SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT:
Rotem Injection 80mg / ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each ml contains:
Artemether Ph. Int 80mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:
Description:
Injection, Colorless, clear viscous solution, in 1ml clear glass ampoule.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:
Treatment of slide-confirmed severe falciparum malaria in areas where there is evidence that quinineis ineffective.

4.2 Posology and method of administration
Artemether Injection is for intramuscular use only.
The recommended dose is as follows: 3.2mg/kg by the intramuscular route as a loading dose on the first day, followed by 1.6mg/kg daily until the patient can take oral therapy to complete a 7-day course. The daily dose can be given as a single injection.
In children, the use of a tuberculin syringe is advisable since the injection volume will be small.

4.3 Contraindications:
Artemether is contra-indicated in patients with hypersensitivity to artemether or other artemisinin compounds.

4.4 Special warnings and precautions for use:
1. Do not exceed the prescribed dose. In case of overdosage, urgent symptomatic treatment in a specialized unit is required.
2. Caution is required in patients with Cardiovascular disease, Hepatic impairment,Renal insufficiency.

4.5 Interaction with other medicinal products and other forms of interaction:
Since electrocardiographic QT prolongation has been reported in some patients treated with artemether, it is recommended to avoid prescription of medications known toproduce a prolongation of QT interval or patients receiving such medication: erythromycin, terfenadine, astemizole, probucol, Class 1a anti-arrhythmic agents (quinidine, procainamide, disopyramide), Class III anti-arrhythmic agents (amiodarone, bretylium), bepridil, sotalol, tricyclic antidepressants, some neuroleptics and phenothiazines are to be monitored closely.

4.6. Fertility, Pregnancy and Lactation:

Usage in pregnancy:
As per information available from World Health Organization, little experience has been gained with the use of this drug in pregnancy but it should not be withheld if it is considered life-saving to the mother.

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.

Nursing Mother:
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:
Dizziness may impair ability to perform skilled tasks, for example, operating machinery or driving.

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 (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 inclinical 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.

<u>Reporting of suspected adverse reactions</u>
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system (see details below).

Paper based reporting: TMDA yellow card
Online reporting: https://sqrt.tmda.go.tz/
USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions

4.9. 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 bringon 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 and Pharmacokinetic properties:

ATC Code: P01BE02

Pharmacodynamics:

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. Artemether is concentrated in the food vacuole. It then splits its endoperoxide bridge as it interacts with haem, blocking conversion to haemozoin, destroying existing haemozoin and releasing haem and acluster of free radicals into the parasite. There is inhibition of protein synthesis during growth of trophozoites. There is no cross resistance with chloroquine. Artemether is not active against hypnozoites. Therefore, an 8-amino-quinoline derivative such as primaquine should be given sequentially after the combination in cases of mixed infections of P. falciparum and P. vivax to achieve hypnozoites eradication. Artemether reduces gametocyte carriage. There is no rationale at present for using artemether for chemoprophylaxis.

Pharmacokinetics:

The drug is slowly absorbed from intramuscular injection. Peak plasma concentrations have been achieved in about 6 hours after intramuscular injection of artemether. Artemether is hydrolyzed after administration to a biologically active metabolite, dihydroartemisinin. Dihydroartemisinin accounts for most or all of clinical antimalarial activity. Total protein binding is 95.4%. The drug is rapidly and extensively metabolised in the liver.

In animal studies, unchanged artemether has not been detected in both faeces and urine due to its rapid and high first-pass metabolism, but several metabolites (unidentified) have been detected in both faeces and urine. The elimination half-life is approximately1 hour, but following intramuscular administration the elimination phase is prolonged because of continued absorption.

The elimination half life of dihydroartemisinin was approximately 2 hours. Artemether has been reported to clear fever in severe falciparum malaria within 30-84 hours.

5.2 Preclinical safety data:

Carcinogenesis:

Carcinogenicity studies were not conducted.

Mutagenesis:

No evidence of mutagenicity was detected.

Animal Toxicology and/or Pharmacology

Neonatal rats (7-21 days old) were more sensitive to the toxic effects of artemether than older juvenile rats or adults. Mortality and severe clinical signs were observed in neonatal rats at doses which were well tolerated in pups above 22 days old.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients
Masester E6000 Glycerol Tricaprylate/ Caprate

6.2 Incompatibilities:
None.

6.3 Shelf life:
36 months.

6.4 Special precautions for storage:
Storage temperature up to 30°C. Protect from light. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

6.5 Nature and contents of container:
A Colorless, clear viscous solution, in 1ml clear glass ampoule, available in pack of 6 Ampoules.

6.6 Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER:
Surge Laboratories (Pvt.) Ltd. 10th, KM Faisalabad Road, Bikhi,District Sheikhupura – Pakistan.

8. MARKETING AUTHORISATION NUMBER
TAN 20 HM 0109

9. DATE OF FIRST AUTHORIZATION
July 09, 2020

10. DATE OF REVISION OF THE TEXT:
November 05, 2023