Annex 1. Summary of Product Characteristics (SmPC)

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Artemether injection 80mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains Artemether 80mg.

3 PHARMACEUTICAL FORM

Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Artemether is indicated for the treatment of malaria caused by all forms of Plasmodium including severe malaria caused by multiple drug resistant strains of P. Falciparum

4.2 Posology and method of administration

Adults: Optimal results have been obtained when Artemether is administered in doses of 240 to 320 mg as a loading dose the first day of treatment. This should be followed by additional injection of one ampoule per day during the following four days as a maintenance dose. However, treatment can also be continued by oral therapy with one of the Artemisinine derivatives like Artesunate tablets, if the patient condition does not require injections.

Children: 3.2 mg/kg on day one and 1.6 mg/kg for the next 4 days. For the maintenance treatment oral formulations should be considered when the clinical condition permits.

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

b) In 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

4.3 Contraindications

Pregnancy: it is advisable not to use drugs during pregnancy but in view of the high risk of malaria during pregnancy for mother and foetus, the responsible physician may consider it essential, as in the case of cerebral malaria, to treat a pregnant woman. Artemisinin derivatives like Artemether are the fastest acting schizontocides and rapid clearance of parasites is essential.

4.4 Special warnings and precautions for use

In cerebral malaria and complicated malaria, general supporting therapy is usually required.

4.5 Interaction with other medicinal products and other forms of interaction

Do not exceed the prescribed dose. In case of overdosage, symptomatic treatment in a specialized unit is recommended. The administration of several times the therapeutic dose was not reported to give serious side effects.

Specific untoward drug interactions have not been found. Potentialisation of other antimalarial drugs is a common feature. Loading dose of Artemether followed by other antimalarial drugs has shown strong beneficial potentialisation effects.

4.6 Pregnancy and lactation

Pregnancy : It is advisable not to use drugs during pregnancy but in view of the high risk of malaria during pregnancy for mother and foetus, the responsible physician may consider it essential, as in the case of cerebral malaria, to treat a pregnant woman. Artemisinin derivatives like Artemether are the fastest acting schizontocides and rapid clearance of parasites is essential.

Breastfeeding: Data on excretion in breast milk are not available.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

At the therapeutic dose there are very few side-effects. There are reports on laboratory abnormalities, i.e. a decrease in reticulocyte count, a transient increase in transaminases and ECG changes (lowering of sinus heart rate, but effects on conduction or on repolarisation have not been observed). At high doses, transient abdominal pain, diarrhoea and tinnitus was reported.

4.9 Overdose

Not known.

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 Artemether causes a marked diminution of nucleic acid synthesis.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tea oil

6.2 Incompatibilities

Not known.

6.3 Shelf life

Three years

6.4 Special precautions for storage

Protected from light and stored at room temperature. KEEP OUT OF REACH OF CHILDREN.

7. Marketing authorisation holder

Shandong Yikang Pharmaceutical Co., Ltd.

No. 3288 Yikang Avenue Tengzhou City, Shandong, China

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorization

10. Date of revision of the text

Dec 2021