SMPC

MICPON Artemether Injection
Artemether Injection 80mg/1ml

PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of the medicinal product

1.1 (Invented) name of the medicinal product

Artemether Injection

1.2 Strength

80 mg/1 ml

1.3 Pharmaceutical form

Injection

2. Qualitative and quantitative composition

Each 1 ml ampoule contains artemether 80 mg.

3. Pharmaceutical form

Injection.

Colorless or yellowish clear oily solution.

4. Clinical particulars

4.1 Therapeutic indications

Artemether Injection is indicated for treatment of acute, uncomplicated malaria infections due to Plasmodium falciparum in patients of 5 kg bodyweight and above. Artemether Injection has been shown to be effective in geographical regions where resistance to chloroquine has been reported.

4.2 Posology and method of administration

Adults: First day: 80 mg administered by IM route twice a day at a 12 hourly interval (=160 mg/day).

Following 4 days: 80 mg administered by IM route once a day.

The dose should not be exceed 480 mg in adults.

Children: First day: 1.6 mg/kg of body weight administered by IM route twice a day at a 12 hourly (= 3.2 mg /Kg body wt/day).

Following 4 days: 1.6 mg/Kg of body weight administered by IM route once a day.

The dose should not be exceed 9.6 mg/ kg in children.

Posology and mode of administration:

Intramuscular Only

4.3 Contraindications

Hypersensitivity to artemether or other artemisinin compounds.

Pregnancy, unless the doctor considers it essential as in the case of cerebral malaria.

4.4 Special warnings and precautions for use

Artemether 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.

In cerebral malaria and complicated malaria, general supporting therapy may be required.

4.5 Interaction with other medicinal products and other forms of interaction

Artemether causes QT prolongation in some patients. Thus concomitant use of erythromycin, terfenadine, procainamide, quinidine, disopyramide, amiodarone, bretylium, bepridil, sotalol, astemizole, probucol, tricyclic antidepressants, phenothiazines may be avoided.

4.6 Pregnancy and lactation

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Artemisinin and its derivatives can be used for treatment of uncomplicated malaria during the second and third trimester of pregnancy in areas of multidrug resistance. Owing to lack of data, use in the first trimester of pregnancy is not recommended.

Artemisinin and its derivatives have not been measured in the milk to nursing mothers. It is very likely that these are present in milk and nursing mothers should not be given artemisinin if they are suffering from uncomplicated malaria either in multidrug resistance or drug sensitive situations. If the nursing mother is suffering from complicated and serious malaria induced by multidrug-resistant P. falciparum and artemisinin is indicated, breast-feeding should be stopped.

4.7 Effects on ability to drive and use machines

Not available.

4.8 Undesirable effects

Artemether has been remarkably well-tolerated, and appears less toxic than quinine or chloroquine; adverse effects include bradycardia, electrocardiogram abnormalities, gastrointestinal disturbances, dizziness, injection site pain, skin reactions, and fever. Transient decreases in neutrophils and reticulocytes have been reported in some patients treated with artemether.

Drug induced fever has been observed with artemether. Mild reactions were seen in patients to whom artemether had been administered intramuscularly. These included nausea, hypotension, dizziness and tinnitus.

These side effects were also reported: dark urine, sweating, somnolence, and jaundice. There were no deaths or any other side effects. No irreversible side effects were seen.

Slight rise of SGOT and SGPT may occur in individual cases. Neurological side effects have not yet been observed in clinical use but clinical trials suggest that coma may be prolonged in patients treated with artemether and there was an increased incidence of convulsions in one trial in cerebral malaria. Transient first degree heart block has been documented in three patients receiving artemether.

Neurotoxicity has been observed in animal studies but not in humans.

Cardiotoxicity has been observed following administration of high doses of Artemether.

4.9 Overdose

There is no experience with overdose with artemether. There is no specific antidote known for the artemisinin derivatives.

However, experimental toxicological results obtained with large doses of artemisinin on the cardiovascular system and the CNS should be considered. Overdosage could bring on cardiac irregularities. An ECG should be taken before initiating treatment in cardiac patients. Irregularities in the pulse should be looked for and cardiac monitoring carried out if necessary. The animal results on the CNS suggest that overdose could result in changes in brain stem function. Clinicians treating cases of overdosage should look for changes in gait, loss of balance, or changes in ocular movements and reflexes.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimalarials, blood schizonticide

ATC code: P01BE02

Artemether is a antimalarial medicines.

Artemisinin and its semisynthetic derivatives act essentially as blood schizonticides.

