

NEW ZEALAND DATA SHEET

Q200 & Q300

Quinine sulfate 200mg and 300mg tablets



Presentation

Q200 Tablets: Clear film coated white biconvex tablet, 3/8" diameter, imprinted Q200 on one side. Each Q200 tablet contains 200mg of quinine sulfate.

Q300 Tablets: Clear film coated white biconvex tablet, 7/16" diameter, imprinted Q300 on one side. Each Q300 tablet contains 300mg of quinine sulfate.

Uses

Actions

Quinine sulfate is a rapidly acting blood schizontocide with activity against *Plasmodium falciparum*, *P.vivax*, *P.ovale* and *P.malariae*. It is active against the gametocytes of *P.malariae* and *P.vivax* but not against *P.falciparum* gametocytes.

The precise mechanism of action of quinine in malaria has not been determined but may be based on its ability to concentrate in parasitic acid vesicles causing an elevation of pH and thereby disrupting intracellular activity. Quinine increases the refractory period of skeletal muscle by direct action on the muscle fibre thereby diminishing the response to tetanic stimulation. It also decreases the excitability of the motor end-plate region, reducing the responses to repetitive nerve stimulation and to acetylcholine.

Pharmacokinetics

Quinine is rapidly and almost completely absorbed from the gastrointestinal tract. Peak concentrations in the circulation are attained about 1 to 3 hours after ingestion and about 70% is bound to proteins in the plasma in healthy subjects rising to about 90% in patients with malaria. Quinine is widely distributed throughout the body. Concentrations attained in the CSF are about 2 to 7% of those in the plasma. Quinine is extensively metabolised in the liver and excreted in the urine. Estimates of the proportion of unchanged quinine excreted in the urine vary from less than 5% to 20%. Excretion is increased in acid urine. The elimination half-life is about 11 hours in healthy subjects but may be prolonged in patients with malaria. The pharmacokinetics of quinine are altered significantly by malaria infection, with reductions in both the apparent volume of distribution and clearance. Quinine crosses the placenta and is excreted in the breast milk.

Indications

Quinine is indicated concurrently with tetracycline or clindamycin or pyrimethamine plus sulphadiazine or sulphadoxine in the treatment of chloroquine-resistant malaria caused by *Plasmodium falciparum*.

Quinine is indicated in the treatment of myotonia.

Dosage and Administration

Q200 and Q300 may be taken with or after meals to minimise gastrointestinal irritation.

Usual Adult and Adolescent Dose

Malaria

For chloroquine-resistant *Plasmodium falciparum* malaria:

Oral, 600 to 650mg every eight hours for at least three days in most areas of the world (seven days in Southeast Asia) with concurrent or consecutive administration of 250mg of tetracycline every six hours for seven days; or concurrent administration of 1.5 grams of sulfadoxine and 75mg of pyrimethamine combination as a single dose; or concurrent or consecutive administration of 900mg of clindamycin three times a day for three days.

Antimyotonic

Oral, 300 to 650mg two or three times a day.

Usual Paediatric Dose

Malaria

For chloroquine-resistant *Plasmodium falciparum* malaria:

Oral, 8.3mg per kg of body weight every eight hours for at least three days in most areas of the world (seven days in Southeast Asia) with concurrent or consecutive administration of 5mg per kg of body weight of tetracycline every six hours for seven days in children over 8 years of age; or concurrent or consecutive administration of 6.7 to 13.3mg per kg of body weight of clindamycin three times a day for three days; or concurrent administration of 1.25mg per kg of body weight of pyrimethamine in combination with 25mg per kg of body weight of sulfadoxine as a single dose.

Antimyotonic

Dosage has not been established.

Contraindications

Quinine is contraindicated in patients with a history of hypersensitivity to quinine, in the presence of haemolysis, and in patients with tinnitus or optic neuritis. It should be used with caution in patients with atrial fibrillation or other serious heart disease. Quinine may cause hypoprothrombinaemia and enhance the effects of anticoagulants. Quinine may aggravate the symptoms of myasthenia gravis and should be used with care if at all in such patients.

Pregnancy in a patient with malaria is not generally regarded as a contraindication to the use of quinine. Risk-benefit should be considered when the following medical problems exist:

- a history of Blackwater fever
- glucose-6-phosphate dehydrogenase (G6PD) deficiency hypoglycemia

Warnings and Precautions

Quinine should be used with caution in patients with atrial fibrillation or other serious heart disease.

Quinine should be avoided in patients with myasthenia gravis as it may aggravate their condition and cause severe respiratory distress and dysphasia.

Glucose-6-phosphate dehydrogenase deficient patients with malaria are at increased risk of haemolysis during quinine therapy. Treatment should be monitored in all patients in case signs of resistance develop.

Quinine can affect the results of certain urine tests for alkaloids and steroids. It may also interfere with tests for plasma catecholamines as well as slowing the erythrocyte sedimentation rate.

Administration of quinine may give rise to cinchonism, which is generally more severe in overdose, but may also occur in normal therapeutic doses. Patients should be warned not to exceed the prescribed dose, because of the possibility of serious, irreversible side effects in overdose. Such symptoms include tinnitus, impaired hearing, headache, nausea and disturbed vision.

Patients hypersensitive to quinidine may be hypersensitive to this medication also. Hypersensitivity to quinine may also occur with symptoms of cinchonism together with urticaria, flushing pruritus, rash, fever, angioedema, dyspnoea and asthma.

