SUMMARY OFPRODUCTCHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICALPRODUCT

Quinine Sulfate Tablets USP 300mg (M-QUINE)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION:

Each Film Coated tabletContains:
Quinine Sulfate USP 300mg
For the full list of excipients, see section6.1.

3. PHARMACEUTICALFORM

Yellow coloured, Circular slightly bi-convex film coated tablet.

4. Clinicalparticulars

4.1 Therapeuticindications

a) Treatment of uncomplicated attacks of falciparum malaria due to chloroquine ormulti-drug resistant strains.

b) Treatment and prevention of nocturnal leg cramps in adults and the elderly, whencramps cause regular disruption of sleep (see section 4.2 and Section 4.4).

4.2 Posology and method of administration

For treatment of uncomplicated (falciparum) malaria:

Adult (including elderly) and children aged 12 years and over: 600mg of Quinine Sulfate every eight hours for 7 days. The dose may depend upon the size of the patient, severity of infection, and evidence of renal or liver disease (when the intervals should be increased), due to a prolonged half-life of the drug.

If quinine resistance is known or suspected on completion of the course additional treatment may be given. This may be one of the following:

1. Doxycycline 200mg daily (as a single dose or in 2 divided doses) for at least 7 days.

2. Clindamycin 300mg four times daily for 5 days.

Children aged 11 years and under: Equivalent of 10mg/kg Quinine Sulfate every eight hours for 7 days,

For the treatment and prevention of nocturnal leg cramps:

Adults (including elderly): The recommended dose is 200mg at bedtime. The maximum dose is 300mg. A reduction in frequency of leg cramps may take up to 4 weeks to become apparent. Patients should be monitored closely during the early stages of treatment for adverse effects. After an initial trial of 4 weeks, treatment should be stopped if there is no benefit. Treatment should be interrupted at approximately three monthly intervals to reassess the benefit of treatment.

Method of Administration

For oral administration.

4.3 Contraindications

- Known hypersensitivity to quinine or any of the excipients in the tablet
- Haemoglobinuria
- Optic neuritis
- Tinnitus
- Myasthenia gravis, quinine may cause severe respiratory distress anddysphagia in these patients.

4.4 Special warnings and precautions for use

Cinchonism

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. Treatment for night cramps should be stopped if symptoms of cinchonism emerge. Such symptoms include tinnitus, impaired hearing; headache, nausea, and disturbed vision (see section 4.8 and 4.9).

Hypersensitivity

Hypersensitivity to quinine may also occur with symptoms of cinchonism together with urticaria, flushing, pruritus, rash, fever, angioedema, dyspnoea and asthma.

Cardiac disorders

Quinine should be used with caution in patients with atrial fibrillation orother serious heart disease. It may cause hypoprothrombinaemia.

Glucose-6-Phosphate Dehydrogenase (G-6-PD) Deficiency

- The administration of quinine to a patient who has previously beensuffering from a chronic and inadequately controlled malarial infectionmay precipitate an attack of blackwater fever. However, in some casesdeficiency of glucose-6-phosphate dehydrogenase may have beeninvolved. Glucose-6-phosphate dehydrogenase deficient patients withmalaria or taking quinine to treat leg cramps may be at increased risk ofhaemolysis during quinine therapy. Quinine may aggravate the symptomsof myasthenia gravis.
- Quinine can affect the results of certain urine tests for alkaloids andsteroids. It may also interfere with tests for plasma catecholamines as wellas slowing the erythrocyte sedimentation rate.

