1.3 Product Information

1.3.1 Summary of product characterization

1. Name of the Medicinal Product

(a) Product Name : Fexona Chloroquine Injection

(b) Strength : 40 mg

(c) Pharmaceutical Dosage Form : Solution for Injection

2. Quality and Quantitative Composition

(a) Qualitative Declaration, the active substance should be declared by its recommended INN. Accompanied by its salt or hydrate form if relevant.

Composition:

Each mL contains:

Chloroquine Phosphate	BP	64.5 mg
Eq. to Chloroquine base		40 mg
Chlorobutanol (As preservative)	BP	5% w/v
Benzyl Alcohol (As preservative)	BP	2% v/v

(b) Quantitative Declaration, the quantity of the active substance must be expressed per dosage unit

Ingredient	Spec.	Label Claim	Overage /Factor	Qty./mL	Qty./Batch For 500 Ltr
Active Ingredient					
Chloroquine Phosphate Eq. to Chloroquine base	B.P.	40 mg	61.25 %	64.5 mg	32.250 kg
Inactive Ingredient					
Benzyl alcohol	B.P.	---	---	2% v/v	10.000 Ltr
Chlorobutanol	B.P.	---	---	5% w/v	25.000 kg
Water for Injection	B.P.	---	---	q.s.	q.s.
Note: Appropriate overages have been added to compensate the loss during manufacturing and to ensure the potency of the active up to shelf life.					

3. Pharmaceutical Form Visual description of the appearance of the product (colour, markings, etc.) e.g.: Clear colourless or almost colourless solution filled in amber glas vials

4. Clinical Particulars

4.1 Therapeutic Indications:

a) Treatment of amoebic hepatitis and abscess.

b) Treatment of discoid and systemic lupus erythematosus.

c) Treatment of rheumatoid arthritis.

4.2 Posology and method of administration:

Adult: 200 to 300 mg chloroquine base by intramuscular or intravenous injection. It should not be given intravenously to children

4.3 Contraindications:

Care is needed in administering chloroquine to patients with impaired liver or renal function or with porphyria

4.4 Special warning and precautions for use:

Administration must be monitored as cardiovascular collapse with or without cardiac arrhythmia may occur especially after intravenous administration and even after the conventional mode of administration.

Pruritus is a common side-effect; headache and visual and gastrointestinal disturbances occasionally arise, but disappear on discontinuation of treatment. Blood dyscrasias have occasionally been reported.

4.5 Interaction with other medicinal products and other forms of interactions:

Antacids and kaolin: Antacids and kaolin can reduce absorption of chloroquine; an interval of at least 4 hours between intake of these agents and chloroquine should be observed. Cimetidine: Cimetidine can inhibit the metabolism of chloroquine, increasing its plasma level. Concomitant use of cimetidine should be avoided. Ampicillin: In a study of healthy volunteers, chloroquine significantly reduced the bioavailability of ampicillin. An interval of at least two hours between intake of this agent and chloroquine should be observed. Cyclosporine: After introduction of chloroquine (oral form), a sudden increase in serum cyclosporine level has been reported. Therefore, close monitoring of serum cyclosporine level is recommended and, if necessary, chloroquine should be discontinued.

4.6 Pregnancy and lactation:

Usage of chloroquine during pregnancy should be avoided except in the suppression or treatment of malaria when in the judgment of the physician the benefit outweighs the potential risk to the fetus.

4.7 Effects on ability to drive and use machine:

Not available

4.8 Undesirable effects:

- Loss of appetite
- Mild dizziness
- Mild diarrhea
- Clumsiness
- Mild headache
- Nausea or stomach cramps

4.9 Overdose:

Overdose symptoms may include headache, drowsiness, nausea, vomiting, vision changes, seizure (convulsions), slow heart rate, weak pulse, fainting, slow breathing (breathing may stop).

5. Pharmacological Properties

5.1 Pharmacodynamic Properties:

Amebicides action: Unknown.

