose of chloroquine (600 mg base). The maximum daily dose of the drug that the infant can receive from breastfeeding was about 0.7% of the maternal start dose of the drug in malaria chemotherapy. Separate chemoprophylaxis for the infant is required (see DOSAGE AND ADMINISTRATION).

Pediatric Use

See WARNINGS and DOSAGE AND ADMINISTRATION.

Geriatric Use

Clinical studies of chloroquine phosphate did not include sufficient numbers of subjects aged 65and over to determine whether they respond differently from younger subjects. However, this drugis known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug maybe greater in patients with impaired renal function. Because elderly patients are more likely to havedecreased renal function, care should be taken in dose selection and it may be useful to monitorrenal function.

ADVERSE REACTIONS

The following adverse reactions have been identified during post-approval use of chloroquine
or other 4-aminoqunoline 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.

Ocular disorders: Maculopathy and macular degenration have been reported and may be irreversible (see WARNINGS), irreversible retinal damage in patients receiving long-term or high-dosage 4-aminoquinoline therapy; visual disturbances (blurring of vision and difficulty of focusing or accommodation); nyctalopia; scotomatous vision with field defects of paracentral, pericentral ring types, and typically temporal scotomas, e.g., difficulty in reading with words tending to disappear, seeing half an object, misty vision, and fog before the eyes. Reversible corneal opacities have also been reported.

Immune system disorders: Urticaria, anaphylactic reaction including angioedema.

Ear and labyrinth disorders: Nerve type deafness; tinnitus, reduced hearing in patients with preexisting auditory damage.

Musculoskeletal and connective tissue-disorders: Sensorimotor disorders, skeletal muscle myopathy or neuromyopathy leading to progressive weakness and atrophy of proximal muscle groups, depression of tendon reflexes and abnormal nerve conduction.

Gastrointestinal disorders: Hepatitis, increased liver enzymes, anorexia, nausea, vomiting, diarrhea, abdominal cramps.

Skin and subcutaneous tissue disorders: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis. Pleomorphic skin eruptions, skin and mucosal pigmentary changes; lichen planus-like eruptions, pruritus,; drug rash with eosinophilia and systemic symptoms (DRESS syndrome); photosensitivity and hair loss and bleaching of hair pigment.

Blood and lymphatic system disorders: Pancytopenia, aplastic anemia, reversible agranulocytosis, thrombocytopenia and neutropenia. Hemolytic anemia in G6PD deficient patients (see PRECAUTIONS).

Nervous system disorders: Convulsions, mild and transient headache, polyneuropathy, acute extrapyramidal disorders (such as dystonia, dyskinesia, tongue protrusion, torticollis) (see WARNINGS and OVERDOSAGE).

Neuropsychiatric disorders: Neuropsychiatric changes including psychosis, delirium, anxiety, agitation, insomnia, confusion, hallucinations, personality changes, depression, and suicidal behavior.

Cardiac disorders: Hypotension, electrocardiographic changes (particularly, inversion or depression of the T-wave with widening of the QRS complex), and cardiomyopathy (which may result in cardiac failure and in some cases a fatal outcome). Cardiac arrhythmias, conduction disorders such as bundle branch block / atrio-ventricular block, QT interval prolongation, torsade de pointes, ventricular tachycardia and ventricular fibrillation have been reported with therapeutic doses of chloroquine as well as with overdose. The risk is greater if chloroquine is administered at high doses. Fatal cases have been reported (see WARNINGS, Cardiac Effects and OVERDOSAGE).

Metabolic and Nutritional disorders: Hypoglycemia (see WARNINGS).

OVERDOSAGE

Signs and Symptoms: Chloroquine is very rapidly and completely absorbed after ingestion. Toxic doses of chloroquine can be fatal. As little as 1 g may be fatal in children. Toxic symptoms can occur within minutes. The symptoms of overdosage may include nausea, vomiting, headache, drowsiness, visual disturbances, cardiovascular collapse, convulsions, hypokalemia, rhythm and conduction disorders including QT prolongation, torsades de pointes, ventricular tachycardia and ventricular fibrillation, followed by sudden potentially fatal respiratory and cardiac arrest. Immediate medical attention is required, as these effects may appear shortly after the overdose. Cases of extrapyramidal disorders have also been reported in the context of chloroquine overdose (see WARNINGS and ADVERSE REACTIONS).
Treatment: Treatment is symptomatic and must be prompt with immediate evacuation of the stomach by emesis or gastric lavage followed by treatment with activated charcoal. Chloroquine overdose is a life-threatening emergency and should be managed with cardio-respiratory and hemodynamic support, monitoring of potassium along with management of arrhythmias and convulsions, as necessary. A patient who survives the acute phase and is asymptomatic should be closely observed until all clinical features of toxicity resolve.