Q200 and Q300 Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy and Lactation

Pregnancy

Quinine may cause congenital abnormalities of the CNS and extremities. Following administration of large doses during pregnancy, phototoxicity and deafness have been reported in neonates. Quinine sulfate should not be used during pregnancy unless the benefits outweigh the risks.

Pregnancy in a patient with malaria is not generally regarded as a contraindication to the use of quinine. As malaria infection is potentially serious during pregnancy and poses a threat to the mother and foetus, there appears to be little justification in withholding treatment in the absence of a suitable alternative.

Breastfeeding

Quinine sulfate is excreted in breast milk, but no problems in humans have been reported. However, quinine sulfate should not be given to nursing mothers unless the benefits outweigh the risks.

Use in Children

Appropriate studies with quinine for use as an antimyotonic have not been performed in the paediatric population. Antimalarial studies performed to date have shown that children have a decreased elimination half-life and volume of distribution; however, paediatrics-specific problems that would limit the usefulness of quinine in children have not been documented.

Adverse Effects

Cinchonism is more common in overdose, but may occur even after normal doses of quinine. In its mild form symptoms include tinnitus, impaired hearing, rashes, headache, nausea and disturbed vision. Its more serious manifestation symptoms may include gastrointestinal symptoms, oculotoxicity, CNS disturbances, cardiotoxicity and death. Visual disorders may include blurred vision, defective colour perception, visual field constriction and total blindness.

Cinchonism may also occur after small doses in patients hypersensitive to quinine but urticaria and flushing of the skin with intense pruritis are the most frequent reactions seen in these patients. Other effects include fever, rashes and dyspnoea.

Hypersensitivity reactions such as angioneurotic oedema may also occur and asthma may be precipitated. Thrombocytopenic purpura has also been associated with quinine hypersensitivity. Haemoglobinuria and myopathy rarely occur. Circulatory collapse may also occur as a result of quinine hypersensitivity and lead to renal failure.

Thrombocytopenia, hypoprothrombinaemia, haemolysis agranulocytosis, hypoglycaemia and acute renal failure have also been reported.

Interactions

The following drug interactions have been noted with quinine sulfate. Combinations containing any of the following medications depending on the amount present may also interact with quinine sulfate.

Anticoagulants, coumarin or indandione-derivative
Antihistamines
Buclizine
Cyclizine
Meclizine
Phenothiazines
Thioxanthenes
Trimethobenzamide
Antimyasthenics
Digitoxin

Digoxin
Hemolytics
Neurotoxic medications
Ototoxic medications
Mefloquine
Neuromuscular blocking agents
Quinidine

Quinine may cause hypoprothrombinaemia and thereby enhance the effect of anticoagulants. Concurrent use of quinidine may increase the possibility of cinchonism.

Quinine may potentiate the effects of digoxin in plasma by up to 100%. Consideration should be given to reducing the maintenance dose of digoxin.

Quinine may cause increased plasma concentrations of flecainide.

Cimetidine, which inhibits metabolism, may cause increased plasma-quinine concentrations.

Quinine sulfate has been observed to interfere with Urinary 17-ketogenic steroid determinations.

Overdosage

Quinine overdosage may lead to serious and irreversible side effects and can be fatal. In acute overdosage, symptoms of cinchonism may occur, including convulsions, nausea, vomiting, tinnitus, deafness, headache, vasodilatation and disturbed vision. The visual disorders may be severe and there may be impaired consciousness, coma, respiratory depression, arrhythmia and cardiogenic shock. Fatalities have been reported in adults after doses of 2-8g. High doses of quinine are teratogenic and may cause miscarriage.

The effects of oculotoxicity may include blurred vision, defective colour perception, visual field constriction and total blindness. The onset of symptoms may vary from a few hours to a day or more after ingestion. Visual disturbances are usually slowly reversible but there may be residual damage.

The effects associated with cardiovascular toxicity include conduction abnormalities, ventricular dysrhythmias, anginal symptoms and hypotension leading to cardiac arrest and circulatory failure. Hypokalaemia may also occur.

Treatment

Quinine is rapidly absorbed. In patients who present within one hour of ingestion an overdose gastric lavage may be considered, but the risk of aspiration must be considered, especially if there is CNS depression or drowsiness. Multiple doses of activated charcoal may be considered. Other treatment is mostly symptomatic to maintain blood pressure, respiration, renal function and treating arrhythmia.

Pharmaceutical Precautions

Store below 25°C. Protect from light.

Medicine Classification

Prescription Medicine.

Package Quantities

Q200 Tablets: 100's & 250's

Q300 Tablets: 500's

Not all strengths and/or pack sizes may be marketed.

Further Information

Quinine Sulfate is (8S,9R)-6'-methoxycinchonan-9-ol sulfate dihydrate. It has a molecular weight of 783.0 and a formula of $(C_{20}H_{24}N_2O_2)_2, H_2SO_4, 2H_2O$.

Each Q200 tablet contains 200mg of active ingredient, quinine sulfate. It also contains lactose, magnesium stearate, povidone, sodium starch glycollate and carnauba wax. The film coating contains ethanol, chloroform, diethyl phthalate and hypromellose. Q200 is gluten free.

Each Q300 tablet contains 300mg of active ingredient, quinine sulfate. It also contains lactose, magnesium stearate, povidone, sodium starch glycollate and carnauba wax. The film coating contains ethanol, diethyl phthalate, purified water and hypromellose. Q300 is gluten free.

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