Storage: Store in a cool and dry place below 30°C, protected from light.
KEEP OUT OF REACH OF CHILDREN.

NAFDAC REG. NO.: B4-6971

2ml x 10amps

QUININE DIHYDROCHLORIDE INJECTION600MG/2ML BP

FECCOX QUININE

Each ampoule contains: Quinine Dihydrochloride 600mg **I.M./I.V.**

SOLE AGENT:
FECCOX PHARM.GEN. ENT. LTD
No 2 JABBA LAYOUT PANISAU,KANO,NIGERIA.

Manufactured by:
Guizhou Tiandi Pharmaceutical Company Ltd
No 6 Baokang Road, Yilong Hongxing Pharmaceutical Park,
Qianxi'nan Buyi and Miao Autonomous Prefecture,
Guizhou Province China

Quinine Dihydrochloride Injection

Batch No.: **Mfg. Date:** **Exp. Date:**

NAFDAC REG. NO.: B4-6971

2ml x 10amps

QUININE DIHYDROCHLORIDE INJECTION600MG/2ML BP

FECCOX QUININE

Each ampoule contains: Quinine Dihydrochloride 600mg **I.M./I.V.**

INDICATION: For detail see enclosed insert.

DOSAGE & ADMINISTRATION: As directed by the physician. Pls refer to insert.

CAREFULLY READ ENCLOSED PACKAGE INSERT BEFORE USE.

Quinine Dihydrochloride Injection

确认!
李文强
2020.3.24

奎宁注射液14.5x7.5x1.4cm

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed.

Summary Product Characteristics

1. **Name of the proprietary product:** ------

   Name of the nonproprietary International Product: Quinine Dihydrochloride Injection BP 600 mg/ 2 ml

   Route of Administration: Intramuscular/ Intravenous

2. **Qualitative and Quantitative composition:**

Batch Size: 100 Liter

Sr. No.	Ingredients	Specification	Qty/Ampoule (mg)	Overages	Qty/batch (kg)	Reason for inclusion
Active						
1.	Quinine Dihydrochloride BP	BP	600.00 mg	Nil	60	Active
Excipients						
2.	Disodium Edetate	BP	0.24	Nil	0.024	Chelating agent
3.	Water for Injection	BP	q.s to 2 ml	Nil	q.s. to 100 Ltr.	Solvent
Total			**2 ml**	---	**100 Ltr.**	---

Where, BP: British Pharmacopoeia, q.s.: quantity sufficient.

3. Pharmaceutical Form: Liquid Injection

4. Clinical Particulars:

4.1 Therapeutic Indications:
INDICATION(S):
For the treatment of acute attacks of malaria, including attacks due to chloroquine-resistant or multi-drug-resistant strains of Plasmodium falciparum.
Quinine is used parenterally for cerebral, severe or complicated malaria, or when vomiting prevents retention of an orally administered drug.
Quinine dihydrochloride is the salt usually employed for the preparation of injections.

4.2 Posology and method of administration:
In severe or complicated malaria, when the patient is unable to take oral medication, a slow intravenous infusion of quinine is used.
In severely ill adults, a loading dose of 20 mg quinine dihydrochloride per kg may be administered by slow, constant rate intravenous infusion diluted in either isotonic fluid or 5% glucose solution (5-10 mL per kg bodyweight depending on the patient's overall fluid balance) over four hours provided that the patient has not received quinine, quinidine or mefloquin during the previous twelve to twenty-four hours, and reliable hospital facilities are available, including cardiac monitoring.
The maintenance dose is 10 mg of quinine dihydrochloride per kg in 250 to 500 mL of diluent, preferably 5% glucose solution, by intravenous infusion over four hours, repeated at eight to twelve hourly intervals.
For children, a dose of 25 to 30 mg per kg body-mass daily in three divided doses has been recommended.
Oral therapy should be substituted as soon as possible and a total of at least seven days therapy should be completed.
If, after forty-eight hours of parenteral treatment, the patient is still unable to take oral treatment, or if there is evidence of significant hepatic impairment, the maintenance dose should be reduced by half.
The recommended drug dosage adjustment for patients with impaired renal function (ie. a GFR less than 10), is a third of the normal dose. However, the loading dose of quinine should not be reduced in patients with renal and hepatic impairment.
If intravenous infusion is not possible, quinine dihydrochloride may be given by intramuscular injection of 10 mg per kg, although this may cause pain and local tissue necrosis.
Monitoring of blood levels and side-effects is recommended during quinine therapy.
NB: Quinine should never be given by rapid intravenous "push" or bolus injections as this may cause severe or even fatal cardiovascular toxicity.

