

Medication Guide

INTRAVENOUS ADMINISTRATION

Adults and children: an initial dose of 20 mg of quinine dihydrochloride / kg is infused over 4 hours followed by 10 mg / kg every 8 hours in adults and every 12 hours in children. The maintenance doses should be reduced threefold in patients with

impaired renal function. Pulse and blood pressure should be closely monitored during administration and the rate of infusion reduced if dysrhythmias occur. The required dose, diluted preferably in 5% (w/v) glucose solution to counteract hypoglycaemia, is given in a total volume of 5-10 ml/kg by infusion into a large vein. In the absence of glucose, physiological saline may be used. This method of administration minimizes the danger of severe hypotension and subsequent respiratory collapse. Parenteral treatment should be discontinued as soon as the patient is able to take quinine orally.

ORAL ADMINISTRATION

Quinine should be given orally to adults per 500 mg base (equivalent to quinine sulfate dihydrate 600 mg) every 8 hours for 7 or 10 days.

Children: 8.2 mg (equivalent to quinine sulfate dihydrate 10 mg)/kg every 8 hours for 7 or 10 days.

The duration of treatment depends on the local susceptibility of *P. falciparum* to quinine and on whether treatment is combined with pyrimethamine/sulfadoxine, clindamycin or tetracycline.

PHARMACOLOGY

When administered by oral route, quinine is rapidly absorbed and plasma peak concentrations are attained 1-3 hours after. It is highly protein-bound but it readily crosses the placental barrier and small amounts penetrate into the cerebrospinal fluid. It is metabolized in the liver, has a plasma half-life of 10 hours and is subsequently excreted in the urine, mainly as hydroxylated metabolites.

Quinine mechanism of action is not yet fully resolved but the accepted hypothesis is based on inhibition of hemozoin biocrystallization in heme detoxification pathway which facilitates the aggregation of cytotoxic heme. Free cytotoxic heme accumulates in the parasites causing therefore their deaths.

ADVERSE EFFECTS

Quinine can adversely affect almost every body system. The most common adverse events associated with quinine use are a cluster of symptoms called "cinchonism", which occurs to some degree in almost all patients taking quinine. Symptoms of mild cinchonism include headache, vasodilatation and sweating, nausea, tinnitus, hearing impairment, vertigo, or dizziness, blurred vision, and disturbance in color perception. More severe symptoms of cinchonism are vomiting, diarrhea, abdominal pain, deafness, blindness, and disturbances in cardiac rhythm or conduction. But most symptoms of cinchonism are reversible and resolve with discontinuation of quinine.

The following adverse reactions have been reported with quinine sulfate. Because these reactions have been 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.