Taj Pharmaceuticals Ltd.

Quinine Sulfate

CAS No. : 130-95-0

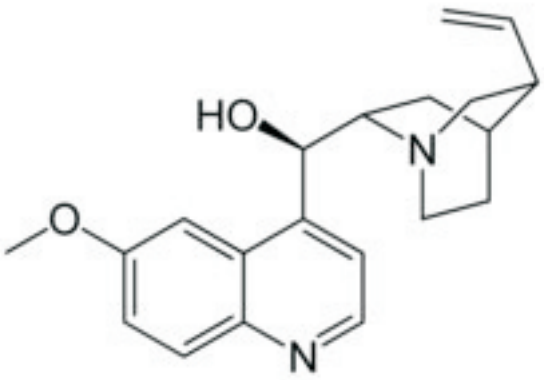
Systematic (IUPAC) name

(R)-(6-methoxyquinolin-4-yl)((2S,4S,8R)- 8-vinylquinuclidin-2-yl)methanol

Identifiers

CAS number 130-95-0
ATC code M09AA01 P01BC01
PubChem 8549
DrugBank APRD00563
ChemSpider 84989

Chemical data



Formula C20H24N2O2
Mol. mass 324.417 g/mol
Physical data
Melt. point 177 °C (351 °F)

Pharmacokinetic data

Bioavailability 76 to 88%
Protein binding ~70%
Metabolism Hepatic (mostly CYP3A4 and CYP2C19-mediated)
Half life ~18 hours
Excretion Renal (20%)

Therapeutic considerations

Pregnancy cat:. C (USA), D (Au)
Legal status: quinine is now banned in Australia unless specifically for Malaria due to its tendency to kill blood platelets.
Routes: Oral, intravenous

Quinine is an effective muscle relaxant, long used by the Quechua Indians of Peru to halt shivering due to low temperatures. The Peruvians would mix the ground bark of cinchona trees with sweetened water to offset the bark's bitter taste, thus producing tonic water.

Quinine has been used in unextracted form by Europeans since at least the early 17th century. Quinine was first used to treat malaria in Rome in 1631. During the 17th century, malaria was endemic to the swamps and marshes surrounding the city of Rome. Malaria was responsible for the death of several popes, many cardinals and countless common Roman citizens. Most of the priests trained in Rome had seen malaria victims and were familiar with the shivering brought on by the febrile phase of the disease. The Jesuit brother Agostino Salumbrino (1561–1642), an apothecary by training who lived in Lima, observed the Quechua using the bark of the cinchona tree for that purpose. While its effect in treating malaria (and hence malaria-induced shivering) was unrelated to its effect in controlling shivering from rigors, it was still a successful medicine for malaria. At the first opportunity, Salumbrino sent a small quantity to Rome to test as a malaria treatment. In the years that followed, cinchona bark was known as Jesuit's bark and became one of the most valuable commodities shipped from Peru to Europe.

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The form of quinine most effective in treating malaria was found by Charles Marie de La Condamine in 1737. Quinine was isolated and named in 1820 by French researchers Pierre Joseph Pelletier and Joseph Bienaimé Caventou. The name was derived from the original Quechua (Inca) word for the cinchona tree bark, "quina" or "quina-quina", which roughly means "bark of bark" or "holy bark". Prior to 1820, the bark was first dried, ground to a fine powder and then mixed into a liquid (commonly wine) which was then drunk. Large scale use of quinine as a prophylaxis started around 1850.

Quinine also played a significant role in the colonization of Africa by Europeans. It has been said that quinine was the prime reason that Africa ceased to be known as the "white man's grave". A historian has stated that "it was quinine's efficacy that gave colonists fresh opportunities to swarm into the Gold Coast, Nigeria and other parts of west Africa".

To maintain their monopoly on cinchona bark, Peru and surrounding countries began outlawing the export of cinchona seeds and saplings beginning in the early 19th century. The Dutch government persisted in its attempt to smuggle the seeds, and by the 1930s Dutch plantations in Java were producing 22 million pounds of cinchona bark, or 97% of the world's quinine production. During World War II, Allied powers were cut off from their supply of quinine when the Germans conquered Holland and the Japanese controlled the Philippines and Indonesia. The United States, however, had managed to obtain four million cinchona seeds from the Philippines and began operation of cinchona plantations in Costa Rica. Nonetheless, such supplies came too late; tens of thousands of U.S. troops in Africa and the South Pacific died due to the lack of quinine. Despite controlling the supply, the Japanese did not make effective use of quinine, and thousands of Japanese troops in the Southwest Pacific died as a result.