DOSAGE AND ADMINISTRATION

The dosage of chloroquine phosphate is often expressed in terms of equivalent chloroquine base. Each 250 mg tablet of chloroquine phosphate contains the equivalent of 150 mg chloroquine base. In infants and children the dosage is preferably calculated by body weight.
Prophylaxis against chloroquine-sensitive *Plasmodium* species
Adult Dose: The dosage for prophylaxis is 250 mg (= 150 mg base) administered once per week on exactly the same day of each week.
Pediatric Dose: The dosage for prophylaxis is 5 mg calculated as base, per kg of body weight, administered once per week on exactly the same day of each week. The pediatric dose should never exceed the adult dose regardless of weight.
If circumstances permit, suppressive therapy should begin two weeks prior to exposure. However, failing this in adults, an initial double (loading) dose of 1 g (= 600 mg base), or in children 10 mg base/kg may be taken in two divided doses, six hours apart. The suppressive therapy should be continued for eight weeks after leaving the endemic area.

Treatment of uncomplicated malaria due to chloroquine-sensitive *Plasmodium* species

Adults: An initial dose of 1 g salt (= 600 mg base) followed by an additional 500 mg (= 300 mg base) after six to eight hours and a single dose of 500 mg (= 300 mg base) on each of two consecutive days. This represents a total dose of 2.5 g chloroquine phosphate or 1.5 g base in three days.
Infants and Children: In infants and children, the recommended dose is 10 mg base/kg followed by 5 mg based/kg at 6, 24 and 36 hours (total dose 25 mg based/kg). The pediatric dose should never exceed the adult dose regardless of weight.
The dosage for adults of low body weight and for infants and children should be determined as follows:
First dose: 10 mg base per kg (but not exceeding a single dose of 600 mg base).

Second dose: (6 hours after first dose) 5 mg base per kg (but not exceeding a single dose of 300 mg base).
Third dose: (24 hours after first dose) 5 mg base per kg.
Fourth dose: (36 hours after first dose) 5 mg base per kg.
***P. vivax* and *P. ovale*:** Concomitant therapy with an 8-aminoquinoline compound is necessary for treatment of the hypnozoite liver stage forms of the parasites.
Extraintestinal Amebiasis: Adults Dosage: 1 g salt (600 mg base) daily for two days, followed by 500 mg (300 mg base) daily for at least two to three weeks. Treatment is usually combined with an effective intestinal amebicide.
Geriatric Use
See PRECAUTIONS, Geriatric Use.

HOW SUPPLIED

Product: 50090-4967

NDC: 50090-4967-3 40 TABLET in a BOTTLE

REFERENCES

1. Marmor MF, Kellner U, and Lai TY, et al. Recommendations on Screening for Chloroquine
   and Hydroxychloroquine Retinopathy (2016 Revision). Ophthalmology 2016. Doi10.1016./
   jophtha.2016.01.058
2. Ullberg S, Lindquist N G, Sjostrand S E: Accumulation of chorioretinotoxic drugs in the foetal eye. Nature 1970; 227: 1257.

Rx Only

Manufactured by:
NATCO PHARMA LIMITED

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Manufactured for:
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Saddle Brook, NJ 07663

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Chloroquine Phosphate

CHLOROQUINE PHOSPHATE

chloroquine phosphate tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50090-4967(NDC:64980-177)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CHLOROQUINE PHOSPHATE (UNII: 6E17K3343P) (CHLOROQUINE - UNII:886U3H6UFF)	CHLOROQUINE PHOSPHATE	250 mg

Inactive Ingredients

Ingredient Name	Strength
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	WHITE (White to Off-White)	**Score**	2 pieces
Shape	ROUND (Round, bi-convex)	**Size**	10mm
Flavor		**Imprint Code**	CN250
Contains			

Packaging

			Marketing Start	Marketing End

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50090-4967-3	40 in 1 BOTTLE; Type 0: Not a Combination Product	03/16/2020	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091621	07/01/2011	

Labeler - A-S Medication Solutions (830016429)

Establishment

Name	Address	ID/FEI	Business Operations
A-S Medication Solutions		830016429	RELABEL(50090-4967) , REPACK(50090-4967)

Revised: 2/2023 A-S Medication Solutions