SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SHAL'ARTEM
Composition:
Each 60 ml contains when reconstituted:
Artemether 180 mg and Lumefantrine 1080 mg
Pharmaceutical form:
Powder for reconstitution for suspension

2. Qualitative and Quantitative Composition

Artemether.....180mg
Lumefantrine.....1080mg
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for reconstitution for suspension,

Light yellow coloured free flowing powder, after reconstitution yellow coloured suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SHAL'ARTEM is indicated for the treatment of malaria in children, 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

SHAL'ARTEM (Artemether and Lumefantrine Dry Syrup) has especially been designed for use in children.
The dose depends on the severity of the case and the clinical situation of the patient

Directions for reconstitution of SHAL'ARTEM Dry Syrup:

Take boiled and cooled water and add it slowly up to the ring mark present on the bottle.
Shake the bottle and if necessary adding more water to adjust the volume up to the ring mark this makes 60 ml of SHAL'ARTEM Dry Syrup.
Use the SHAL'ARTEM Dry Syrup within 7 days after reconstitution. Shake the bottle every time before use.
A standard 3-day treatment schedule, with a total of 6 doses, is recommended as follows.

Child body weig	Day 1	Day 2		Day 3	
		Morning	Evening	Morning	Evening

ht						
5-less than 15kg	At 0 hour	8 hours	24 hours	36 hours	48 hours	60 hours
	7ml	7ml	7ml	7ml	7ml	7ml

SHAL'ARTEM Dry Syrup should be taken with foods or drinks having high quantity of fat such as milk.
If vomiting occurs within one hour of taking SHAL'ARTEM Dry Syrup a repeat dose should be taken.

4.3 Contraindications
SHAL'ARTEM is contraindicated in those with hypersensitivity to the active substances or any of the excipients, in the first trimester of pregnancy, patients with a family history of congenital prolongation of the QTc interval or sudden death or with any other clinical condition known to prolong the QTc interval such as patients with a history of symptomatic cardiac arrhythmias, patients with clinically relevant bradycardia or with severe cardiac disease, family history of sudden death, disturbances of electrolyte balance, e.g. hypokalaemia or hypomagnesaemia.
SHAL'ARTEM is not indicated for prophylaxis of malaria.

4.4 Special warnings and precautions for use
Use with caution in patients with severe hepatic or renal insufficiency and patients refusing food intake. Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

4.5 Interaction with other medicinal products and other forms of interaction
The sequential oral administration of mefloquine prior to artemether and lumefantrine combination had no effect on plasma concentrations of artemether or the artemether/ dihydroartemisinin (DHA) ratio but
there was a significant (around 30-40%) reduction in plasma levels (Cmax and AUC) of lumefantrine, possibly due to lower absorption secondary to a mefloquine-induced decrease in bile production. Such
patients should therefore be encouraged to eat at dosing times to compensate for this decrease in bioavailability. Quinine alone caused a transient prolongation of the QTc interval, which was consistent with its known cardiotoxicity. This effect was slightly but significantly greater when quinine was infused after artemether and lumefantrine combination. Hence when artemether and lumefantrine combination is given to patients following administration of mefloquine or quinine, close monitoring of food intake (for mefloquine) or the ECG (for quinine) should be carried out. In patients previously treated with halofantrine,
L- Artem should be administered at least one month after the last halofantrine dose.
Due to limited data on safety and efficacy, the combination should not be given concurrently with other antimalarial unless there is no other treatment option. However, if a patient deteriorates while taking the combination, alternative treatments for malaria should be commenced without delay. In such cases,

monitoring of the ECG is recommended and steps should be taken to correct electrolyte disturbances.

4.6 Pregnancy and lactation

Pregnancy

Risk Summary

Published data from clinical studies and pharmacovigilance data have not established an association with artemether/lumefantrine use during pregnancy and major birth defects, miscarriage, or adverse maternal or fetal outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations:

Disease-Associated Maternal and/or Embryo/Fetal Risk: Malaria during and after pregnancy increases the risk for adverse pregnancy and neonatal outcomes, including maternal anemia, severe malaria, spontaneous abortion, stillbirths, preterm delivery, low birth weight, intrauterine growth restriction, congenital malaria, and maternal and neonatal mortality.

Data

Human Data: While available studies cannot definitively establish the absence of risk, a meta-analysis of observational studies including over 500 artemether-lumefantrine exposed women in their first trimester of pregnancy, data from observational, and open label studies including more than 1200 pregnant women in their second-or third trimester exposed to artemether-lumefantrine compared to other antimalarials, and pharmacovigilance data have not demonstrated an increase in major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published epidemiologic studies have important methodological limitations which hinder interpretation of data, including inability to control for confounders, such as underlying maternal disease, and maternal use of concomitant medications and missing information on the dose and duration of use.

