EMZOR CHLOROQUINE SYRUP 50MG/5ML

1. Name of the medicinal product

Chloroquine Syrup

2. Qualitative and quantitative composition

Each 5ml contains:

Chloroquine Phosphate equivalent to	80.0mg
Chloroquine base	50.0mg

Excipient(s) with known effect:

Sucrose

Methyl, Ethyl, Propyl and Butyl Hydroxybenzoic Acid Esters

Propylene Glycol

Colouring (Ponceau 4R) E124

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution

4. Clinical particulars

4.1 Therapeutic indications
For the prophylaxis, suppression and treatment of malaria.

4.2 Posology and method of administration
Method of administration

Oral

Posology

Table 1	
Age Group	Dose
Children up to 1 year:	2.5-5ml
1 to 3 years:	7.5-10ml
3 to 6 years:	10-15ml
6 to 9 years:	15-22.5ml
9 to 12 years:	22.5-30ml
Adults:	30ml

PROPHYLAXIS OR SUPPRESSION OF MALARIA, NON-IMMUNE

A single weekly dose, as shown in Table 1, beginning two weeks before and continuing four weeks after exposure to infection

PROPHYLAXIS OR SUPPRESSION OF MALARIA, PARTIALLY-IMMUNE

Half the dose in table 1 every two weeks will afford a high degree of protection.

TREATMENT OF MALARIA, NON-IMMUNE

Give twice the dose in Table 1, then give the same dose as in table 1 six hours later and then once a day for two days.

TREATMENT OF MALARIA, PARTIALLY IMMUNE

Give twice the dose in table 1 once only

No distinction is made between the dose for adults and the elderly.

4.3 Contraindications

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Hypersensitivity to chloroquine or to any of the excipients listed in section 6.1

Concomitent use with amiodarone. (See section 4.5)

4.4 Special warnings and precautions for use
When used as malaria prophylaxis official guidelines and local information on prevalence of resistance to anti-malarial drugs should be taken into consideration.

Irreversible retinal damage and corneal changes may develop during long term therapy and after the drug has been discontinued. Ophthalmic examination prior to, and at 3-6 monthly intervals during use is required if patients are receiving chloroquine:

- At continuous high doses for longer than 12 months

- As weekly treatment for longer than 3 years

- When total consumption exceeds 1.6g/kg (cumulative dose 100g)

Patients should be advised to stop taking the drug immediately and seek the advise of their doctor if any disturbances of vision occur.

Bone marrow suppression may occur rarely so full blood counts should be carried out during extended treatment. Caution is required if drugs known to induce blood disorders are used concurrently.

Use with caution in patients with impaired hepatic function, particularly cirrhosis.

Use with caution in patients with porphyria as the disease may be precipitated. This may be especially apparent in patients with a high alcohol intake.

Use with caution in patients with a renal impairment.

Use with caution in patients with a history of epilepsy, convulsions and other neurological disorders.

Use with caution in patients with psoriasis as chloroquine may precipitate a severe attack.

Use with caution in patients with severe gastro-intestinal disease.

Use with caution in patients with glucose-6-phosphate dehydrogenase deficiency, as there may be risk of haemolysis.

Chloroquine has been shown to cause severe hypoglycaemia including loss of consciousness that could be life threatening in patients treated with and without antidiabetic medications. Patients treated with chloroquine should be warned about the risk of hypoglycaemia and the associated clinical signs and symptoms. Patients presenting with clinical symptoms suggestive of hypoglycaemia during treatment with chloroquine should have their blood glucose level checked and treatment reviewed as necessary.

A small number of cases of diffuse parenchymal lung disease have been identified in patients taking chloroquine. A response after therapy with steroids has been observed in some of these cases.

Cases of drug rash with eosinophilia and systemic symptoms (DRESS) syndrome have been identified in patients taking chloroquine. Recovery after discontinuation of treatment and response after therapy with steroids has been observed.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltese insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
If the patient is taking amiodarone then chloroquine may increase the risk of cardiac arrhythmias including ventricular arrhythmias, bradycardias and cardiac conduction defect. Concurrent use is contraindicated. Co-administration with other drugs that have antiarrhythmogenic properties, e.g. moxifloxacin, droperidol, may increase the risk of cardiac arrhythmias.

Antacids and adsorbents (e.g. kaolin) may reduce the absorption of chloroquine, so should be administered at least four hours apart.