- Quinine should not be withheld from pregnant women who have lifethreatening malaria (see section 4.6).
- Treatment with quinine should be monitored in case signs of resistancedevelop.
- Before use for nocturnal leg cramps, the risks, which include significantadverse effects and interactions (see sections 4.5 and 4.8), should becarefully considered relative to the potential benefits. These risks arelikely to be of particular concern in the elderly. Quinine should only beconsidered when cramps are very painful or frequent, when other treatablecauses of cramp have been ruled out, and when nonpharmacologicalmeasures have not worked. Quinine Sulfate should not be used for thisindication during pregnancy (see Section 4.6).
- Quinine may cause unpredictable serious and life-threatening thrombocytopenia, which is thought to be an idiosyncratic hypersensitivity reaction. Quinine should not be prescribed or administered to patients who have previously experienced any adverse reaction to quinine, including that in tonic water or other beverages. Patients should be instructed to stop treatment and consult a physician if signs of thrombocytopenia such as unexplained bruising or bleeding occur.
- Excessive amounts of beverages containing quinine should not be consumed while taking quinine, as this may increase the risk of adverse reactions and toxicity.
- Reduce the dosage (or increase intervals between doses) in renal or hepatic disease.
- Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactosemalabsorption or sucraseisomaltase insufficiency should not take this medicine, as it contains lactose.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of other drugs on quinine

Quinine is metabolised via hepatic oxidative cytochrome P450 pathways,predominantly by CYP3A4. There is the potential for increased quininetoxicity with concurrent use of potent CYP3A4 inhibitors, which include azoleantifungal drugs and HIV protease inhibitors.

Sub-optimal quinine serum levels may result from concomitant use ofCYP3A4 inducers, which include rifampicin, barbiturates, carbamazepine andphenytoin.

Care should be taken when quinine is used in combination with other CYP3A4substrates, especially those causing prolongation of the QT interval.

Effect of quinine on other drugs

The plasma concentration of mefloquine may be increased. Concomitantadministration of mefloquine and quinine may produce electrocardiogramabnormalities and increase the risk of convulsions.

Amantadine: Quinine can reduce the renal clearance of amantadine.

Ciclosporin: Quinine can decrease plasma concentrations of ciclosporin.

Cardiac glycosides: Quinine increases plasma concentrations of cardiacglycosides and reduced dosage of concomitant cardiac glycosides such asdigoxin to half the maintenance dose may be necessary.

Other drug interactions

There is an increased risk of ventricular arrhythmias with other drugs whichprolong the QT interval, including amiodarone, moxifloxacin, pimozide,thioridazine and halofantrine. Co-administration of other drugs known to altercardiac conduction (e.g. anti-arrhythmic or ß-adrenergic blocking agents, calciumchannel blockers, some antihistamines or H1-blocking agents, tricyclic antidepressantsand antipsychotics) might also contribute to a prolongation of the QT interval.

Antiarrhythmics: Concomitant use of amiodarone should be avoided due to theincreased risk of ventricular arrhythmias. The plasma concentration offlecainide is increased by quinine. Concomitant use of quinidine may increasethe possibility of cinchonism.

Antibacterials: There is an increased risk of ventricular arrhythmias whenmoxifloxacin is given with quinine. Rifampicin can reduced the serum levelsof quinine, therefore reducing its therapeutic effect.

Concurrent use with oral hypoglycaemics may increase the risk ofhypoglycaemia.

Anticoagulants Quinine may cause hypoprothrombinaemia and enhance theeffects of anticoagulants, i.e. Warfarin.

Antihistamines: Concomitant use of terfenadine should be avoided due to theincreased risk of ventricular arrhythmias.

Antimalarials: According to the manufacturer of artemether with lumefantrineconcomitant use should be avoided. Chloroquine and quinine appear to beantagonistic when given together for *P falciparum* malaria. There is a decreasein plasma concentrations of primaquine.

Concomitant use of quinidine may increase the possibility of cinchonism.

Antipsychotics: There is an increased risk of ventricular arrhythmias andconcomitant use should be avoided with pimozide or thioridazine.

Suxamethonium: Quinine enhances the neuromuscular effects ofsuxamethonium.

Ulcer-healing drugs: Clearance of quinine was reduced and half-life increasedin patients pre-treated with cimetidine.

