1.3.1 Summary of Product Characteristics (SmPC)

1.3.1.1 Name of the Medicinal Product

International Non– Proprietary Name (INN): Artemether

1.3.1.2 ATC and Forensic Classification

ATC Classification: Antimalarial.

1.3.1.3. Qualitative and quantitative composition

Each 1 ml Ampoule contains Artemether 80mg

1.3.1.4. Pharmaceutical form

Liquid injection ;

1ml Ampoule containing a colourless or yellowish clear oily liquid

1.3.1.5. Clinical particulars

1.3.1.5.1 Therapeutic indications

It is indicated for the treatment of all kinds of malarial including the chloroquine-resistant P. falciparum malarial and the first aid of critical malaria.

1.3.1.5.2 Posology and method of administration

The drug is used for intramuscular injection, five days course with the initial dose of 3.2mg/kg, followed by 1.6 mg/kg for the following 4 days.
The initial dose of adults is 160 mg (2 ampoules), followed by 80 mg (1 ampoule) every time from the 2^{nd} to 5^{th} day. The dose for children or overweight patients should be decreased or increase on the basis of the individual weight or under the doctor's prescription.
Administration for children:
For children, the dose should be chosen as follows:

Age (year)	**Weight**	**Total dose**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**
<1	<8kg	75mg	25mg	12.5mg	12.5mg	12.5mg	12.5mg
1-3	8-12.5kg	120mg	40mg	20mg	20mg	20mg	20mg
3-6	12.5-17.5kg	150mg	50mg	25mg	25mg	25mg	25mg
6-9	17.5-25kg	240mg	80mg	40mg	40mg	40mg	40mg
9-12	25-32kg	300mg	100mg	50mg	50mg	50mg	50mg
12-16	32-47kg	360mg	120mg	60mg	60mg	60mg	60mg

The dose for the children out of the above ranges should be decreased or increase on the basis of the individual weight or under the doctor's prescription.

1.3.1.5.3 Contraindications

Artemether is contraindicated in patients with hypersensitivity to artemether or other artemisinin compounds or any excipient in the injection.
Artemether is not recommended in the first trimester of pregnancy because of limited data.

1.3.1.5.4 Special warnings and precautions for use

Clinical dosage exhibits slight adverse reactions.

Artemether has been remarkably well-tolerated, and appears less toxic than quinine or chloroquine; adverse effects include bradycardia, electrocardiogram abnormalities, gastrointestinal disturbances (nausea, abdominal pain, diarrhoea - oral therapy only), 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

1.3.1.5.5 Interaction with other medicinal products and other forms of interaction

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 have shown strong beneficial potentialisation effects.

1.3.1.5.6 Pregnancy and lactation

Artemether is not recommended in the first trimester of pregnancy because of limited data.

1.3.1.5.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Due to the occurrence of some adverse reactions (see section 4.8) the ability to drive and use machines may be impaired.

1.3.1.5.8 Undesirable effects

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

There is no experience with overdosage 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.
In case of overdosage, symptomatic treatment is recommender under the instruction of doctors.

1.3.1.6 Pharmacological properties

1.3.2.6.1 Pharmacodynamic properties

Artemether is active against all Plasmodia including those which may be resistant to other antimalarials.
Artemether has very rapid schizontocidal activity. The schizontocidal activity of artemether is mainly due to destruction of the asexual erythrocytic forms of P. falciparum and P. vivax. There is inhibition of protein synthesis during growth of trophozoites. There is no cross resistance with chloroquine.
It is not hypnozoiticidal but it reduces gametocyte carriage.
There is no rationale at present for using artemether for chemoprophylaxis.

1.3.1.6.2 Pharmacokinetic properties

Intramuscular Artemether is rapidly absorbed reaching therapeutic levels within the first hour. Cmax is obtained within 4-6 hours. It is metabolized in the liver to the demethylated derivative dihydroartemisinin. The elimination is rapid, with a T1/2 of 1-3 hours. Dihydroartemisinin, being a potent antimalarial itself, has a similar T1/2 of. The degree of binding to plasma proteins varied markedly according to the species studied. The binding of β -Artemether with plasma protein is of the order of 50 %. Distribution of radioactive-labelled β -Artemether was found to be equal between cells and plasma.

1.3.1.6.3 Preclinical safety data

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. This proves the quite low toxicity of Artemether.

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1.3.1.7 Pharmaceutical Particulars

1.3.1.7.1 Incompatibilities

Not applicable.

1.3.1.7 2 Shelf life: 36 Months

1.3.1.7.3 Special precautions for storage :

Store below 30°C. Protect from light.

1.3.1.7.4 Nature and contents of container

80mg/ ml – Clear Type II glass ampoule packs of 6 ampoules per box.

1.3.1.7.5 Special precautions for disposal

Single use only. Discard any unused contents.

1.3.1.8. Marketing authorisation holder

Ningbo Voice Biochemic Co., Ltd.
298 West Zhonghsan Road, Ningbo . P.R. China