24 mm

For the use only of Registered Medical Practitioner or a Hospital or a Laboratory.

HCQS

Hydroxychloroquine Tablets BP 200 mg

DESCRIPTION

Hydroxychloroquine is a 4-aminoquinoline derivative. Chemically it is 2-[[4-[(7-Chloro-4-quinolyl) amino]pentyl] ethylamino] ethanol sulphate, having molecular weight (base) 433.9 (335.9). Its molecular formula is $C_{18}H_{26}ClN_3O.H_2SO_4$.
White, circular, biconvex film coated tablets.

COMPOSITION

Each film-coated tablet contains:
Hydroxychloroquine Sulfate Ph. Eur. 200mg

PHARMACOLOGY

Hydroxychloroquine is structurally and pharmacologically very similar to chloroquine. It differs from chloroquine by having a hydroxyethyl group in place of an ethyl group on the -4-N atom. It has been found to be useful as an anti-inflammatory, and anti-thrombotic agent. It also produces beneficial effects in conditions associated with light sensitivity.
The cellular and molecular mechanisms involved in all these recognised pharmacological actions of hydroxychloroquine are largely unknown.
Hydroxychloroquine is thought to act as a mild immunosupressant, inhibiting the production of rheumatoid factor and acute phase reactants. In rheumatoid arthritis, hydroxychloroquine acts as a DMARD (disease modifying antirheumatic drug). It has several pharmacological actions, which may be involved in their therapeutic effect in the treatment of rheumatoid disease, but the role of each is not known. These include interaction with sulphydryl groups, interference with enzyme activity (including phospholipase, NADH-cytochrome C reductase, cholinesterase, collagenase, proteases and hydrolases), DNA binding, stabilisation of lysosomal membranes, inhibition of prostaglandin formation, inhibition of polymorphonuclear cell chemotaxis and phagocytosis, possible interference with interleukin 1 production from monocytes and inhibition of neutrophil superoxide release.
Hydroxychloroquine therapy may lead to the regression of the skin lesions of discoid or systemic lupus erythematosus.

PHARMACOKINETICS

Hydroxychloroquine is rapidly and almost completely absorbed orally. Bioavailability is approximately 74%. It is widely distributed in body tissues such as the eyes, kidneys, liver, and lungs where retention is prolonged. Concentrations are 2-5 times higher in erythrocytes than in plasma. Very low concentration is present in intestinal wall. The drug crosses placenta also. It has moderate protein binding (approximately 45%). It is metabolized in liver, to active de-ethylated metabolites. Hydroxychloroquine has a terminal elimination half-life of approximately 50 days in blood and approximately 32 days in plasma. 23-25% of hydroxychloroquine is excreted in urine in unchanged form. Hydroxychloroquine is excreted very slowly; may persist in urine for months or years after medication is discontinued. It is also excreted in bile. Hemodialysis does not remove appreciable amount of hydroxychloroquine from blood.

INDICATIONS

Hydroxychloroquine is indicated for:
1. Acute or chronic rheumatoid arthritis
2. Systemic and discoid lupus erythematosus

DOSAGE AND ADMINISTRATION

Adults (including the elderly)
The minimum effective dose should be employed. This dose should not exceed 6.5mg/kg/day (calculated from ideal body weight and not actual body weight) and will be either 200mg or 400mg per day.
In patients able to receive 400mg daily
Initially 400mg daily in divided doses. The dose can be reduced to 200mg when no further improvement is evident. The maintenance dose should be increased to 400mg daily if the response lessens.
Children
The minimum effective dose should be employed and should not exceed 6.5mg/kg/day based on ideal body weight. The 200mg tablet is therefore not suitable for use in children with an ideal body weight of less than 31kg.
Each dose should be taken with a meal or glass of milk.
Hydroxychloroquine is cumulative in action and will require several weeks to exert its beneficial effects, whereas minor side effects may occur relatively early. For rheumatic disease treatment should be discontinued if there is no improvement by 6 months. In light-sensitive diseases, treatment should only be given in periods of maximum exposure to light.

CONTRAINDICATIONS

Hydroxychloroquine is contraindicated:
i. In patients who are hypersensitive to 4-aminoquinoline compounds
ii. In patients with retinal or visual field changes attributable to any 4-aminoquinoline compound
iii. For long term therapy in children
iv. Pre-existing maculopathy of the eye
v. Pregnancy

WARNINGS & PRECAUTIONS

Hydroxychloroquine
Suicidal behaviour and psychiatric disorders
Suicidal behaviour and psychiatric disorders have been reported in some patients treated with hydroxychloroquine. Psychiatric side effects typically occur within the first month after the start of treatment with hydroxychloroquine and have been reported also in patients with no prior history of psychiatric disorders.
Patients should be advised to seek medical advice promptly if they experience psychiatric symptoms during treatment.
General
The occurrence of retinopathy is very uncommon if the recommended daily dose is not exceeded. The administration of doses in excess of the recommended maximum is likely to increase the risk of retinopathy, and accelerate its onset.
All patients should have an ophthalmological examination before initiating treatment with HCQS. Thereafter, ophthalmological examination must be repeated at least every 12 months.
The examination should include testing visual acuity, careful ophthalmoscopy, fundoscopy, central visual field testing with a red target, and colour vision.
This examination should be more frequent and adapted to the patients in the following situations:
- Daily dosage exceeds 6.5 mg/kg lean body weight. Absolute body weight used as a guide to dosage could result in an overdosage in the obese.
- Renal insufficiency
- Visual acuity below 6/8
- Age above 65 years.
- Cumulative dose more than 200 g.