Anti-inflammatory action: Unknown. Drug may antagonize histamine and serotonin and inhibit prostaglandin effects by inhibiting conversion of arachidonic acid to prostaglandin F2; it also may inhibit chemotaxis of polymorph nuclear leukocytes, macrophages, and eosinophils. Chloroquine's spectrum of activity includes the asexual erythrocytic forms of Plasmodium malariae, P. ovale, P. vivax, many strains of P. falciparum, and Entamoeba histolytica.

5.2 Pharmacokinetic Properties:

Absorption: Absorbed readily and almost completely.

Distribution: 55% bound to plasma proteins. Concentrated in erythrocytes, liver, spleen, kidneys, heart, and brain and is strongly bound in melanin-containing cells.

Metabolism: About 30% of an administered dose is metabolized by the liver to monodesethyl-chloroquine and desethylchloroquine.

Excretion: About 70% of dose is excreted unchanged in urine; unabsorbed drug is excreted in feces. Small amounts of the drug may be present in urine for months after the drug is discontinued. Renal excretion is enhanced by urinary acidification.

5.3 Preclinical Safety Data:

Chloroquine causes a toxic myopathy but also produces a toxic neuropathy. Chloroquine is used for the treatment of severe rheumatoid arthritis, systemic lupus erythematosus, and other dermatological diseases. The clinical features of chloroquine-induced neuropathy are those of symmetrical sensorimotor polyneuropathy. Both axonal damage and primary demyelination have been reported. A prominent pathological feature of chloroquine neuropathy is ultrastructural intracytoplasmic lamellar inclusions, resembling those described in amiodarone neuropathy, within Schwann cells and in perineurial and endothelial cells but not in axons. Only long-term treatment has been associated with chloroquine neuropathy, followed by complete recovery after drug withdrawal.

Chloroquine is quinolone derivative known to exert dose-related retinal toxicity, albe it in a variable manner. It is thought that variability in the presentation of chloroquine retinopathy may be the result of perturbations in drug bioavailability subsequent to oral ingestion. In order to better understand the ramifications of bioavailability on the development of retinal injury subsequent to chloroquine use, this study investigated the relationship between retinal injury and chloroquine administration via intraperitoneal rather than oral administration. Four-week-old C57/6J mice underwent daily intraperitoneal injection of 10 mg kg−1 chloroquine hydrochloride for a total of 62 days. Following treatment, tissue was fixed in preparation for analysis by light and transmission electron microscopy. Treated animals demonstrated marked abnormality of the outer retinal layers described as complete loss of the outer plexiform layer as well as photoreceptors and photoreceptor nuclei. The retinal pigmented epithelium demonstrated focal atrophy, loss of nuclei and pigment irregularity. Findings in the inner retina were notable for the loss of Müller cells and the presence of membranous cytoplasmic bodies. Retinae of control animals were entirely normal. In contrast to previous studies in the murine model examining chloroquine retinopathy subsequent to oral administration, this study suggests that intraperitoneal chloroquine administration facilitates retinal toxicity, presumably due to heightened drug absorption and

bioavailability. It is posited that an increased rate of drug accumulation within the retina leads to an enhanced Lysosomotropic drug effect due to inability of the lysosome to compensate for chloroquine-induced elevation in pH through re-acidification of the

6.0 Pharmaceutical Particulars

(a) List of excipients:

S. No.	Ingredients	Specification
1	Benzyl alcohol	B.P.
2	Chlorobutanol	B.P.
3	Water for injection	B.P.

(b) Incompatibilities: Not known

(c) Shelf life: 36 Months

(d) Special precautions for storage:

Store Protected from light and moisture below 30°C.

(e) Nature and contents of container:

Pack 10 x 30 ml vial in a carton with insert.

7.0 Marketing Authorization Holder

Name **:** Fexona Pharmaceutical Co., Ltd.

Address **:** 19, Akinlawon street, Ijesha Surulere, Lagos- Nigeria

Phone **:** +2348032587764

E-mail **:** fexonapharmltd@yahoo.com

8.0 Marketing Authorization Numbers

Not applicable

9.0 Date of first authorization/renewal of the authorization

Not applicable

10.0 Date of revision of the text

07/02/2023