4.6 Fertility, 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. Treatment of falciparum malaria: Pregnancy in patients with malaria is not generally regards 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.

Prophylaxis of nocturnal leg-cramps: Quinine Sulfate should not be used during pregnancy to treat cramps.

Lactation

Quinine Sulfate is excreted in breast milk, but no problems in humans havebeen reported. However, quinine Sulfate should not be given to nursingmothers unless the benefits outweigh the risks.

4.7 Effects on ability to drive and use machines

Quinine may cause visual disturbances and vertigo, hence patients should be advised that if affected they should not drive or operate machinery.

4.8 Undesirable effects

Cinchonism is more common in overdose, but may occur even after normaldoses of quinine. In its mild form symptoms include tinnitus, impairedhearing, rashes, headache, nausea and disturbed vision. Its more severemanifestations symptoms may include gastrointestinal symptoms,oculotoxicity, CNS disturbances, cardiotoxicity and death (see section 4.9).

Visual disorders may include blurred vision, defective colour perception,visual field constriction and total blindness

MedDRA system organclass	AdverseReaction
Blood and lymphatic systemdisorders	Thrombocytopenia, intravascular coagulation,hypoprothrombinaemia, haemoglobinuria, oliguria,haemolytic- uremic syndrome, pancytopenia, haemolysis,agranulocytosis,
Immune systemdisorders	Generalised hypersensitivity reactions includingangioneuroticoedema andfever
Metabolism and nutritiondisorders	Hypoglycaemia
Psychiatricdisorders	Agitation,confusion

Nervous systemdisorders	Headache,vertigo
Eyedisorders	Blurred vision, defective colour perception, visual fieldconstriction
Ear and labyrinthdisorders	Tinnitus, impairedhearing
Cardiacdisorders	Atrioventricular conduction disturbances,hypotension, prolongation of the QT interval, widening of the QRScomplex and T waveflattening
Respiratory, thoracic andmediastinal disorders	Bronchospasm
Gastrointestinaldisorders	Nausea, vomiting, diarrhoea, abdominalpain
Skin and subcutaneous tissuedisorders	Flushing, rash, urticaria, eczematous dermatitis, oedema,erythema, lichen planus,
Musculoskeletal and connectivetissue disorders	Muscle weakness, aggravation of myastheniagravis
Renal and urinarydisorders	Renal insufficiency, acute renalfailure
Reproductive system and breast disorders	Toxic doses of quinine may induce abortion, but it is unwise to withhold the drug if less toxic antimalarials are not available

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinalproduct is important. It allows continued monitoring of the benefit/risk balanceof the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme(www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in theGooglePlay or Apple App Store.

4.9 Overdose

Symptoms:

Quinine over dosage may lead to serious and irreversible side effects and can be fatal. In acute over dosage, symptoms of cinchonism may occur, including convulsions, nausea, vomiting, tinnitus, deafness, headache, vasodilatation, disturbed vision, QT prlogation and renal failure**.** The visual disorders may be severe and there may be impairment of consciousness, coma, respiratory depression, arrhythmia and cardiogenic shock. Fatalities have been reported in adults after doses of 2 – 8 g. High doses of quinine are teratogenic and may cause miscarriage. Hypokalaemia and hypoglycaemia may also occur.

Treatment:

Children (< 5 years) who have ingested any amount should be referred tohospital. Older children and adults should be referred to hospital if more than30 mg/kg of quinine base has been taken.

Consider activated charcoal (50 g for adults; 1 g/kg for children) if the patientpresents within 1 hour of ingestion of more than 30 mg/kg quinine base or anyamount in a child under 5 years. Multiple dose activated charcoal will enhancequinine elimination.

Observe patients for at least 12 hours after ingestion. Monitor cardiacconduction and rhythm, serum electrolytes, blood glucose and visual activity.

Other treatment is mostly symptomatic to maintain blood pressure, respiration,renal function and treating arrhythmia, convulsions, hypoglycaemia andacidosis.