Concomitant use of drugs such as multidrug and toxin extrusion protein (MATE1) inhibitors (e.g., ciprofloxacin, cimetidine, omeprazole, pyrimethamine) may impact the renal clearance of chloroquine, which could theoretically lead to increased levels of chloroquine and potentially overdosage (see section 4.9). In addition, care should be taken when alkalinization of urine occurs as this may reduce chloroquine renal excretion.

Chloroquine increases risk of convulsions with mefloquine (anti-malarial drug).

Chloroquine antagonises the anticonvulsant effect of antiepileptics.

Chloroquine may possibly increase the plasma concentration of digoxin.

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When co-administered with ciclosporin, chloroquine increases plasma ciclosporin concentration resulting in increased risk of toxicity.

Chloroquine has been reported to reduce the bioavailability of praziquantel. Caution is advised during co-administration.

Chloroquine has the potential to increase symptoms of myasthenia gravis and thus diminish effect of neostigmine and pyridostigmine.

Concomitant administration of chloroquine with rabies vaccine may affect the antibody response.

Concomitant administration of chloroquine inactivates oral typhoid vaccine, so the vaccine should be completed at least three days before the first dose of chloroquine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Should not be used during pregnancy unless, in the judgement of the physician, potential benefit outweighs the risk. When given at high doses throughout pregnancy it has been reported to give rise to foetal abnormalities including visual loss, ototoxicity and cochlea-vestibular dysfunction.

Malaria in pregnant women increase the risk of maternal death, miscarriages, still-births and low birth weight infants with the associated risk of neonatal death. Travel to malarious areas should be avoided during pregnancy but if this is not possible women should receive effective prophylaxis.

Breast-feeding

Emzor chloroquine Syrup is excreted in breast milk, although amounts are probably too small to be harmful when used for malaria prophylaxis but as a consequence they are insufficient to protect the infant.

4.7 Effects on ability to drive and use machines

At start of treatment chloroquine has a temporary effect on visual accommodation, causing blurred and/or double vision. Therefore patients should be advised that the product may affect their ability to drive or operate machinery.

4.8 Undesirable effects

The following CIOMS frequency rating is used when applicable:

Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%; Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (frequency cannot be estimated from available data)

Cardiac disorders

- Uncommon: cardiomyopathy has been reported during long term therapy at high doses, which may result in cardiac failure and in some cases a fatal outcome.

- Rare: cardiac arrhythmias, including QT prolongation, torsade de pointes, ventricular tachycardia and ventricular fibrillation have been reported with therapeutic doses of chloroquine as well as with overdose. The risk is greater if chloroquine is administered at high doses. Fatal cases have been reported.

- Not known - hypotension.

Nervous system disorders

- Very common: headache

- Common: convulsions have been reported rarely (these may result from cerebral malaria).

- Uncommon: neuropathy

- Rare: polyneuropathy

- Not known: acute extrapyramidal disorders (such as dystonia, dyskinesia, tongue protrusion, torticollis).

Psychiatric disorders

- Very common: insomnia

- Common: depression

- Rare: psychiatric disorders such as anxiety, agitation, confusion, hallucinations, delirium

- Not known: suicidal behaviour

Eye disorders

- Common: transient blurred vision

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- Rare: reversible corneal opacity, cases of retinopathy as well as cases of irreversible retinal damage have been reported during long term, high dose therapy.

- Not known: maculopathy and macular degeneration have been reported and may be irreversible, macular defects of colour vision, optic atrophy, scotomas, field defects, blindness and pigmented deposits, difficult in focusing, diplopia.

Gastro-intestinal disorders

- Very common: gastrointestinal disturbances such as nausea, vomiting, diarrhoea.

- Not known: abdominal cramps

Blood and lymphatic system disorders

- Rare: bone marrow depression, including aplastic anaemia, agranulocytosis, pancytopenia, thrombocytopenia, neutropenia

Hepatobiliary disorders

- Rare: changes in liver function, including hepatitis and abnormal liver function tests

- Immune system disorders

- Common: allergic and anaphylactic reactions, including angioedema

Ear and labyrinth disorders

- Uncommon: ototoxicity such as tinnitus, hypoacusis, nerve deafness.