HCQS should be discontinued immediately in any patient who develops a pigmentary abnormality, visual field defect, or any other abnormality not explainable by difficulty in accomodation or presence of corneal opacities. Patients should continue to be observed for possible progression of the changes.
Patients should be advised to stop taking the drug immediately and seek the advise of their prescribing doctor if any disturbances of vision are noted, including abnormal colour vision.
HCQS should be used with caution in patients taking medicines, which may cause adverse ocular or skin reactions.
Caution should also be applied when it is used in the following:
- Patients with hepatic or renal disease, and in those taking drugs known to affect those organs. Estimation of plasma hydroxychloroquine level should be undertaken in patients with severely compromised renal or hepatic function and dosage adjusted accordingly.
- Patients with severe gastrointestinal, neurological or blood disorders.

Although the risk of bone marrow depression is low, periodic blood counts are advisable as anaemia, aplastic anaemia, agranulocysis, a decrease in white blood cells, and throbocytopenia have been reported. HCQS should be discontinued if abnormalities develop.
Caution is also advised in patients with sensitivity to quinine, those with glucose-6-phosphate dehydrogenase deficiency, those with porphyria cutanea tarda which can be exacerbated by hydroxychloroquine and in patients with psoriasis since it appears to increase the risk of skin reactions.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Small children are particularly sensitive to the toxic effects of 4-aminoquinolines; therefore patients should be warned to keep HCQS out of reach of children.
All patients on long-term therapy should undergo periodic examination of skeletal muscle function and tendon reflexes. If weakness occurs, the drug should be withdrawn.
Drug Induced Phospholipidosis
Cases of hydroxychloroquine induced phospholipidosis have been reported during use of HCQS tablet 200mg (see section Adverse Effects).
Drug-induced phospholipidosis may occur in different organ systems such as cardiac, renal, or muscle. Monitoring for toxicity is advised.
Discontinue hydroxychloroquine if cardiac, renal, or muscle toxicity related to drug induced phospholipidosis is suspected or demonstrated by tissue biopsy.
Aggravation of Myasthenia Gravis
Aggravation of symptoms of myasthenia gravis (generalized weakness

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including shortness of breath, dysphagia, diplopia, ptosis etc.) have been reported in myasthenic patients receiving hydroxychloroquine therapy. Discontinue hydroxychloroquine if aggravation of symptoms related to myasthenia gravis is suspected.

Effects on ability to drive and use machines:

Impaired visual accommodation soon after the treatment has been reported and patients should be warned regarding driving or operating machinery. If the condition is not self-limiting, it will resolve on reducing the dose or stopping treatment.

Pregnancy

Hydroxychloroquine crosses the placenta. Data are limited regarding the use of hydroxychloroquine during pregnancy. It should be noted that 4-aminoquinolines in therapeutic doses have been associated with central nervous system damage, including ototoxicity (auditory and vestibular toxicity, congenital deafness), retinal hemorrhages and abnormal retinal pigmentation. Therefore hydroxychloroquine should not be used in pregnancy.

Data from a population-based cohort study including 2045 hydroxychloroquine exposed pregnancies suggests a small increase in the relative risk (RR) of congenital malformations associated with hydroxychloroquine exposure in the first trimester (n = 112 events). For a daily dose of ≥ 400 mg the RR was 1.33 (95% CI, 1.08 – 1.65). For a daily dose of < 400 mg the RR was 0.95 (95% CI, 0.60 – 1.50).

Lactation

Careful consideration should be given to using hydroxychloroquine during lactation, since it has been shown to be excreted in small amounts in human breast milk, and it is known that infants are extremely sensitive to the toxic effects of 4-aminoquinolines.

ADVERSE DRUG REACTIONS

Hydroxychloroquine

SOC Psychiatric disorders

Common: Affect lability

Uncommon: Nervousness

Not known: suicidal behaviour, psychosis, depression, hallucinations, anxiety, agitation, confusion, delusions, mania and sleep disorders.

Skin and subcutaneous tissue disorders:

Frequency 'not known': Sweet's syndrome

The lower toxicity of hydroxychloroqine makes it more popular than chloroquine for use in conditions where relatively high drug dosages are required over long periods.

