Summary OF Product Characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

ARTEMETIN-BETA
(Artemether Injection 80mg/ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Artemether….80mg
Excipients……q.s

S. No.	Ingredient	Specification Reference	Qty. per Ampoule (mg)	Qty. for 300,000Ampoules(Kgs)	Function
1.	Artemether	CP	80	24	Active ingredient
2.	Tea-seed oil	CP	1	300	Excipient

3. Pharmaceutical Form:

Sterile Clear Solution for Intramuscular Injection.

4. CLINICAL PARTICULARS:

4.1. Therapeutic Indication

ARTEMETIN-BETA for intramuscular injection is indicated in adults and children for the treatment of severe Plasmodium falciparum malaria infection. It should be used only when Artesunate injection is not available. Radical cure should be effected with a full dose of an effective oral antimalarial medication. ARTEMETIN-BETA INJECTION should be given for a minimum of 24 hours, and continued until the patient is able to take oral antimalarial medication.

Consideration should be given to official treatment guidelines for malaria (e.g. by WHO, see References)

4.2. Posology and Method of Administration

Posology

The total daily dose of ARTEMETIN-BETA INJECTION should not exceed 160 mg/day.

Adults

On the first day: 2 ampoules once a day (i.e. 160 mg/day). During the subsequent days:

1 ampoule/day (i.e. 80 mg/day), for a maximum of 4 days.

Children

On the first day: 3.2 mg/kg once a day (i.e. 0.2 ml/5 kg/day) During the subsequent days:

1.6mg/kg/day (i.e. 0.1 ml/5 kg/day) for a maximum of 4 days.

Renal/hepatic impairment

No dose adjustments are necessary in patients with renal or hepatic impairment.

Method of Administration

ARTEMETIN-BETA INJECTION is exclusively administered via deep intramuscular (IM) route. Injections must be administered under strictly aseptic conditions. For children, since the injected volumes are small, it is advisable to use a 1-ml syringe to ensure that the correct dose is given and to administer IM injections into the anterior thigh. Avoid combining other medicinal products in the same syringe.

4.3. Contraindications

- Hypersensitivity to Artemether
- Hypersensitivity to Arachis (peanut) oil

4.4. Special Warnings and Precautions for Use

Prolongation of the QT-interval: ARTEMETIN-BETA INJECTION may prolong the QTc interval and increase the risk of cardiac arrhythmias (see sections 4.5, 4.8 and 5.3). Therefore, ARTEMETIN-BETA INJECTION should be avoided in:

I. Patients with a family history of congenital prolongation of the QTc interval or sudden death, or with any other clinical condition known to prolong the QTc interval, such as patients with a history of symptomatic cardiac arrhythmias, clinically relevant bradycardia or congestive heart failure.

II. Patients with known disturbances of electrolyte balance, e.g. hypokalaemia (see section 4.5) or hypomagnesaemia.

III. Patients taking drugs that prolong the QTc interval, such as class IA and III antiarrhythmics, certain neuroleptics and antidepressants, certain antibiotics (some macrolides and fluoroquinolones), certain non-sedating antihistamines (terfenadine, astemizole) and cisapride (see section 4.5). In these patients, ECG and serum potassium monitoring is advised.

Pregnancy: ARTEMETIN-BETA INJECTION should not be used in the first trimester of pregnancy in situations where other suitable and effective antimalarials are available (see section 4.6).

Malaria Prophylaxis: ARTEMETIN-BETA INJECTION has not been evaluated for malaria prophylaxis. Severe Malaria not caused by P. falciparum: ARTEMETIN-BETA INJECTION has not been evaluated for the treatment of severe malaria due to P. vivax. Uncomplicated malaria: According to WHO malaria treatment guidelines, uncomplicated P. falciparum malaria must be treated with artemisinin-based combination therapy and not by artemisinin derivatives alone or any other monotherapy. ARTEMETIN-BETA INJECTION contains arachis (peanut) oil and may cause hypersensitivity reactions (urticaria, anaphylactic shock)

4.5. Interaction with Other Medicinal Products and Other Forms of Interaction

Inadvisable concomitant medications: Artemether IM. should not be used in patients taking drugs that are known to prolong the QTc interval, as effects may be additive and increase the risk of cardiac arrhythmia. Such as: - Class IA antiarrhythmics (quinidine, hydroquinidine, disopyramide) - Class III antiarrhythmics (amiodarone, sotalol, dofetilide, ibutilide) - Certain neuroleptics (amisulpride, chlorpromazine, cyamemazine, droperidol, flupentixol, fluphenazine, haloperidol, levomepromazin, pimozide, pipamperone, pipotiazine, propericiazine, sertindole, sulpiride, sultopride, tiapride, zuclopenthixol) - Certain antiparasitic drugs (halofantrine, lumefantrine, pentamidine) - And other drugs such as bepridil, cisapride, diphemanil, dolasetron, methadone, mizolastine,terfenadine, toremifen, moxifloxacin, sparfloxacin, erythromycin IV, spiramycinIV, vincamine IV.