Synthetic quinine
Main article: quinine total synthesis

Cinchona trees remain the only economically practical source of quinine. However, under wartime pressure, research towards its synthetic production was undertaken. A formal chemical synthesis was accomplished in 1944 by American chemists R.B. Woodward and W.E. Doering. Since then, several more efficient quinine total syntheses have been achieved, but none of them can compete in economic terms with isolation of the alkaloid from natural sources. The first synthetic organic dye, mauveine, was discovered by William Henry Perkin in 1856 while he was attempting to synthesize quinine.

Dosing and indication

As of 2006, quinine is no longer recommended by the WHO as first line treatment for malaria and should be used only when artemesinins are not available. Quinine is a basic amine and is therefore always presented as a salt. Various preparations that exist include the hydrochloride, dihydrochloride, sulfate, bisulfate and gluconate. This makes quinine dosing complicated since each of the salts has a different weight.
The following amounts of each form are equal:

* quinine base 100 mg
* quinine bisulfate 169 mg
* quinine dihydrochloride 122 mg
* quinine hydrochloride 111 mg
* quinine sulfate (actually (quinine)2H2SO4·2H 2O) 121 mg
* quinine gluconate 160 mg.

All quinine salts may be given orally or intravenously; quinine gluconate may also be given intramuscularly (IM) or rectally (PR). The main problem with the rectal route is that the dose can be expelled before it is completely absorbed; this can be corrected by giving a half dose again.

The IV dose of quinine is 8 mg/kg of quinine base every eight hours; the IM dose is 12.8 mg/kg of quinine base twice daily; the PR dose is 20 mg/kg of quinine base twice daily. Treatment should be given for seven days.

The preparations available in the UK are quinine sulfate (200 mg or 300 mg tablets) and quinine hydrochloride (300 mg/ml for injection). Quinine is not licensed for IM or PR use in the UK. The adult dose in the UK is 600 mg quinine dihydrochloride IV or 600 mg quinine sulfate orally every eight hours. For nocturnal leg cramps, the dosage is 200–300 mg at night.

In the United States, quinine sulfate is commercially available in 324-mg tablets under the brand name Qualaquin; the adult dose is two tablets every eight hours. There is no injectable preparation of quinine licensed in the U.S.: quinidine is used instead.

USES

This medication is used to treat a parasite infection of the red blood cells (malaria caused by Plasmodium falciparum). Quinine sulfate belongs to a class of drugs known as antimalarials. It works by killing the form of the malaria parasite that infects the red blood cells.It has not been shown to work for this use and may cause serious side effects.

HOW TO USE

Read the Patient Information Leaflet provided by your pharmacist before you start using quinine and each time you get a refill. If you have any questions, consult your doctor or pharmacist.

Take this medication by mouth with or without food exactly as prescribed by your doctor. This medication is usually taken every 8 hours for 7 days or as directed by your doctor. If you have stomach upset with quinine, take it with food.

Dosage is based on your kidney function, medical condition, and response to therapy.

It is very important to continue taking this medication exactly as prescribed by your doctor. This medication works best when the amount of drug in your body is kept at a constant level. Therefore, take this drug at evenly spaced intervals. To help you remember, take it at the same times each day.

Do not take more or less of this drug than prescribed. Do not stop taking it before completing this prescription unless directed to do so by your doctor, even if you feel better. Skipping or changing your dose without approval from your doctor may cause the amount of parasite to increase, make the infection more difficult to treat (resistant), or worsen side effects.

SIDE EFFECTS

Headache, flushing, unusual sweating, nausea, ringing in the ears, decreased hearing, dizziness, blurred vision, and temporary changes in color vision may occur. Less common side effects may include signs of low blood sugar (e.g., sweating, shakiness, confusion, extreme hunger). If you experience these symptoms, promptly drink some fruit juice or have a snack, and call your doctor immediately. If any of these effects persist or worsen, tell your doctor or pharmacist promptly. Tell your doctor immediately if any of these rare but very serious side effects occur: signs of a serious immune system problem (e.g., unusual tiredness, joint/muscle aches, unusual fever, butterfly-shaped facial rash, swollen glands), easy bruising/bleeding, signs of serious infection (e.g., high fever, severe chills, persistent sore throat), signs of a sudden loss of red blood cells called hemolytic anemia (e.g., severe tiredness, brown urine, pale lips/nails/skin, rapid breathing at rest), signs of severe liver problems (e.g., persistent nausea/vomiting, abdominal pain, severe weakness, yellow skin/eyes, unusually dark urine), decrease in the amount of urine. A very serious allergic reaction to this drug is rare.

However, seek immediate medical attention if you notice any symptoms of a serious allergic reaction, including: rash, itching, swelling, severe dizziness, trouble breathing.

PRECAUTIONS

Before taking quinine, tell your doctor or pharmacist if you are allergic to it; or to quinidine or mefloquine; or if you have any other allergies.