Ocular side effects

Retinopathy with changes in pigmentation and visual field defects can occur, but appears to be uncommon, if the recommended daily dose is not exceeded. In its early form it appears reversible on discontinuation of hydroxychloroquine. If allowed to develop, there may be a risk of progression even after treatment withdrawal.

Corneal changes including oedema and opacities have been reported. They are symptomless or may cause disturbances such as halos, blurring vision or photophobia. They may be transient and are reversible on stopping treatment.

Blurring of vision due to disturbances of accommodation, which is dose dependant and reversible on cessation of therapy may also occur.

Dermatological side effects

Skin rashes some times occur; pigmentary changes in skin and mucous membrane, bleaching of hair and hair losses have also been reported. These usually resolve readily on stopping treatment. Isolated cases of exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP) have been reported. Hydroxychloroquine can also precipitate or exacerbate porphyria and may precipitate attack of psoriasis.

Gastrointestinal side effects

These include nausea, diarrhea, anorexia, abdominal cramps and rarely, vomiting. These symptoms usually resolve immediately on reducing the dose or stopping treatment.

Isolated cases of abnormal liver function tests and rare cases of fulminant hepatic failure have been reported.

CNS side effects

Irritability, nervousness, emotional changes, nightmares, psychosis, headache, dizziness, vertigo, tinnitus, nystagmus, nerve deafness, convulsions, ataxia.

Neuromuscular side effects

Skeletal muscle palsies or skeletal muscle myopathy or neuromyopathy leading to progressive weakness and atrophy of proximal muscle groups which may be associated with mild sensory changes, depression of tendon reflexes and abnormal nerve conduction.

Hematologic side effects

Various blood dyscrasias such as aplastic anemia, agranulocytosis, leukopenia, thrombocytopenia (hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency).

Metabolism and nutrition disorders

Frequency 'not known': phospholipidosis*

*Cases of hydroxychloroquine induced phospholipidosis have been reported. Drug-induced phospholipidosis may occur in different organ systems such as cardiac, renal, or muscle causing toxicity (see section Warnings and Precautions).

Miscellaneous

Weight loss, lassitude, exacerbation or precipitation of porphyria and nonlight-sensitive psoriasis.

Cardiomyopathy has been rarely reported with high daily dosages of hydroxychloroquine.

DRUG INTERACTION

Hydroxychloroquine sulfate has been reported to increase plasma digoxin levels. Serum digoxin levels should be closely monitored in-patients receiving combined therapy.

Hydroxychloroquine sulfate may also be subjective to several known interactions of chloroquine even though specific reports have not been appeared. These include: potentiation of its direct blocking at the neuromuscular junction by aminoglycoside antibiotics; inhibition of its metabolism by cimetidine which may increase plasma concentration of the drug; antagonism effect of neostigmine and pyridostigmine; reduction of the antibody response to primary immunisation with intradermal human-diploid cell rabies vaccine.

As with chloroquine, antacids may reduce absorption of hydroxychloroquine so it is advised that a 4 hour interval be observed between hydroxychloroquine and antacid dosing.

Concurrent use of penicillamine with hydroxychloroquine may increase penicillamine plasma concentrations, increasing the potential for serious hematologic and/or renal adverse reactions, as well as the possibility of severe skin reactions.

Elevated cyclosporine concentrations may occur, when aminoquinolines (e.g. Hydroxychloroquine) is given along with cyclosporine, increasing the risk of nephrotoxicity. Consider monitoring cyclosporine and serum creatinine levels. Adjust cyclosporine dose accordingly.

OVERDOSAGE

Overdosage with the 4-aminoquinolines is especially dangerous in infants. About 1-2g has proved fatal. Death can occur within 2h of overdosage. An adult male is reported to have survived an overdose of 36 tablets (200mg per tablet) and a plasma level of 6.1mg/L.

The symptoms of massive overdose may include headache, visual disturbances, cardiovascular collapse and convulsions, followed by sudden and early respiratory and cardiac arrest. Since these effects may appear soon after taking a massive dose, treatment should be prompt and symptomatic. The stomach should be immediately evacuated either by emesis or by gastric lavage. Finely powdered charcoal in a dose at least five times of the overdose may inhibit further absorption if introduced into the stomach by tube following lavage and within 30 minutes of ingestion of the overdose.

Consideration should be given to administration of parenteral diazepam in cases of overdosage; it has been shown to reverse chloroquine cardiotoxicity.

Respiratory support may be needed and the need for intubation or tracheostomy considered. Shock should be treated by the administration of fluid (with plasma expanders if necessary) with central venous pressure monitoring. In severe cases, the administration of dopamine should be considered.

A patient who survives the acute phase and is asymptomatic should be closely observed for at least 6 hours.

STORAGE

Store below 30ºC, in a dry place

KEEP OUT OF REACH OF CHILDREN

PRESENTATION

Blister strip of 10 tablets

Pack of 30's tablets per box

DATE OF REVISION

Dec. 2025

Product Registration Holder:
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