4.6. Fertility, Pregnancy and Breastfeeding

Pregnancy

Malaria is known to be particularly hazardous during pregnancy. The benefits and risks of therapy with artemether IM to the mother and fetus must be assessed by the health care provider.

There is insufficient data from the use of artemether IM in pregnant women. In animal studies artemether IM, as well as other artemisinin derivatives, has been shown to cause post-implantation losses and serious birth defects when administered during the first trimester of pregnancy (see sections 4.4 and 5.3).

Blood and lymphatic system disorders: Frequency not known: transient decrease in reticulocytes and, more rarely, leukocytes. Cardiac disorders: Very common: prolongation in QT interval. Common: bradycardia (mostly reported as mild and transient), first-degree atrioventricular block. Ear and labyrinth disorders: Rarely: transient cases of deafness. General disorders and administration site conditions: Very common: injection site pain. Hepatobiliary disorders: Very rare: transient and moderate elevation of liver transaminases (ALT, AST). Cases of nausea, vomiting and abdominal pain, coma, and convulsions have been also reported. They may be in part due to the disease process. If any of the side effects is serious or unexpected, you should inform the supplier (see section 7) and/or health authority, as per local regulation.

During the 1st trimester of pregnancy ARTEMETIN-BETA INJECTION should not be used unless clearly necessary e.g. if treatment is life-saving for the mother and if another antimalarial is not suitable, not available or not tolerated.

During 2nd and 3rd trimesters of pregnancy, ARTEMETIN-BETA INJECTION may be used with caution, only if other antimalarials are unsuitable.

Breastfeeding

The safety of Artemether IM during breastfeeding has not been established. However, the amounts of antimalarials in breast milk are small. Therefore, lactating women can receive artemisinin-based therapies (including ARTEMETIN-BETA INJECTION) for malaria treatment.

4.7. Effects on the Ability to Drive and Use Machines

There are no data available with regard to the effects on the ability to drive and to use machines.

4.8. Undesirable Effects

- Palpitations
- Electrocardiogram QT Prolonged
- Headache
- Dizziness
- Paraesthesia
- Ataxia
- Hypoaesthesia

4.9. Overdose

In cases of suspected over dosage, symptomatic and supportive therapy should be given as appropriate, which should include ECG and Blood Potassium Monitoring.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamics Properties

Pharmacotherapeutic group: Antimalarials, Blood Schizonticide, ATC code: P01BE02

Artemether is the methyl ether of dihydroartemisinin (DHA). It acts essentially as a blood schizonticide. The presence of the endoperoxide bridge (generating single oxygen and free radicals) appears to be essential for antimalarial activity. No cross- resistance exists with chloroquine. The antimalarial action of artemether involves the rapid destruction of Plasmodia by inhibition of protein synthesis during trophozoite growth.

5.2. Pharmacokinetic Properties

The pharmacokinetics of ARTEMETIN-BETA INJECTION following IM administration appear to be highly variable especially in severely ill children. Available data suggest that absorption kinetics of the drug are variable, probably related to drug formulation rather than to pathophysiological factors. The wide range of Cmax, Tmax and AUC values observed for the parent drug and DHA, the major metabolite, indicates that the absorption kinetics of IM artemether is slow and unpredictable in extent, and that hydrolysis into DHA is limited.

Pharmacokinetic parameters of artemether administered by the intramuscular route in healthy male adults:

Pharmacokinetic parameter (Mean ± SD)	**Dose 3.2 mg/kg**
T_{max} (hours)	4.1 ± 0.7
C_{max} (µg/ml)*	1.2 ± 0.9
AUC (µg.h/ml)*	9.2 ± 5.1
$t_{1/2}$ (hours)	7.1 ±0.5
V_d (l/kg)	4.7 ± 3.0

5.3. Preclinical Safety Data

Single dose toxicity studies: Artemether was found to exhibit an IM LD50 of 263 mg/kg in mice. One monkey tolerated an IM dose of 141 mg/kg, rabbits showed no toxicity at an IM dose of 160 mg/kg. Subacute toxicity studies: In the subacute toxicity studies (14-day and 4-week) by the IM route in rats and dogs, haematological, neurological and electrocardiographic signs appeared to be the most sensitive parameters of the toxicity of artemether.

