SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

QUININE SULPHATE TABLETS B.P. 300 MG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Label claim

Each Sugar coated tablet contains:

Quinine Sulphate B.P. 300mg

List of Excipients:

Maize Starch, Cros carmellose sodium, Sodium Methyl Paraben, Sodium Propyl Paraben, Gelatin, Magnesium Stearate, Talcum, Aerosil, Gum Acacia, Sugar, Titanium Dioxide, Solvent Methylene Chloride, Carnauba wax, Bees wax.

3. PHARMACEUTICAL FORM

White coloured, circular, biconvex sugar coated tablets with "QUININE 300" printed on one side of each tablet and other side plain.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the treatment of falciparum malaria.

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

4.2 Posology and method of administration

Posology

For the treatment of falciparum malaria

Adults

600mg (two tablets) every eight hours for seven days.

Paediatric population

*Children:*10mg/kg bodyweight every eight hours for seven 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.

Paediatric population

Children under ten years: Not recommended

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 use

4.3 Contraindications

Quinine is contraindicated in patients with a history of hypersensitivity to the active substance or any of the excipients listed in section 6.1, in tinnitus or optic neuritis, in myasthenia gravis and in the presence of haemolysis or haemoglobinuria. As quinine has been implicated in precipitating blackwater fever**,** it is generally contraindicated in patients who have already suffered an attack.

4.4 Special warnings and precautions for use

Before use for nocturnal leg cramps, the risks, which include significant adverse effects and interactions (see sections 4.5 and 4.8), should be carefully considered relative to the potential benefits. These risks are likely to be of particular concern in the elderly. Quinine should only be considered when cramps are very painful or frequent, when other treatable causes of cramp have been ruled out, and when non-pharmacological measures have not worked. Quinine Sulfate should not be used for this indication 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.

Cardiac disorders

Quinine has dose-dependent QT-prolonging effects. Caution is recommended in patients with conditions which predispose to QT-prolongation and in patients with atrioventricular block. Quinine should be used with caution in patients with atrial fibrillation, heart block, other cardiac conduction defects, or other serious heart disease. Quinine may cause hypoprothrombinaemia and enhance the effects of anticoagulants.

Quinine has been implicated in precipitating blackwater fever when given for prolonged periods, although in some cases, glucose-6-phosphate dehydrogenase deficiency may have been involved. Patients with glucose-6-phosphate dehydrogenase deficiency may be at increased risk of haemolysis during quinine therapy and may develop acute haemolytic anaemia.

Patients with rare hereditary problems of galactose intolerance, total lactose deficiency or glucose-galactose malabsorption should not take this medicine.

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 sections 4.8 and 4.9).

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

This medicine contains methyl hydroxyl benzoate (E218) which may cause allergic reactions (possibly delayed).

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 quinine toxicity with concurrent use of potent CYP3A4 inhibitors, which include azole antifungal drugs and HIV protease inhibitors.

Sub-optimal quinine serum levels may result from concomitant use of CYP3A4 inducers, which include rifampicin, barbiturates, carbamazepine and phenytoin.

Care should be taken when quinine is used in combination with other CYP3A4 substrates, especially those causing prolongation of the QT interval.

Other drug interactions

Amantadine: reduced renal clearance of amantadine with risk of amantadine toxicity (including headache, nausea, dizziness).

Analgesics: increased risk of ventricular arrhythmias with levacetylmethadol (avoid concomitant use).

Anti-arrhythmics: plasma concentration of flecainide increased. Increased risk of ventricular arrhythmias with other drugs which prolong the QT interval, including amiodarone (avoid concomitant use). Concomitant use of quinidine may increase the possibility of cinchonism.

Antibacterials: increased elimination of quinine reported with rifampicin. There is an increased risk of ventricular arrhythmias with moxifloxacin.

Anticoagulants: quinine may cause hypoprothrombinaemia and enhance effects of anticoagulants.

Caution is advised when administering quinine with drugs which could prolong the QT interval.

Quinine may increase the levels of phenobarbital and of carbamazepine. Patients should be monitored closely during concomitant use of quinine with these agents.

Anti-histamines: increased risk of ventricular arrhythmias with astemizole and terfenadine.

Other antimalarials: There may be an increased risk of side effects if quinine is used with other antimalarials, for example, chloroquine, halofantrine and mefloquine (increased risk of convulsions), although this should not prevent their use in severe cases. Quinine may increase the plasma concentration of mefloquine. Chloroquine and quinine appear to be antagonistic when given together for P falciparum malaria. There is an increased risk of ventricular arrhythmias with halofantrine.

Antipsychotics: increased risk of ventricular arrhythmias with pimozide or thioridazine (avoid concomitant use).

Cardiac glycosides: Quinine may increase the plasma concentration of digoxin and it has been recommended that the maintenance dose of digoxin should be halved during concurrent therapy.

Ulcer healing drugs: cimetidine inhibits metabolism (increased plasma quinine concentration).

Quinine can decrease plasma concentrations of ciclosporin.

Concurrent use with oral hypoglycaemics may increase the risk of hypoglycaemia .

Quinine enhances the neuromuscular effects of suxamethonium.

