SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

1.1 Invented name of the medicinal product:

ARTIM (Artemether Injection, 80mg/ml)

1.2 Strength:

80mg/ml

1.3 Pharmaceutical Form:

Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Name of the product	:	ARTIM
Generic Name	:	Artemether Injection, 80mg/ml
Strength	:	80mg
Formula & Composition	:	Each ml contains: Artemether IH …….80 mg Butylate Hydroxy Anisole BP ……. 0.2 mg Butylate Hydroxy Toluene BP ……. 0.2 mg Ethyl Oleate BP ……. Q.S.
Batch Size	:	100 Lit

Ingredient	**Specification**	**Label claim / ml**	**Quantity/Batch (in Kg)**
Active Ingredient			
Artemether	IH	80	8.055 Kg
Inactive Ingredient			
Butylate Hydroxy Anisole	BP	0.2 mg	20 gm
Butylate Hydroxy Toluene	BP	0.2 mg	20 gm
Ethyl Oleate	BP	q.s	100.0Lit

BP- British pharmacopeia

IH - In House

3. PHARMACEUTICAL FORM

Injection

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

ARTEMETHER 80 mg/ml is indicated for the treatment of malaria caused by all species of Plasmodium, including severe malaria caused by multiple drug resistant strains of Plasmodium falciparum.

4.2 Posology and method of administration

The dosage depends on the severity of the case and the clinical state of the patient. Formulations for intramuscular injection of Artemether are mostly used in case of severe malaria, such as cerebral malaria, but also in case of patients showing gastrointestinal problems.

Loading dose for adults and children: 3.2 mg/kg body weight administered as a single intramuscular injection on the first day.

Maintenance dose for adults and children: 1.6 mg/kg/day administered as intramuscular injection once a day during the following four days.

Maintenance treatment can also be continued by oral Artemisinin-based combination therapy (ACT) if the patient's condition does not require injections. The drug is given by intramuscular injection in the gluteal muscle or the quadriceps. Combination of other drugs in the same syringe should be avoided. Aseptic conditions must be respected when injecting Artemether.

Note:

a) A full course therapy of five days is essential in order to avoid recrudescence.

b) In case of severe malaria it may be necessary to increase the loading dose and to prolong treatment for seven days if parasitaemia is not cleared during the first few days.

Method of administration

Intramuscular

4.3 Contraindications

Artemether 80 mg/ml is indicated for use in children and adults.

There is no known contra-indication for the use of Artemether in the treatment of malaria. The use of Artemether should be avoided during pregnancy, particularly during the first trimester.

4.4 Special warning and Precautions for use.

The use of Artemether should be avoided during pregnancy, particularly during the first trimester.

4.5 Interactions with other medicinal products and other forms of interaction

Specific drug interactions were not observed. Artemether potentialises the antimalarial activity of other antimalarials.

4.6 Pregnancy and Lactation

Fertility

Not known.

Pregnancy

The use of Artemether should be avoided during pregnancy, particularly during the first trimester.

Lactation

Not known.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

Adverse events were usually not reported with the recommended dose. Laboratory abnormalities such as increase in transaminases and decrease in reticulocyte count are rare and transient and usually without clinical manifestations. A decrease in sinus frequency without changes in the electrocardiogram has also been reported. At high doses, transient abdominal pain, tinnitus and diarrhea have been described.

4.9 Overdose

Do not exceed the prescribed dose. A specific antidote is not known. The administration of several times the therapeutic dose was not reported to cause serious adverse events. In case of accidental and severe overdose, symptomatic treatment in a specialized center is recommended.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Artemether acts essentialy as a blood schizonticide. The presence of the endoperoxide bridge (generating singlet oxygen and free radicals) appears to be essential for the antimalarial activity. Inhibition of protein synthesis as the basic mechanism of action was suggested in studies showing 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 and of the oxidative effect caused by the opening of the peroxide group. Other in vitro tests suggest that Artemether causes a marked diminution of nucleic acid synthesis. Recent studies using electronic microscopy showed rupture of membrane structures of the parasites, leading to destruction of the parasite within a few hours.

Mechanism of action

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

Intra-muscular Artemether is rapidly absorbed, reaching therapeutic levels within the first hour and C-max within 4–9 hours. Artemether is metabolized in the liver to the demethylated derivative dihydroartemisinin.

The elimination is rapid with a T ½ of 1 – 3 hours. Dihydroartemisinin, being a potent antimalarial itself, has a T ½ of about 1 – 3 hours. The degree of binding to plasma proteins varied markedly according to the studied species, but it is about 50% in man. The distribution

of radioactive marked Artemether was found to be equal between cells and plasma.

5.3 Preclinical safety data

Single dose toxicity

Artemether was found to exhibit an i.m. LD50 of 263 mg/kg in mice. One monkey tolerated an i.m. dose of 141 mg/kg, rabbits showed no toxicity at an i.m. dose of160 mg/kg. (China Cooperative Research Group, 1982b).

Repeated dose toxicity

Rats receiving total intramuscular doses of 40 to 360 mg/kg over a 9 to 14 day period exhibited some body weight loss and a slight hepatic fatty degeneration in the high dose group (China Cooperative Research Group, 1982b).

Dogs were given two three day courses of i.m. injections with an interval of 7 days; a second group was given these three-day courses over a period of 3 months. Total doses applied were 24 and 972 mg/kg, respectively (daily doses not stated). There were no abnormal findings reported, with the exception of body weight loss and slight hepatic fatty degeneration in the high-dose group (China Cooperative Research Group, 1982b).

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

Following excipients are used in ARTIM:

Butylate Hydroxy Anisole BP

Butylate Hydroxy Toluene BP

Ethyl Oleate BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months from the date of manufacture.

6.4 Special precautions for storage

Store below 30°C, protected from light.

6.5 Nature and contents of container

1 ml USP type I amber ampoule with brown ring is filled, sealed and labeled. 6 such ampoules are to be placed in a transparent tray. The tray is inserted in carton with inside KILITCH printing along with literature.

6.6 Special precautions for disposal

Keep out of reach of children.

7. REGISTRANT

Manufactured for :

Name: EUROMED LTD.

Address:'B' Insurance House, 34/36 Association Venue (Opp. Total Filling Station) Ilupeju, Lagos, Nigeria

Manufactured by:

Name: KILITCH DRUGS INDIA LTD.

Address: Plot no. C-301/2, M.I.D.C. T.T.C., Industrial area, Pawane, Navi Mumbai- 400 705. Maharashtra, INDIA

Telephone: +91 22 27680913

Fax no.: 022-61214101

E-mail: bhavinmehta@kilitch.com

8. DRUG PRODUCT MANUFACTURER

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9. NAFDAC REGISTRATION NUMBER(S)

C4-1387