Reproductive toxicity studies: In rats, fertility was not modified at the doses of 5 mg/kg/day or 10 mg/kg/day but showed a statistically significant decrease at the dose of 20 mg/kg/day. In this study, the dose of 10 mg/kg/day had no effects on reproduction function, in particular on fertility, although a slight toxicity was still observed at this dose in the parents. IM artemether at the doses of 10.7 and 21.4 mg/kg/day was embryolethal in the gestating female rat. A dose of 5.4 mg/kg/day, artemether was neither embryolethal nor teratogenic, although foetus weight was significantly lower compared to control females. IM treatment of gestating female rats during the critical phase of embryogenesis with artemether 2 mg/kg/day and 4 mg/kg/day was neither embryolethal, nor foetolethal, nor teratogenic. However, a tendency for delayed occipital ossification was noted in foetuses from females of the 4 mg/kg/day group. At the dose of 8mg/kg/day, IM artemether was embryolethal but no malformations were observed in live fetuses at this dose. In rabbits, artemether at the doses of 5.4, 10.7 and 21.4 mg/kg/day was fully embryotoxic. The higher dose was toxic in the mothers as shown by weight loss. Nothing in the frequency or type of abnormality observed in this study indicates a teratogenic effect of IM artemether at the doses of 0.5 and 1 mg/kg/day in rabbits.

Mutagenicity: Artemether did not show any mutagenic activity neither in in vitro nor in vivo tests.

Neurotoxicity: Artemether was shown to be consistently neurotoxic by the IM route in mice, rats and dogs. However, neurotoxicity was seen with very high IM doses, and with treatment duration far in excess of the duration of IM treatment in malaria patients. Effect of artemether on electrocardiogram: The alteration of cardiac repolarization, namely an increase in heart rate corrected QT interval (QTc) observed in rats and dogs appears to be a target sign of artemether, although at the high dose used, changes in the electrocardiogram may also be due to the general deterioration of the animals.

Carcinogenesis: No studies of the carcinogenic potential of artemether have been conducted.

6. Pharmaceutical Particulars:

6.1. List of Excipients

Tea-seed oil

6.2. Incompatibilities

None known

6.3. Shelf Life

36 months from the date of manufacture.

6.4. Special Precautions for Storage

Store in a cool and dry place, protected from light

6.5. Nature and Contents of Container

1ml packed in one ampoule, such 6 ampoules packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

6.6. Special Precautions for Disposal and other Handling

No special requirements

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

LABETA DRUGS LIMITED
125C, Olaitan street, Surulere, Lagos.
greenabeta_nig@yahoo.com
+238174828411

8. DRUG PRODUCT MANUFACTURER

ANHUI CHENGSHI PHARMACEUTICAL CO. LIMITED.
No. 5068; Huaigshang Road Bengbu, Anhui; China.
Telephone: 13151968065
E-mail: 2014104343@qq.com

9. NAFDAC REGISTRATION NUMBER

A4-5947

蒿甲醚小盒110230906
成品尺寸：90x68x15mm
SXMJ-2023.09.08(15:35)

C95Y85
M5Y100
MY100
K100

ARTEMETIN-BETA

Each 1ml ampoule contains Artemether 80mg

DOSAGE AND ADMINISTRATION:

	Adults	Children
Day 1	160mg (2 Amps.)	4.0mg/kg body weight
Day 2	80mg (1Amp.)	2.0mg/kg body weight
Day 3	80mg (1 Amp.)	2.0mg/kg body weight
Day 4	80mg (1 Amp.)	2.0mg/kg body weight
Day 5	80mg (1 Amp.)	2.0mg/kg body weight

Manufactured by:
Anhui Chengshi Pharmaceutical Co.,Ltd.
No.5068, Huaishang Road, Bengbu,Anhui Province, China

LaBeta®

Batch No.:110230906
Mfg.Date: 09/2023
Exp.Date: 09/2026

SOLE AGENT:
LABETA DRUGS LIMITED
125C OLAITAN STREET,SURULERE, LAGOS.

ARTEMETIN-BETA

Artemether Injection

80mg/1ml x6 Ampoule
for I.M use only

ARTEMETIN-BETA
NAFDAC REG.NO.:A4-5947

LaBeta®

Store below 25°C, dry and dark place.
Keep out of reach of children.

Warning:
To be sold by retail on the prescription
of a registered medical practitioner only


C95Y85
M5Y100
MY100
K100
蒿甲醚中盒110230906
成品尺寸：90x68x15mm
SXMJ-2023.09.08(15:39)
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