Route of Administration: Intravenous (I.V.)/intramuscular (I.M.) administration

4.3 Contraindications
Quinine is contraindicated in patients with the following:

Prolonged QT interval
One case of a fatal ventricular arrhythmia was reported in an elderly patient with a prolonged QT interval at baseline, who received quinine sulfate intravenously for *P. falciparum* malaria .

Glucose-6-phosphate Dehydrogenase (G6PD) Deficiency

Hemolysis can occur in patients with G6PD deficiency receiving quinine.

Known Hypersensitivity Reactions to Quinine or any of the Excipients in the Tablet
These include, but are not limited to; the following :

- Thrombocytopenia
- Idiopathic thrombocytopenia purpura (ITP) and Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- Blackwater fever (acute intravascular hemolysis, hemoglobinuria, and hemoglobinemia)

Known Hypersensitivity to Mefloquine or Quinidine
Cross-sensitivity to quinine has been documented.

Myasthenia Gravis
Quinine has neuromuscular blocking activity, and may exacerbate muscle weakness.

Optic Neuritis
Quinine may exacerbate active optic neuritis.

4.4 Special warnings and precautions for use
Before use for nocturnal leg cramps, the risks, which include significant adverse effects and interactions should be carefully considered relative to the potential benefits (Pls refer to drug interactions and undesirable effects). 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 sulphate should not be used for this indication during pregnancy.

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.

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 black water 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.

Owing to the presence of lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase 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 (pls refer to undesirable effects).

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

4.5 Interaction with other medicinal products and other forms of interaction:
The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Antacids, aluminum-containing (concurrent use of aluminum-containing antacids with quinine may decrease or delay the absorption of quinine)

Anticoagulants, coumarin- or indandione-derivative (hypoprothrombinemic effects may be increased when these agents are used concurrently with quinine because of decreased hepatic synthesis of procoagulant factors; hypoprothrombinemia can be prevented by coadministration of vitamin K; dosage adjustments may be necessary during and after quinine therapy)

Antimyasthenics (concurrent use of medications with neuromuscular blocking action may antagonize the effect of antimyasthenics on skeletal muscle; temporary dosage adjustments of antimyasthenics may be necessary to control symptoms of myasthenia gravis during and following concurrent use)
Cimetidine (concurrent use of cimetidine with quinine may reduce the clearance of quinine)

Digitoxin or Digoxin (concurrent use of digoxin with quinine may result in increased digoxin serum concentrations and increased digoxin effect by decreasing the nonrenal clearance of digoxin; concurrent use of quinidine with digitoxin has been reported to result in increased digitoxin serum concentrations and increased digitoxin effect as well; because of the similarities of the digitalis glycosides and the similarities of quinine and quinidine, serum digoxin and digitoxin concentrations should be monitored periodically during concurrent therapy with quinine, and dosage adjustments made as indicated)

Hemolytics, other or Neurotoxic medications, other or Ototoxic medications, other, (concurrent use of these medications with quinine may increase the potential for toxicity)

» Mefloquine (concurrent use with quinine may result in an increased incidence of seizures and of electrocardiogram abnormalities, predisposing the patient to arrhythmias; it is recommended that mefloquine be administered at least 12 hours after the last dose of quinine) (patients taking weekly mefloquine prophylaxis may be found to have mefloquine-resistant malaria that requires treatment with quinine; because mefloquine has a very long half-life [approximately 20 days], it will remain in the body long after the drug has been discontinued. Although there is insufficient information available, it is recommended that if quinine must be given, the patient be hospitalized, if possible, and monitored for QT prolongation and possible rhythm disturbances. Seizure activity also may be potentiated in these patients. In patients considered to be at high risk for

a seizure, additional precautions and interventions may be indicated)

Neuromuscular blocking agents (neuromuscular blockade may be potentiated when these agents are used concurrently with quinine)

Quinidine (concurrent use with quinine may increase the possibility of QT prolongation or cinchonism)

4.6 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 sulphate 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 sulphate should not be used during pregnancy to treat cramps.

