1.3 Product Information

1.3.1 Summary of product characteristics (SmPC)

1. Name of the medicinal product

Artesunate For Injection 60 mg/Vial

2. Qualitative and Quantitative composition:

Each vial contains:
Artesunate (As Sterile Lyophilized powder) (In House) (60 mg)
1 ml ampoule of Sodium bicarbonate injection BP (5.0% w/v)
5 ml of Sodium chloride injection BP (0.9% w/v)

Qualitative and Quantitative formula:

Standard batch size: 5.750 KG / 93,042 Vials						
Sr. No.	**Ingredient**	**Reference**	**Quantity/ Vial**	**Overages %**	**Quantity/ Batch**	**Function**
1.	ARTESUNATE (STERILE)	IH	60.0 mg	3.0%	5.750* Kg	Active Ingredient

Note:*Considering 100% assay.

3. Pharmaceutical form

Dry Powder Injection

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the treatment of severe malaria caused by Plasmodium falciparum, in adults and children.

4.2 Posology and method of administration

Adults and children: Artesunate injection is administered at a dose of 2.4 mg of artesunate/kg body weight, by intravenous (I.V.) or intramuscular (l.M.) injection, at 0, 12 and 24 hours, then once daily until oral treatment can be substituted.
Administration: The powder for injection is difficult to dissolve and care should be taken to ensure that it is completely dissolved before parenteral administration The formulation should be used immediately after reconstitution. If the solution is cloudy or precipitate is present, the

parenteral solution should be discarded. Do not use water for injection for reconstitution of the artesunate powder or for dilution of the resulting solution prior to injection.
The powder for injection should be reconstituted with 1 ml of sodium bicarbonate 5% w/v, shake vigorously till the solution become clear.
For I.V. Use: Add 5 ml of sodium chloride 0.9% w/v and mix again to prepare final concentration of 10 mg/ml for I. V. use. The required amount of drug for I. V. use should be administered slowly over a period of 2-3 minutes. For I.M. Use: Add 2 ml of sodium chloride 0.9% w/v and mix again to prepare final concentration of 20 mg/ml for I.M. use.

Method of administration: Intravenous or Intramuscular.

4.3 Contraindication

It is contraindicated in patients with hypersensitivity to artesunate or other artemisinin derivatives.

4.4 Special warning and precautions for use

Non-falciparum malaria: Artesunate has not been evaluated in the treatment of severe malaria due to Plasmodium vivax, Plasmodium malariae or Plasmodium ovale. In cerebral malaria and complicated malaria, general supporting therapy is usually required.

Renal/hepatic impairment: Dose adjustment is not necessary in patients with hepatic or renal impairment.

Pregnancy: There has been limited clinical experience with the use of artesunate in pregnancy. In animal studies, artesunate has been associated with foetal toxicity during the first trimester of pregnancy. To date, clinical data regarding safety in the first trimester have not indicated an increased risk of foetal harm. Treatment with artesunate should not be withheld during the first trimester if it is potentially life-saving for the mother.

Lactation: The active metabolite of artesunate is excreted at low levels in breast milk. The drug levels are not expected to cause any adverse effects in breast fed infants. The amount of drug present in breast milk does not protect the infant from malaria.

4.5 Interaction with other medicinal products and other forms of interaction

Few clinical drug-drug interaction studies have been performed; however no clinically significant interactions have been identified**.**

4.6 Pregnancy and lactation

Pregnancy: There has been limited clinical experience with the use of artesunate in pregnancy. In animal studies, artesunate has been associated with foetal toxicity during the first trimester of pregnancy. To date, clinical data regarding safety in the first trimester have not indicated an increased risk of foetal harm. Treatment with artesunate should not be withheld during the first trimester if it is potentially life-saving for the mother.

Lactation: The active metabolite of artesunate is excreted at low levels in breast milk. The drug levels are not expected to cause any adverse effects in breast fed infants. The amount of drug present in breast milk does not protect the infant from malaria

4.7 Effect on ability to drive and use machines

Patients receiving Artesunate for injection should be warned that dizziness may occur, in which case they should not drive or use machines.

4.8 Undesirable effects

Blood and lymphatic systems disorders: Neutropenia and anaemia (both occasionally severe), thrombocytopenia, pure red cell aplasia, post-treatment anaemia, mild and transient decrease in reticulocyte count.

Nervous system disorders·: Dizziness, light-headaches, headache, insomnia, tinnitus, peripheral neuropathy.

Respiratory disorders: Cough, nasal symptoms

Gastrointestinal disorders: Altered taste, nausea, vomiting, abdominal pain or cramps, diarrhoea, raised serum amylase, pancreatitis.

Hepatobiliary disorders: Transient rises in liver transaminases (AST, ALT), hepatitis.

Skin and subcutaneous tissue disorders: Rash, alopecia.

