1.3 Product Information

1.3.1 Summary Of product characteristics (SmPC)

1 Name of the medicinal product

Artemether Inj 80 mg/ml

2 Qualitative and Quantitative composition:

Each ml contains:

Artemether……80 mg

Water for Injection BP…….QS

Qualitative and Quantitative formula:

						Standard batch size: 50.0 Liters
Sr. No.	**Ingredient**	**Reference**	**Quantity/ ml**	**Overages %**	**Quantity/ Batch**	**Function**
1.	Artemether	IH	80 mg	--	4.00 Kg	Active Ingredient
2.	Butalate hydroxyl anisole	BP	0.2 mg	--	10.0 gm	Preservative
3.	Butalate hydroxyl toluene	BP	0.2 mg	--	10.0 gm	Antioxidant
4.	Ethyl oleate	BP	874.0 mg	--	43.7 Kg	Solvent

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3 Pharmaceutical form

Liquid Injection

A clear, colourless to yellowish liquid.

4 Clinical particulars

4.1 Therapeutic indication

Artemether Injection are indicated for

Treatment of slide-confirmed severe falciparum malaria in areas where there is evidence that quinine is ineffective. Radical cure should then be effected with a full dose of an effective oral antimalarial such as mefloquine.

4.2 Posology and method of administration

Adults and children:

3.2 mg/kg by intramuscular on the first day followed by 1.6 mg/kg once daily

weight	80 mg ampoule	
	Loading dose	Maintenance dose
3 – 4 kg	0.2 ml	0.1 ml
4 – 6 kg	0.3 ml	0.15 ml
7 – 9 kg	0.4 ml	0.2 ml
10 – 14 kg	0.6 ml	0.3 ml
15 – 19 kg	0.8 ml	0.4 ml
20 – 29 kg	1.2 ml	0.6 ml
30 – 39 kg	1.6 ml	0.8 ml
40 – 49 kg	2 ml	1 ml
50 – 59 kg	2.6 ml	1.2 ml

4.3 Contraindication

Artemether Injection are contraindicated in First trimester of pregnancy.

Hypersensitivity to artesunate including cases of anaphylaxis have been reported during the use of parenteral artesunate (including Artesunate for Injection). If hypotension, dyspnea, urticaria, or generalized rash occurs during administration of Artesunate for Injection, consider discontinuing Artesunate for Injection administration and continuing therapy with another antimalarial drug

4.4 Special warning and precautions for use

Artemether Injection 80 mg/ml should be used for the treatment of severe falciparum malaria only where there is evidence that the antimalarial efficacy of quinine is declining.

For children, since the injected volumes will be small, it is advisable to use a 1-ml syringe to ensure that the correct dose is given.

4.5 Interaction with other medicinal products and other forms of interaction

The following interactions include those observed with Artemether Injection 80 mg/ml

- The metabolism of Artemether can be decreased when combined with Acalabrutinib.
- The risk or severity of QTc prolongation can be increased when Acebutolol is combined with Artemether.
- The metabolism of Artemether can be decreased when combined with Acetylsalicylic acid.
- The serum concentration of Artemether can be decreased when it is combined with Alpelisib.
- The risk or severity of QTc prolongation can be increased when Alfuzosin is combined with Artemether.

4.6 Pregnancy and lactation

Pregnancy:

Little experience has been gained with the use of this drug in pregnancy but it should be withheld if it is lifesaving to the mother. It should be used with caution in the first trimester of pregnancy since some fetus absorption has been observed

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1.3.1.4.7 Effect on ability to drive and use machines

Patients receiving Artemether should be warned that dizziness or fatigue/asthenia may occur in which case they should not drive or use machines.

4.8 Undesirable effects

- headache, dizziness;
- fever, cough, feeling weak or tired;
- muscle pain, tenderness, or weakness;
- joint pain;
- vomiting;
- loss of appetite.

4.9 Overdose

Headache, drowsiness, respiratory and cardiovascular depression, arrhythmias, shock, visual disturbances, convulsions, respiratory and cardiac arrest. Overdosage is more likely in

children and with intravenous administration. Treatment of overdosage is symptomatic and supportive.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Artemether acts essentially as a blood schizonticide. The presence of the endoperoxide bridge (generating singlet oxygen and free radicals) appears to be essential for antimalarial activity. Inhibition of protein synthesis as the basic mechanism of action is suggested in studies which showed morphological changes in ribosomes as well as in the endoplasmic reticulum. Morphological changes of the parasitic membranes induced by Artemether have been described, being the result of free-radical action. Other in vitro tests suggest that β -Artemether causes a marked diminution of nucleic acid synthesis

Mechanism of action

Involves an interaction with ferriprotoporphyrin IX ("heme"), or ferrous ions, in the acidic parasite food vacuole, which results in the generation of cytotoxic radical species.

The generally accepted mechanism of action of peroxide antimalarials involves interaction of the peroxide-containing drug with heme, a hemoglobin degradation byproduct, derived from proteolysis of hemoglobin. This interaction is believed to result in the formation of a range of potentially toxic oxygen and carbon-centered radicals.

5.2 Pharmacokinetic properties

Intramuscular Artemether is rapidly absorbed reaching therapeutic levels within the first hour. Cmax is obtained within 4-6 hours. It is metabolized in the liver to the demethylated derivative dihydroartemisinin. The elimination is rapid, with a T1/2 of 1-3 hours. Dihydroartemisinin, being a potent antimalarial itself, has a similar T1/2 of. The degree of binding to plasma proteins varied markedly according to the species studied. The binding of β -Artemether with plasma protein is of the order of 50 %. Distribution of radioactivelabelled β -Artemether was found to be equal between cells and plasma.

5.3 Preclinical safety data

None stated.

6 Pharmaceutical particulars

6.1 List of excipients

Artemether injection 80 mg/ml contains:

ButalateHydroxy anisole BP

ButalateHydroxy Toluene BP

Ethyl oleate BP

6.2 Incompatibilities: --

Not applicable.

6.3 Shelf life

Unopened 24 months, after opening 28 days.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light.

6.5 Nature and contents of container

Primary packing:

1 ml Amber glass ampoules.

Secondary packing:

A PVC Tray containing 6 Amber glass ampoules of 1 ml each packed in carton along with leaflet.

6.6 Special precautions for disposal:

No specific requirement.

7 Marketing authorization holder

Applicant:

PRIYA PHARMACEUTICAL NIGERIALIMITED.,
No. 2F, Cl , Airport road , Kano, Kano State, Nigeria

Manufacturer:

M/s. Kamla Lifesciences Ltd.
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