This medication should not be used if you have certain medical conditions. Before using this medicine, consult your doctor or pharmacist if you have: previous serious side effects with quinine (e.g., blood problems), certain heart problems (congenital or acquired long QT syndromes, torsade de pointes), very low blood potassium, a certain enzyme problem (glucose-6-phosphate dehydrogenase deficiency-G6PD), a certain nerve/muscle disease (myasthenia gravis), a certain eye nerve problem (optic neuritis).

Before using this medication, tell your doctor or pharmacist your medical history, especially of: certain heart rhythm problems (atrial fibrillation/flutter), kidney problems, severe liver problems, family history of favism/G6PD deficiency.

This drug may make you dizzy. Use caution while driving, using machinery, or doing any activity that requires alertness. Avoid alcoholic beverages.

Before having surgery, tell your doctor or dentist that you are taking this medication.
Caution is advised when using this drug in the elderly because they may be more sensitive to the effects of the drug, especially dizziness, irregular heartbeat, and low blood sugar.

MISSED DOSE

If you miss a dose, take it as soon as you remember. If it is within 4 hours of the time for the next dose, skip the missed dose and resume your usual dosing schedule. Do not double the dose to catch up.

STORAGE

Store at room temperature between 77-86 degrees F (25-30 degrees C) away from light and moisture. Do not store in the bathroom. Keep all medicines away from children and pets.

DOSAGE

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Dosage is based on your kidney function, medical condition, and response to therapy.

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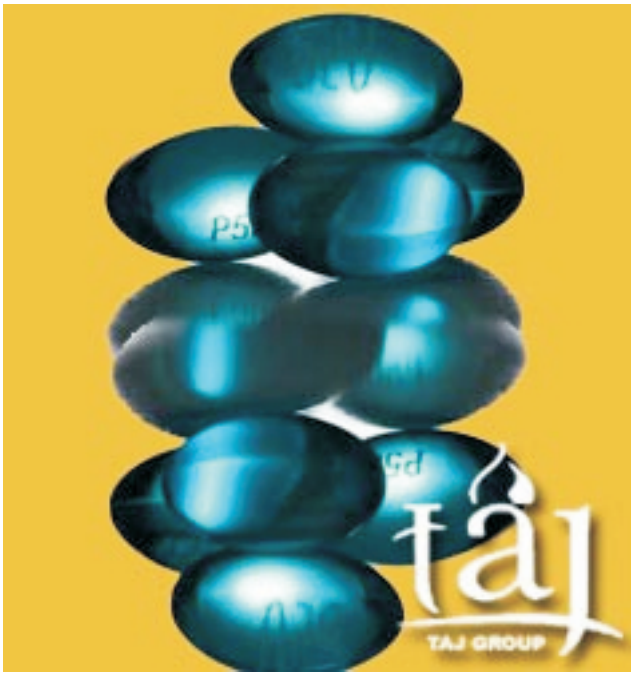
* quinine dihydrochloride 122 mg
* quinine hydrochloride 111 mg
* quinine sulfate



quinine gluconate 160 mgAll quinine salts may be given orally or intravenously (IV); quinine gluconate may also be given intramuscularly (IM) or rectally (PR).
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DRUG DESCRIPTION

Quinine is a natural white crystalline alkaloid having antipyretic (fever-reducing), antimalarial, analgesic (painkilling), and anti-inflammatory properties and a bitter taste. It is a stereoisomer of quinidine.

Quinine was the first effective treatment for malaria caused by Plasmodium falciparum, appearing in therapeutics in the 17th century. It remained the antimalarial drug of choice until the 1940s, when other drugs took over. Since then, many effective antimalarials have been introduced, although quinine is still used to treat the disease in certain critical situations Quinine is also used to treat nocturnal leg cramps and arthritis, and there have been attempts (with limited success) to treat prion diseases. It was once a popular heroin adulterant and is now not as popular in the world.
quinine sulfateis an antimalarial drug chemically described as cinchonan-9-ol, 6'-methoxy-, (8a, 9R)-, sulfate (2:1) (salt), dihydrate with a molecular formula of (C20H24N2O2)2•H2SO4•2H2O and a molecular weight of 782.96.
Quinine sulfate occurs as a white, crystalline powder that darkens on exposure to light. It is odorless and has a persistent very bitter taste. It is only slightly soluble in water, alcohol, chloroform, and ether.
Qualaquin is supplied for oral administration as capsules containing 324 mg of the active ingredient quinine sulfate USP, equivalent to 269 mg free base. Inactive ingredients: corn starch, magnesium stearate, and talc.

Note /Government Notification: These chemicals are designated as those that are used in the manufacture of the controlled substances and are important to the manufacture of the substances. For any (Control Substance) products Import and Export *** subjected to your country government laws /control substance ACT.

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The Controlled Substances Act (CSA) was enacted into law by the Congress of the United States as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1] The CSA is the federal U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. The Act also served as the national implementing legislation for the Single Convention on Narcotic Drugs

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http://www.tajapi.com
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