Note: that each 200 mg tablet is equivalent to 165 mg quinine base,each 300 mg tablet is equivalent to 248 mg quinine base.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:Quinine alkaloid,

ATC code:P01BC01.

Quinine is a rapidly acting blood schizontide with activity against Plasmodiumfalciparum, P. vivax, P. ovale and P. malariae. It is active against thegametocytes of P. malariae and P. vivax, but not against P. falciparumgametocytes. Since it has no activity against exoerythrocytic forms quinine does not produce a radical cure in vivax or ovale malarias. Quininesupresses the asexual cycle of development of the malarial parasite in theerythrocytes through interference with its DNA.

On skeletal muscle quinine has dual action; it acts directly on muscle fibre andalso effects muscular transmission by increasing the threshold of excitabilityof the motor end-plate.

5.2Pharmacokineticproperties

Quinine is rapidly and almost completely absorbed from the gastro-intestinaltract. Peak concentrations in the circulation are attained about 1 to 3 hoursafter ingestion. About 70% is bound to proteins in plasma in healthy subjectsrising to 90% in patients with malaria. Quinine is widely distributedthroughout the body. Concentrations in CFS are 2 to 7% of those in theplasma. Quinine is extensively metabolized in the liver and excreted in theurine. Unchanged quinine in urine vary from less than 5 to 20%. Excretion isincreased in acid urine. Elimination half-life is about 11 hours in healthysubjects but may be prolonged in patients with malaria. Pharmacokinetics arcaltered significantly by malarial infection, with reduction in volume ofdistribution and clearance.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose (Monohydrate) BP
- Maize Starch BP
- Sodium Lauryl Sulphate BP
- Talc USP
- Gelatin NF
- HPMC E-15 BP
- Sodium Propyl Paraben BP
- Magnesium Stearate BP
- Microcrystalline Cellulose (PH 101) BP
- Colloidal silicon dioxide NF
- Titanium dioxide BP
- Tartrazine Lake INH
- PEG 400 NF
- Isopropyl Alcohol BP
- Methylene Chloride NF

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.

6.5 Nature and contents ofcontainer

Presentation: Quinine Sulfate Tablets USP 300mg (M-QUINE) is available as10 x 10’s, 100 x 10's PVC Blister pack and 1000's Bulk pack..

Primary Container (s):

Quinine Sulfate Tablets USP 300mg (F/C) (M-QUINE) is available as PVC Blister pack.

10x10's& 100x 10’s - Each blister contains 10 tablets

Description and composition of primary packaging materials:

Blister pack:

- Printed blister Foil
- PVC Film clear

Bulk pack: Poly bag

Secondary packing:

Such blisters are packed in cartons of GSM 300, made of ITC cyber XL board with aqua varnish.Carton is printed in Multicolor.

Leaflet: leaflet made with 70 GSM Map Lithopaper.

Outer Container:

Such cartons are packed in Export Worthy 5/7 Ply Shippers. These shippers are labelled with product name and relevant batch details and sealed with BOPP tape. Shippers are then strapped with Polypropylene tapes.

Transportation: Should be transported with precautions.

The Cautions Like- This Side Up

- Not For Loose Handling
- Protect from Water
- Avoid Vigorous Transportation Not all pack sizes may be marketed.

6.6 Special precautions for disposal and otherhandling

None

7. MARKETING AUTHORIZATIONHOLDER

Name and Permanent address of the Marketing authorization holder:

Medopharm

"MEDO HOUSE"

25, Puliyur II Main road, Trustpuram, Chennai-600 024, Tamil Nadu, India.

PH: +91 44-30149992/30149955

Fax: 260211 286283

Manufacturing Site address:

MEDOPHARM
34-B Industrial Area,

Malur-563160, Kolar District,

KarnatakaIndia

8. NUMBER (S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

08379/09885/NMR/2022

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

13.01.2023

10. DATE OF REVISION OF THE TEXT

13.07.2023