PATIENT INFORMATION LEAFLET

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Quinine Sulphate 300 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 300 mg quinine sulphate.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The name of your product is Quinine Sulphate 300 mg film-coated tablets. The active ingredient is quinine sulphate.
Quinine Sulphate belongs to a group of medicines called anti-protozoal agents and they are used to treat malaria and prevent night cramps in adults and the elderly when sleep is regularly disrupted.

4.2 Posology and method of administration

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The tablets should be swallowed with a drink of water.

Doses:
For the treatment of malaria (you may be given another medicine for malaria with or after this course of quinine):

Adults (including the elderly) and children aged 12 years and over: The usual dose is 2 tablets every 8 hours for 7 days.

Children under 12 years: 10 mg per kg of body weight every 8 hours for 7 days.

If you have kidney or liver disease you may be given a different dose.

For the treatment of night cramps:

Adults and elderly: Take 1 tablet at night. It may take up to 4 weeks before you notice any reduction in the frequency of leg cramps.

The tablet can be divided into equal doses.

4.3 Method of administration

Oral administration

4.4 Contraindications

This medicine is contraindicated in patients with:
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- optic neuritis.
- tinnitus.
- haemoglobinuria.
- myasthenia gravis. Quinine Sulphate may cause severe respiratory distress and dysphagia in these patients.

4.5 Special warnings and precautions for use

Talk to your doctor or pharmacist before taking Quinine Sulphate:
- if you have irregular heart beats or other heart disease.
- if you have had malaria for a long time.
- if you suffer from severe glucose-6-phosphate dehydrogenase deficiency (G6PD), this can cause episodes of anaemia after eating certain foods such as fava beans (favism) or certain drugs including drugs to prevent malaria and dapsone.
- if you have liver or kidney problems.

You should not take more than the prescribed dose as a condition called 'cinchonism' may occur even with normal doses. Please see section 4.9 'Undesirable effects' for symptoms of cinchonism and tell your doctor if you experience any of them.

4.6 Special warnings and precautions for use – Paediatric population

Please refer to section 4.5.

4.7 Interaction with other medicinal products and other forms of interaction

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Especially:
- anticoagulants (to stop your blood from clotting such as warfarin).
- cardiac glycosides (for your heart such as digoxin).
- chloroquine, mefloquine, artemether with lumefantrine or primaquine (also to treat malaria).
- cimetidine (to treat stomach ulcers or acid reflux and indigestion).
- amantadine (to treat Parkinson's Disease or some viral infections).
- ciclosporin (to prevent transplant rejection).
- flecainide, quinidine or amiodarone (to treat irregular heart beats).
- terfenadine (for allergic reactions).

- pimozide or thioridazine (to treat some mental disorders).
- moxifloxacin, rifampicin or antifungals (to treat infections).
- medicines to treat diabetes.
- suxamethonium (muscle relaxant).
- HIV medicines.
- Barbiturates or carbamazepine or phenytoin (medicines to treat epilepsy).
- medicines which are known to cause disturbances in heart rhythm.

4.8 Interaction with other medicinal products and other forms of interaction – Additional information on special populations

Please refer to section 4.7.

4.9 Interaction with other medicinal products and other forms of interaction – Paediatric population

Please refer to section 4.7.

4.10 Fertility, pregnancy and lactation

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Quinine Sulphate tablets should not be used for night cramps during pregnancy.

4.11 Effects on ability to drive and use machines

Do not drive or operate machinery if you experience any problems with your vision while you are taking this medicine.

4.12 Undesirable effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Contact your doctor at once if the following effects occur:
- allergic reactions –itchy skin rash, swelling of the lips, face, throat or tongue, flushing, fever, asthma or sensitivity to light.
- cinchonism –abdominal pain, diarrhoea, disturbed vision (blurred vision, changes in colour perception or field of vision, total blindness), headache, feeling or being sick, ringing in the ears or impaired hearing, rashes, loss of consciousness, fits, shock due to heart problems, irregular heart beats, death. If these occur while taking Quinine Sulphate tablets for leg cramps, treatment should be stopped and a doctor contacted straight away.
- changes to blood cells, if you notice that you are bruising or bleeding easily, have frequent nose bleeds, or you have more sore throats and infections than usual tell your doctor who may want to give you a blood test.