Lactation
Quinine sulphate 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 sulphate should not be given to nursing mothers unless the benefit outweighs the risks.

4.7 Effects on the 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

4.9 Overdose

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

5. Pharmacological Particulars:

5.1 Pharmacodynamic properties

Pharmacological Class: Antimalarials

ATC Code: P01BC01

Mechanism of action

Antiprotozoal—The precise mechanism of action of quinine in malaria has not been determined but may be based on its ability to concentrate in parasitic acid vesicles, causing an elevation of pH in intracellular organelles. This is thought to disrupt the intracellular transport of membrane components and macromolecules, and phospholipase activity. Quinine has a schizonticidal action. Its ability to

concentrate in parasitized erythrocytes may account for its selective toxicity against the erythrocytic stages of the four malarial parasites, including Plasmodium falciparum strains resistant to chloroquine. The drug is also gametocidal against Plasmodium vivax and Plasmodium malariae.

Antimyotonic—Quinine increases the refractory period of skeletal muscle by direct action on the muscle fiber and the distribution of calcium within the muscle fiber, thereby diminishing the response to tetanic stimulation. It also decreases the excitability of the motor end-plate region, reducing the responses to repetitive nerve stimulation and to acetylcholine.

5.2 Pharmacokinetic properties

Absorption:

Rapidly and almost completely absorbed. Bioavailability is approximately 80% in healthy subjects.

Distribution:

Distribution of quinine may vary depending on the degree of illness; the volume of distribution is smaller in patients with cerebral malaria and increases with recovery. Children and pregnant women have a smaller volume of distribution than do nonpregnant female adults and male adults. Plasma and red blood cell (RBC) concentrations appear to be similar before infection; however, during a malaria attack, plasma concentrations are considerably higher than RBC concentrations. Quinine does not freely cross the blood-brain barrier; the cerebrospinal fluid to plasma ratio is approximately 7%. Quinine crosses the placenta and is distributed into breast milk; peak concentrations are reached in breast milk approximately 90 minutes after oral administration.

Adults—
Cerebral malaria—Approximately 1.2 liters per kg.
Uncomplicated malaria—Approximately 1.7 liters per kg.
Children—
Uncomplicated malaria—
Approximately 0.8 liter per kg.

Protein binding:

Higher (> 90%) in patients with cerebral malaria, pregnant women, and children;
approximately 85 to 90% in patients with uncomplicated malaria; and approximately 70% in healthy adults.

Biotransformation:

Hepatic; > 80% metabolized by the liver. Metabolites have less activity than the parent drug.

Half-life:

Adults:
Cerebral malaria: Approximately 18 hours.
Uncomplicated malaria: Approximately 16 hours.
Healthy persons: Approximately 11 hours.

Children:
Uncomplicated malaria: Approximately 12 hours.
Acute overdose:

Approximately 26 hours.

Time to peak serum concentration
Acute malaria—Approximately 5.9 hours.
Convalescence—Approximately 3.2 hours.

Mean serum concentration
Approximately 7 mcg per mL, following chronic administration of total daily doses of 1 gram. Plasma concentrations are higher in patients with cerebral malaria due to reduced clearance and volume of distribution; concentrations decrease as patient recovers.

Elimination:
Primarily renal, with about 20% excreted as unchanged drug. Excretion of quinine is increased in acidic urine.
Dialysis—Exchange transfusion, hemodialysis, peritoneal dialysis, and hemofiltration have little effect on plasma quinine concentrations.

5.3 Pre-clinical Safety:
It is a well-established drug for which there are adequate published data

6. Pharmaceutical Particulars:

List of Excipients:

Disodium Edetate	BP
Water for Injection	BP

6.2 Incompatibilities:
Nil.

6.3 Shelf Life: 36 months.

6.4 Special Precautions for storage:
Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container:
An amber colored glass Ampoule of 2 ml, such 10 ampoules packed in a plastic tray and one such tray is packed in a carton along with pack insert.

6.6 Special precautions for disposal and other handling:
None.

7. Marketing Authorization Holder: FECCOX PHARMACY AND GENERAL ENTERPRISE LTD

8. Marketing Authorization Number: ---

9. Date of first Authorization /renewal of the authorization: ---

10. Date of revision of text: August 2023