

## **1.3 PRODUCT INFORMATION**

### **1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SPC)**

#### **1. Name of the medicinal product**

##### **1.1 Name of the medicinal product**

Derms 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**

The drug is for intramuscular injection, for a period of 5 days and not exceeding a total of 480mg for adults.

The initial dose for adults is 160mg (2 ampoules), followed by 80mg (1 ampoule) every time from the 2<sup>nd</sup> to 5<sup>th</sup> day. The dose for children or overweight patients should be decreased or increased on the basis of the individual weight or under the doctor's prescription.

	Day-1	Day-2	Day-3	Day-4	Day-5
Adults	160 mg (2 ampoules)	80 mg (1 ampoule)	80 mg (1 ampoule)	80 mg (1 ampoule)	80 mg (1 ampoule)
Children	4mg/kg bodyweight	2mg/kg bodyweight	2mg/kg bodyweight	2mg/kg bodyweight	2mg/kg bodyweight

#### **4.3 Contraindications**

Hypersensitivity.

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.

#### **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**

In the body, artemether is metabolized into the active metabolite dihydroartemisinin. The drug works against the erythrocytic stages of *P. falciparum* by inhibiting nucleic acid and protein synthesis. Artemether is administered in combination with lumefantrine for improved efficacy.

Artemether has a rapid onset of action and is rapidly cleared from the body. It is thought that

artemether provides rapid symptomatic relief by reducing the number of malarial parasites.

Lumefantrine has a much longer half life and is believed to clear residual parasites.

## **5.2 Pharmacokinetic properties**

Absorption of artemether is improved 2- to 3-fold with food. It is highly bound to protein (95.4%).

Peak concentrations of artemether are seen 2 hours after administration.

Artemether is metabolized in the human body to the active metabolite, dihydroartemisinin, primarily by hepatic enzymes CYP3A4/5. Both the parent drug and active metabolite are eliminated with a half-life of about 2 hours.

### **Mechanism of Action**

Artemether is an artemisinin derivative and the mechanism of action for artemisinins is unknown. One of the proposed mechanisms is that through inhibiting anti-oxidant and metabolic enzymes, artemisinin derivatives inflict oxidative and metabolic stress on the cell. Some pathways affected may concern glutathione and glucose metabolism. As a consequence, lesions and reduced growth of the parasite may result.

Another possible mechanism of action suggests that artemisinin drugs exert their cidal action through inhibiting PfATP6. Since PfATP6 is an enzyme regulating cellular calcium concentration, its malfunctioning will lead to intracellular calcium accumulation, which in turns causes cell death.

### **Metabolism**

Rapidly hydrolysed to the active metabolite dihydroartemisinin.

### **Excretion**

Elimination half-life: about 4-11 hr after IM.

## **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**

Tea Tree Oil

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years

### **6.4 Special precautions for storage**

Store in room temperature below 30°C.

### **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.

## **7. MARKETED BY:**

Derm Pharmaceutical Limited

19, Alhaji Salami Street, Aguda Surulere, Lagos State, Nigeria.

## **8. MANUFACTURED BY:**

Shanxi Zhongbao Shuguang Pharmaceutical Co. Ltd

No.1, Kangle St., Qi County, Jinzhong City, Shanxi Province, P.R., China.