Musculoskeletal and connective tissue disorders: Arthralgia, muscle disorders

General disorders and administration site conditions: Fatigue, malaise, fever, pain at injection site.

Immune system disorders: Hypersensitivity

4.9 Overdose

Experience of acute overdose with artesunate is limited. The overdose of artesunate is associated with pancytopenia, melena, seizures, multi organ failure and death. Treatment of overdose should consist of general supportive measures.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Artesunate is a hemisuccinate derivative of dihydro-artemisinin, which is itself formed by the reduction of artemisinin. The mechanism of action of the artemisinins likely involves cleavage of the internal endoperoxidc bridge through reaction with haeme within the infected erythrocyte, thereby generating free radicals which alkylate vital parasite proteins. However, artemisinins have also been reported to inhibit an essential parasite calcium adenosine triphosphatase. The artemisinins are distinguished from other antimalarials by their ability to kill all erythrocytic stages of the malaria parasite, including the relatively inactive ring stage and late schizonts, as well as the gametocytes responsible for malaria transmission. Artesunate and the artemisinins are the most rapid acting of the antimalarials, and they have also been shown to enhance splenic clearance of infected erythrocytes by reducing cytoadherence.

5.2 Pharmacokinetic properties

Absorption: After intravenous injection artesunate is very rapidly biotransformed to its active metabolite, dihydroartemisinin (DHA). Consequently, artesunate half-life (t1/2) is estimated to be less than 5 minutes. Artesunate is rapidly absorbed following intramuscular injection, and peak plasma levels are generally achieved within 30 minutes of administration.

Distribution: Dihydroartemisinin (DHA) has been shown to substantially accumulate in P. falciparum infected erythrocytes. Plasma protein binding of dihydroartemisinin is determined to be 93% in patients and 88% in healthy volunteers.

Metabolism Elimination: Artesunate is extensively and rapidly hydrolysed by plasma esterases, with possible minimal contribution by CYP2A6. The main metabolite, dihydroartemisinin, accounts for most of the in vivo antimalarial activity of IV administration. DHA is further metabolized in the liver via glucuronidation and is excreted in the urine;

adihydroartemisinin-P-glucuronide has been identified as the major urinary product in patients with falciparum malaria.

5.3 Preclinical safety data

Not applicable

6 Pharmaceutical particulars

6.1 List of excipients

Not Applicable as it is a Dry Powder Injection.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

A white Crystalline powder is filled in 7.5 ml Moulded Clear Vial USP Type III with Grey Bromo Butyl Rubber Stopper & 20 mm flip off Aluminium Seals. Such one vial is packed in a transparent tray pack with 1 ml Sodium bicarbonate Injection BP (5.0% w/v) & 5 ml Sodium Chloride Injection BP (0.9% w/v). Such one Tray is packed in a printed carton with packing insert.

7 Marketing authorization holder

Applicant:

M/s. UGOLAB PRODUCTIONS NIG LTD

No. 31A BURMA ROAD, SABON GARI, KANO, KANO STATE, NIGERIA.

Manufacturer:

M/s. Kamla Lifesciences Ltd.

G-84/1, Tarapur, MIDC, Boisar, District-Palghar 401506

PATIENT INFORMATION LEAFLET (PIL)
ARTESUNATE FOR INJECTION 60 MG/VIAL

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again before, during or after use of this medicine.
- If you have any further questions, ask your health care provider.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please inform your health care provider.

In this leaflet:

1. What Artesunate for Injection 60 mg/vial is and what it is used for.
2. What you need to know before you take Artesunate for Injection 60 mg/vial.
3. How to take Artesunate for Injection 60 mg/vial
4. Possible side effects
5. How to store Artesunate for Injection 60 mg/vial
6. Contents of the pack and other information

1. WHAT ARTESUNATE FOR INJECTION 60 MG/VIAL IS AND WHAT IT IS USED FOR

Artesunate is a soluble artemisinin derivative indicated for the emergency treatment of severe and/or complicated malaria caused by P. falciparum and P. vivax.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ARTESUNATE FOR INJECTION 60 MG/VIAL.

Do not take use ARTESUNATE FOR INJECTION 60 MG/VIAL if you are allergic to artesunate.

Warnings and precautions

Severe Falciparum malaria infections usually require additional therapy, like infusions and paracetamol. When the critical phase of the Falciparum malaria infection has passed, it is advised to weekly check your blood for parasites. If reinfection or recrudescence occurs, you should be treated with another antimalarial drug. Other antimalarials are also necessary when a mixed infection with P. vivax has been established or is suspected. In a clinical observational study with Artesunate for Injection 60 mg/vial late-onset haemolytic anaemia and persistent haemolytic anaemia have been seen (see also section 3 “what to do after treatment with artesunate”). There are no adjustments in dosing necessary if you have a decreased renal or hepatic function.