The presence of the endoperoxidebridge appears to be essential for antimalarial activity: generation of singlet oxygen and formation of free radicals.

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 dihydroartemisinin have been described, being the result of free radical action.

The observation that membranous structures are disrupted have lead, once again, to the hypothesis that the site of action of artemisinin could be the membranous structures.

Other in vitro tests suggest that artemisinin causes a marked diminution of nucleic acid synthesis.

5.2 Pharmacokinetic properties

Oral ß-Artemether is rapidly absorbed reaching Cmax Within 2-3 hours. Intramuscular ß-Artemether is rapidly absorbed reaching Cmax Within 4-9 hours. It is metabolized in the liver to the demethylated derivative dihydroartemisinin. The elimination is rapid, with a TI/2 of 4 hours.

Dihydroartemisinin has a Tl/2 of more than 10 hours.

The degree of binding to plasma proteins varied markedly according to the species considered. The binding of ß-Artemether with plasma protein was 58% in mice, 61% in monkeys and 77% in humans. The binding of β -Artemether with plasma protein is of the order of 50%. Radioactivity of free ß-Artemether in plasma was found to be equal to that in red blood cells indicating an equal distribution of free drug between cells and plasma.

Artemisinin and related compounds are difficult to assay in body fluids.

Measurement can be done by high-performance liquid chromatography with UV detection and electrochemical detection. These drugs bind avidly and irreversibly to membranes, including those of normal erythrocytes and may also bind covalently to plasma proteins.

In view of these difficulties, some groups have developed bio-assays as useful, if imprecise, measures of biological activity.

Distribution and excretion

Artemisinin and its derivatives are metabolised rapidly in vivo to dihydroartemisinin.

This active metabolise may be eliminated more slowly than the parent compound. Intramuscular ß-Artemether is rapidly absorbed reaching Cmax within 4 - 9 hours. Oral, ß-Artemether is rapidly absorbed reaching Cmax within 2 - 3 hours.

The elimination is rapid, with a Tl/2 of 4 hours.

Pharmacokinetics of oral ß-Artemether in healthy males and patients with acute, uncomplicated, falciparum malaria.

The pharmacokinetics of a single oral dose of ß-Artemether 200 mg were investigated in 6 healthy male volunteers. The pharmacokinetics of multiple doses of oral ß-Artemether 200 mg as an initial dose followed by 100 mg at 12h later, then 100 mg daily for 4 days were investigated in 8 male patients with acute uncomplicated falciparum malaria.

In the healthy volunteers, median maximum plasma concentrations of ß-Artemetherof 118 ng/ml were reached at 3h.

ß-Artemether undergoes rapid and extensive conversion to dihydroartemisinin.

The active metabolise, dihydroartemisinin, reached Cmax at the median time of 6h, attaining higher plasma concentrations than the parent drug.

In the patients ß-Artemether was rapidly absorbed; median absorption half-life was 0.29h Cmax of 199 ng/ml was reached at 2.3h after the first dose. Steady state was reached after the third dose (24h). The plasma levels indicate high bioavailability.

Metabolism

The major metabolise of B-Artemether is the demethylated product dihydroartemisinin. The following are considered to be metabolises.

3 a-hydroxydeoxydihydroqinghaosu

2 a-hydroxyartemether

9 a-hydroxyartemether

5.3 Preclinical safety data

Toxicity

Animal studies on acute toxicity show that the LD50 of Artemether in mice is a single i.g. administration of 895mg/kg and a single i.m. injection of 296mg/kg dose; in rats, the LD50 is a single i.m. injection of 597mg/kg dose.

Carcinogenicity

Carcinogenicity studies with the artemether were not conducted.

6. Pharmaceutical particulars

6.1 List of excipients

Soybean Oil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store between 8-25°C. Protect from light.

Keep medicines out of the reach of children.

6.5 Nature and contents of container

Type I clear glass ampoule containing 1 ml solution for injection.

Package of 6 ampoules per box.

6.6 Special precautions for disposal

Not applicable.

6.7 Applicant/manufacturer

Jiangsu Ruinian Qianjin Pharmaceutical Co. Ltd.

Chuanbu Village, Dingshu Town, Yixing City, Jiangsu Province, China

6.8 Marketing authorisation holder

MICPON PHARMACY LTD.

162 SAIKO ROAD MINNA, NIGER STATE, NIGERIA.

6.9 Date of first authorisation/renewal of the authorisation

12/03/2012

6.9 Date of revision of the text

23/06/2023