4.6 Fertility, pregnancy and lactation

Pregnancy

Large doses of quinine can induce abortion. Congenital malformations of the optic and auditory nerves have been reported after quinine has failed to induce abortion. Quinine Sulfate should not be used during pregnancy unless the benefits outweigh the risks. However, pregnancy in a patient with malaria is not generally regarded as a contraindication to the use of quinine and it should not be withheld from pregnant women with life threatening malaria if other agents are inappropriate. Quinine Sulfate should not be used during pregnancy to treat cramps.

Breast-feeding

Quinine Sulfate is excreted in breast milk, but no problems in humans have been reported. Infants at risk for glucose-6-phosphate dehydrogenase deficiency should not be breast-fed until this disease can be ruled out. However, quinine Sulfate should not be given to nursing mothers unless the benefit 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

MedDRA system organ class	Adverse Reaction

Blood and lymphatic system disorders	Thrombocytopenia, intravascular coagulation, hypoprothrombinaemia, haemoglobinuria, oliguria, haemolytic-uremic syndrome, pancytopenia, haemolysis, agranulocytosis, thrombocytopenic purpura
Immune system disorders	Generalised hypersensitivity reactions including angioneurotic oedema and fever
Metabolism and nutrition disorders	Hypoglycaemia
Psychiatric disorders	Agitation, confusion
Nervous system disorders	Headache, vertigo
Eye disorders	Blurred vision, defective colour perception, visual field constriction
Ear and labyrinth disorders	Tinnitus, impaired hearing
Cardiac disorders	Atrioventricular conduction disturbances, hypotension, prolongation of the QT interval, widening of the QRS complex and T wave flattening
Respiratory, thoracic and mediastinal disorders	Bronchospasm
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, abdominal pain
Skin and subcutaneous tissue disorders	Flushing, rash, urticaria, eczematous dermatitis, oedema, erythema, lichen planus, pruritis, photosensitivity
Musculoskeletal and connective tissue disorders	Muscle weakness, aggravation of myasthenia gravis
Renal and urinary disorders	Renal insufficiency, acute renal failure

Reporting of suspected adverse reactions

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

4.9 Overdose

Acute intoxication can be seen after ingestion of doses of 4-12g, but a dose of 8g can prove lethal. The average fatal dose for an adult is about 8g although deaths have been reported from as little as 1.5g in an adult and 900mg in a child.

Symptoms: Quinine overdosage may lead to serious side effects including irreversible visual loss, and can be fatal.

Symptoms include vomiting, tinnitus, deafness, headache, and visual disturbance.

Features of a significant overdose include convulsions, impairment of consciousness, respiratory depression, QT prolongation, ventricular arrhythmia, cardiogenic shock and renal failure. 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 to hospital. Older children and adults should be referred to hospital if more than 30 mg/kg of quinine base has been taken.

Each 300 mg tablet is equivalent to 248 mg quinine base.

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

Observe patients for at least 12 hours after ingestion. Monitor cardiac conduction and rhythm, serum electrolytes, blood glucose and visual acuity.

Other treatment is symptomatic to maintain blood pressure, respiration, renal function and to treat arrhythmia, convulsions, hypoglycaemia and acidosis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Quinine alkaloid, ATC code: P01B C01

Quinine is a highly active blood schizonticide and suppresses the asexual cycle of development of malaria parasites in the erythrocytes. It has no action on the tissue forms of the malaria parasites and therefore will not prevent relapse of *Plasmodium vivax*, P. *ovale* or P. *malariae* infections.

5.2 Pharmacokinetic properties

Quinine is almost completely absorbed from the gastrointestinal tract. Maximal blood concentrations are attained within one to three hours of ingestion. Most of the quinine is bound to plasma proteins. Quinine readily diffuses across the placenta. Quinine is extensively metabolised, mainly in the liver, and only a small proportion is excreted unchanged.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch, Cros carmellose sodium, Sodium Methyl Paraben, Sodium Propyl Paraben, Gelatin, Magnesium Stearate, Talcum, Aerosil, Gum Acacia, Sugar, Titanium Dioxide, Solvent Methylene Chloride, Carnauba wax, Bees wax.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a cool dark place below 30ºC & keep out of reach of children.

6.5 Nature and contents of container

10 X 10 Tablets in blister & 1 x 500 Tablets in Jar.

6.6 Instructions for use and handling and disposal

No special requirements.

7. Marketing authorization holder

Name : **GREAT TIMEC PHARMA COMPANY LIMITED**

Address : 19B, Niger Bridge head, Housing Estate,
Fegge, Onitsha, Anambra, Nigeria

Name and address of manufacturer*

Applicant's Name: Nem Laboratories Pvt. Ltd.

Address : 133 Krishna Ind. Estate, Vasai (E)
Thane 401210, Maharashtra-India
Tel. no. +91(250) 2390002/3

8. Number(s) in the national register of finished pharmaceutical products

NAFDAC REGN. NO.: B4-1169

9. Date of first authorization/renewal of the authorization

7th November 2012

10. DATE OF REVISION OF THE TEXT

6th November 2017