Other medicines and ARTESUNATE FOR INJECTION 60 MG/VIAL

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This particularly applies if you use one of the following medicines: chloroquine and chloroquine derivatives, omeprazole, free radical scavengers (like ascorbic acid and vitamin E).

Taking other medicines with ARTESUNATE FOR INJECTION 60 MG/VIAL

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This particularly applies if you use one of the following medicines: chloroquine and chloroquinederivatives, omeprazole, free radical scavengers (like ascorbic acid and vitamine E)

Pregnancy

Not enough data are available on the use of this medication during pregnancy. Ask your doctor for advice before taking this medicine.

Breast-feeding

Limited information indicates that dihydroartemisinin, the active metabolite of artesunate is present at low levels in breast milk. It is advised to (temporarily) stop breast-feeding.

Driving and using machines

No information is available

3. HOW TO TAKE ARTESUNATE FOR INJECTION 60 MG/VIAL

The dose of artesunate for injection 60 mg/vial is determined by the specialist internal medicine. artesunate for injection 60 mg/vial is administrated by intravenous injection.

How much to take

The recommended dose is 2.4 mg per kg body weight at T=0, T=12, T=24 hours and subsequently every 24 hours. After at least 24 hours (3 doses) switch to oral therapy as soon as possible. To minimize the chance of recrudescence it is important that you are treated with an antimalarial drug for 7 consecutive days.

If the product is contraindicated in a particular age group, this should be stated under this section.

Use in children

The recommended dose for children weighing 20 kg or more as for adults is: 2.4 mg per kg body weight. The recommended dose for children weighing less than 20 kg is 3 mg per kg body weight.

How should this product be prepared?

• Add the sodium bicarbonate solution (1 ml) to the vial with the powder

• Shake until the solution is clear

• Let the gas (CO2) escape from the vial through a needle

• Add 5 ml glucose 5% or 5 ml sodium chloride 0.9% solution to the vial • Swirl to form a homogeneous solution

• This solution should be administered

After reconstitution 1 ml of solution contains 10 mg artesunate. The total solution is 6 ml. Pull the required volume up and inject intravenously, over 1-2 minutes. The solution should not be added to an infusion.

If you take more ARTESUNATE FOR INJECTION 60 MG/VIAL.

Contact your doctor as soon as possible

If you forget to take ARTESUNATE FOR INJECTION 60 MG/VIAL.

Do not take a double dose to make up for a forgotten dose.

4. POSSIBLE SIDE EFFECTS

Like all medicine , Artesunate for Injection 60 mg/vial can cause side effects, but not everybody gets them. Some of these may be difficult to detect, and may be similar to detect, and may be similar to effect of the disease itself.

Common Side Effects

Dizziness, feeling sick, vomiting, light-headedness, headache, sleeplessness, hearing problems, 'flu-like effects (including fever, tiredness, bone and muscle pain), cough, altered taste, abdominal pain, diarrhoea, rash, and pain at injection site.

Uncommon Side Effects

Anaemia (low red blood cell count), neutropenia (low white blood cell count), reduction in platelets (which are important for blood clotting) and allergic reactions.

Rare Side Effects

Inflammation of the liver (hepatitis, with yellowing of eyes and skin) and inflammation of the pancreas (pancreatitis).

Very Rare Side Effects

Severe reduction in red blood cells, tingling sensation and nerve pain.

If You Get Side Effects

Consult your Doctor.

5. HOW TO STORE ARTESUNATE FOR INJECTION 60 MG/VIAL

Keep out of the reach and sight of children.

ARTESUNATE FOR INJECTION 60 MG/VIAL, is stored in the original packing, below 30° C, until it is ready to be used to create a solution. The reconstituted and diluted solutions should be stored below 30°

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

Do not use this medicine if the solution is not clear.

Remark: After reconstitution the solution must be used within 1 hour

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

What Artesunate for Injection contains

- The active substance is Artesunate
- The other ingredient is Sodium bicarbonate solution for dissolving the artesunate.
- The other ingredient is Sodium Chloride which is used for maintaining Tonicity.

What Artesunate for Injection 60 mg/vial looks like and content of the pack

7.5 ml moulded clear vial USP type III with label packed in tray with 1 ml clear ampoule of Sodium bicarbonate 5.0% w/v and 5 ml clear ampoule of Sodium Chloride (0.9% w/v). The tray is inserted into the carton with a leaflet inside of it.

Manufactured by:
M/s. Kamla Lifescience Ltd.
Plot no.G-84/1, Tarapur M.I.D.C, Boisar,
Tal. & Dist. Palghar, Maharashtra, India-401506.

Submitted by:
M/s. UGOLAB PRODUCTIONS NIG LTD
No. 31A BURMA ROAD, SABON GARI,
KANO, KANO STATE, NIGERIA.