Musculoskeletal and connective tissue disorders

- Uncommon: myopathy

Skin and subcutaneous tissue disorders

- Very common: pruritis,

- Common: skin eruptions, urticaria

- Uncommon: alopecia, bluish-black pigmentation of the nails and mucosae (long term use).

- Rare: exacerbation of psoriasis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis

- Very rare: exfoliative dermatitis and similar desquamation-type events.

- Not known: depigmentation, photosensitivity, Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome)

Metabolism and nutrition disorders

- Not known: hypoglycaemia

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 national reporting system: Yellow Card Scheme: Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Chloroquine is highly toxic in overdose and children are particularly susceptible. The chief symptoms of overdosage include circulatory collapse due to a potent cardiotoxic effect, respiratory arrest and coma. Symptoms may progress rapidly after initial headache, drowsiness, visual disturbances, nausea and vomiting. Cardiac complications may occur without progressively deepening coma.

Death may result from circulatory or respiratory failure or cardiac arrhythmia. If there is no demonstrable cardiac output due to arrhythmias, asystole or electromechanical dissociation, external chest compression should be persisted with for as long as necessary, or until adrenaline and diazepam can be given (see below).

Gastric lavage should be carried out urgently (as soon as possible within 2 hours of the overdose), first protecting the airway and instituting artificial ventilation where necessary. There is a risk of cardiac arrest following aspiration of gastric contents in more serious cases. Activated charcoal left in the stomach may reduce absorption of any remaining chloroquine from the gut (minimum 5 times the suspected maximum dose of chloroquine phosphate). Circulatory status (with central venous pressure measurement), respiration, plasma electrolytes and blood gases should be monitored, with correction of hypokalaemia and acidosis if indicated. Cardiac arrhythmias should not be treated unless life threatening; drugs with quinidine-like effects should be avoided. Intravenous sodium bicarbonate 1-2mmol/kg over 15 minutes may be effective in conduction disturbances, and DC shock is indicated for ventricular tachycardia and ventricular fibrillation.

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Early administration of the following has been shown to improve survival in cases of serious poisoning:

1. Adrenaline infusion 0.25micrograms/kg/min initially, with increments of 0.25micrograms/kg/min until adequate systolic blood pressure (more than 100mg/Hg) is restored; adrenaline reduces the effects of chloroquine on the heart through its inotropic and vasoconstrictor effects.

2. Diazepam infusion (2mg/kg over 30 minutes as a loading dose, followed by 1-2mg/kg/day for up to 2-4 days). Diazepam may minimise cardiotoxicity.

Acidification of the urine, haemodialysis, peritoneal dialysis or exchange transfusion have not been shown to be of value in treating chloroquine poisoning. Chloroquine is excreted very slowly, therefore cases of overdosage require observation for several days.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antimalrials, Aminoquinolines, ATC code: P01B A01

Chloroquine Phosphate is an antimalarial, active against susceptible strains of *Plasmodium falciparum, P.ovale, P. Vivax* and *P. Malariae.*

5.2 Pharmacokinetic properties
Chloroquine Phosphate is rapidly and almost completely absorbed from the gastro intestinal tract following oral administration. It is then widely distributed in the body tissues with the highest concentrations being found in kidneys, lungs, liver and spleen. In addition it is also concentrated in melanin containing cells such as in the eyes and skin. It both crosses the placenta and is found in breast milk. Chloroquine remains in the system for a long period after discontinuation of therapy. Metabolism is mainly in the liver with elimination being via the urine.

5.3 Preclinical safety data
None stated.

6. Pharmaceutical particulars

6.1 List of excipients
Sucrose, Methyl, Ethyl, Propyl and Butyl Hydroxybenzoic Acid Esters, Propylene Glycol, Flavouring, Sodium Saccharin, Glycerin, Colouring (Ponceau 4R (E124)) and Purified Water.

6.2 Incompatibilities
Not known

6.3 Shelf life
48 months

6.4 Special precautions for storage
Protect from light. Store below 30°C.

6.5 Nature and contents of container
Glass bottle containing 60ml of Emzor chloroquine Syrup.

6.6 Special precautions for disposal and other handling
None stated

7. Marketing authorisation holder

Emzor Pharmaceutical Industries Limited

No 10 Kolawole Shonibare Street,Ajao Estate,Lagos

8. Marketing authorisation number(s)

N/A

9. Date of first authorisation/renewal of the authorisation

N/A

10. Date of revision of the text

N/A