Animal Data: Pregnant rats dosed orally during the period of organogenesis [gestational days (GD) 7 through 17] at 50 mg/kg/day artemether-lumefantrine combination (corresponding to 7 mg/kg/day artemether or higher, a dose of less than half the maximum recommended human dose (MRHD) of 1120 mg artemether-lumefantrine per day (based on body surface area (BSA) comparisons), showed increases in fetal loss, early resorptions, and postimplantation loss. No adverse effects were observed in animals dosed at 25 mg/kg/day artemether-lumefantrine (corresponding to 3.6 mg/kg/day of artemether), about one-third the MRHD (based on BSA comparison). Similarly, oral dosing in pregnant rabbits during organogenesis (GD 7 through GD 19) at 175 mg/kg/day, (corresponding to 25 mg/kg/day artemether) about 3 times the MRHD (based on BSA comparisons) resulted in abortions, preimplantation loss, post implantation loss and decreases in the number of live fetuses. No adverse reproductive effects were detected in rabbits at 105 mg/kg/day artemether-lumefantrine (corresponding to 15 mg/kg/day artemether), about 2 times the MRHD. Artemether and other artemisinins are

associated with maternal toxicity and embryotoxicity and malformations in animals at clinically relevant exposures; however, lumefantrine doses as high as 1000 mg/kg/day, showed no evidence to suggest maternal, embryo-or fetotoxicity or teratogenicity in rats and rabbits. The relevance of the findings from the animal reproductive studies to human risk is unclear.

Lactation
There are no data on the presence of artemether or lumefantrine in human milk, the effects on the breastfed infant or the effects on milk production. Artemether and lumefantrine are transferred into rat milk. When a drug is transferred into animal milk, it is likely that the drug will also be transferred into human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need and any potential adverse effects on the breastfed infant or from the underlying maternal condition.

4.7 Effects on ability to drive and use machines
Driving and use of machinery is not recommended because SHAL'ARTEM Dry Syrup may causes impairment in balance.

4.8 Undesirable effects
Common adverse events reported with artemether and lumefantrine combination included headache, dizziness, sleep disorder, abdominal pain, anorexia, diarrhea, vomiting, nausea, palpitation, cough, arthralgia, myalgia, pruritus, rash, asthenia and fatigue.
Somnolence, involuntary muscle contractions, paraesthesia, hypoaesthesia, abnormal gait, ataxia were other adverse effects reported with artemether and lumefantrine combination.
Rare adverse event included hypersensitivity.
Unspecified personality disorders have also been reported in children <5 years treated with artemether and lumefantrine combination.
Reporting of Adverse Drug Reactions
Healthcare professionals are asked to report any suspected adverse drug reactions via the Pharmacy and Poisons Board's; Pharmacovigilance-Electronic-Reporting-System (PvERS)https://pharmacyboardkenya.org

4.9 Overdose
In cases of suspected overdosage, symptomatic and supportive therapy should be given as appropriate. ECG and blood potassium levels should be monitored.

5.1 Pharmacodynamic Properties
SHAL'ARTEM is a fixed dose artemisinin-based combination therapy (ACT) combining Artemether, an artemisinin derivative, and Lumefantrine, a synthetic antimalarial drug.
Both Artemether and Lumefantrine act as blood schizontocides. The site of anti-parasitic action of both components of the combination is the food vacuole of the malarial parasite, where they are thought to interfere with the conversion of haem,

a toxic intermediate produced during haemoglobin breakdown, to the non-toxic haemozoin, malaria pigment.

5.2 Pharmacokinetic Propeties
Artemether is absorbed fairly rapidly with peak plasma concentrations reached about 2 hours after dosing. Absorption of Lumefantrine, a highly lipophilic compound, starts after a lag period of up to 2 hours, with peak plasma concentration about 6-8 hours after dosing. Food enhances the absorption of both Artemether and Lumefantrine. Artemether and Lumefantrine are both highly bound to human serum proteins in vitro (95.4% and 99.7%, respectively). The artemisinin metabolite dihydroartemisinin is also bound to human serum proteins (47%-76%). Artemether is rapidly and extensively metabolised by human liver microsomes. The main active metabolite is dihydroartemisinin. Lumefantrine is also metabolised predominantly by the enzyme CYP3A4 in human liver microsomes. Artemether and dihydroartemisinin are rapidly cleared from plasma with an elimination half-life of approximately 2-3 hours.
Conversely, Lumefantrine is eliminated very slowly with a terminal half-life of 2-3 days in healthy volunteers and 4-6 days in patients with falciparum malaria. No urinary excretion data are available for humans.

5.3 Preclinical safety data
No preclinical findings of relevance have been reported.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Carmellose Sodium BP, Sucrose BP, Sodium methyl hydroxybenzoate BP, Sodium propyl hydroxybenzoate BP, Anhydrous Citric Acid BP, Saccharin Sodium BP, Colloidal Anhydrous Silica BP and Flavour Pineapple DM.

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 30°C. Protect from sunlight. Keep out of reach of children.

6.5 Nature and contents of the container
60ml HDPE bottle with10ml measuring cup packed in a carton along with a leaflet.

6.6 Special precautions for disposal and other handling
None

7. MARKETING AUTHORIZATION HOLDER
M/s SHALINA HEALTHCARE DMCC
30th Floor, Almas Towers, Jumeirah Lakes Towers,
Dubai-UAE. Country: Dubai

8. MARKETING AUTHORIZATION NUMBER
H2015/CTD647/306.

9**. DATE OF FIRST REGISTRATION /RENEWAL OF THE <REGISTARTION>**
Date of first authorization: 27th Oct.2015
Date of latest renewal: 31/03/2026

10**. DATE OF REVISION OF TEXT**

31/03/2026