Tell your doctor if you notice any of the following side effects or notice any other effects not listed:
- diarrhoea, feeling or being sick, abdominal pain, low blood sugar.

- muscle weakness, excitement, agitation, 'spinning sensation', confusion, loss of consciousness, coma, death.
- headache, changes in vision, 'ringing' in the ears, loss of hearing.
- swollen, itchy, flaky, red or raised patches of skin, rashes, sensitivity to light.
- aggravation of Myasthenia gravis.
- kidney damage, water retention, slowed heart rate, hypotension, changes in heart rhythm and the way the heart beats, eczema, miscarriages (at very high concentrations), difficulty breathing**.**

4.13 Overdose

Symptoms
Quinine overdosage may lead to serious side effects including irreversible visual loss, and can be fatal. In acute overdosage, symptoms of cinchonism may occur, including convulsions, nausea, vomiting, tinnitus, deafness, headache, vasodilation and disturbed vision.

Features of a significant overdose include convulsions, impairment of consciousness, coma, respiratory depression, QT prolongation, ventricular arrhythmia, cardiogenic shock and renal failure. High doses of quinine are teratogenic and may cause miscarriage. Fatalities have been reported in adults after doses of 2-8 g. 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. Quinine is rapidly absorbed. 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*:* Antiprotozoals; Antimalarials*,* ATC Code*:* P01BC01

Quinine is a cinchona alkaloid and a 4-methanol-quinolone antimalarial agent which 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 mature gametocytes of *P. falciparum*. The precise mechanism of action of quinine is unclear but it may interfere with lysosome function or nucleic acid synthesis in the malaria parasite. Since it has no activity against exoerythrocytic forms, quinine does not produce a radical cure in vivax or ovale malarias.

Quinine has effects on the motor end-plate of skeletal muscle and prolongs the refractory period. Like quinidine, quinine is a sodium channel blocker and, therefore, has local anaesthetic, and both anti- and proarrhythmic activity.
The precise mechanism of action of quinine is unclear but it may interfere with lysosome function or nucleic acid synthesis in the malaria parasite.

5.2 Pharmacokinetic properties

The pharmacokinetics of quinine are altered significantly by malaria infection, the major effects being reduction in both its apparent volume of distribution and its clearance.

Absorption
Quinine is rapidly and almost completely absorbed from the gastrointestinal tract and peak concentrations in the circulation are attained about 1 to 3 hours after oral administration of the sulphate.

Distribution
Plasma protein binding is about 70% in healthy subjects and rises to 90% or more in patients with malaria. Quinine is widely distributed throughout the body. Concentrations attained in the CSF of patients with cerebral malaria have been reported to be about 2 to 7% of those in the plasma.

Metabolism
Quinine is extensively metabolised in the liver and rapidly excreted mainly in the urine. Estimates of the proportion of unchanged quinine excreted in the urine vary from less than 5% to 20%.The pharmacokinetics of quinine are altered significantly by malaria infection, with reductions in both the apparent volume of distribution and clearance.

Elimination
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. Small amounts of quinine also appear in bile and saliva. Quinine crosses the placenta and is excreted in breast milk.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core
Povidone
Microcrystalline cellulose
Pregelatinised starch
Sodium lauryl sulfate
Colloidal silicon dioxide
Magnesium stearate
Talc

Coating
Hypromellose
Macrogol 400
Titanium dioxide
Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

5 years

6.4 Special precautions for storage

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

Store below 25 ºC. Protect from light and moisture.

6.5 Nature and contents of container

PVC/Aluminium blisters. Pack size of 100 film-coated tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

Remedica Ltd
Aharnon Str., Limassol Industrial Estate,
3056 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

Date of first authorization:

10. DATE OF REVISION OF THE TEXT

For internal use only: rw-pl-quinine-sulphate-fc-tabs-a0