Summary of Product Characteristics (SPC)

1. NAME OF THE MEDICINAL PRODUCT

SHAL'ARTEM FORTE (Artemether & Lumefantrine Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Approved name	Specifications	Quantity in mg per tablet
Artemether	IH	80.0
Lumefantrine	IH	480.0
Maize Starch	BP	5.00
Sodium Starch Glycolate	BP	30.00
Hydroxypropylcellulose	BP	30.00
*Isopropyl Alcohol	BP	*143.47
Microcrystalline Cellulose	BP	29.00
Colloidal Anhydrous Silica	BP	7.00
Purified Talc	BP	7.00
Magnesium Stearate	BP	20.00
Opadry Yellow 21K520012 (Yellow Iron Oxide USP, Lake Quinoline Yellow, Titanium Dioxide BP, Triacetin, Ethylcellulose, Hypromellose)	IH	15.00
*Methylene Chloride	BP	*130.00

Note: BP = British Pharmacopoeia * Does not appear in final finished product
IH = In house Specifications

3. PHARMACEUTICAL FORM

Tablet (Oral)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Shal'Artem Forte are indicated for the treatment of Plasmodium falciparum malaria cases resistant to both chloroquine and sulphadoxine pyrimethamine combination.

4.2 Posology and method of administration

Shal'Artem Forte should be taken with high fat food or drinks such as milk. Note that patients with acute malaria are frequently averse to food. Patients should be encouraged to resume normal eating as soon as food can be tolerated since this improves absorption of Artemether and Lumefantrine. In the event of vomiting within one hour of administration a repeat dose should be taken.

Shal'Artem Forte Tablet Dosage (In Adults): One tablet as a single dose at the time of initial diagnosis, and then 8, 24, 36 and 48 hours thereafter.

Total Tablets	Dosage regimen					
	Day 1		Day 2		Day 3	
6	0 Hrs.	8 Hrs.	24 Hrs.	36 Hrs.	48 Hrs.	60 Hrs.
	1 tablet	1 tablet	1 tablet	1 tablet	1 tablet	1 tablet

4.3 Contraindications

Shal'Artem Forte are 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 / Shal'Artem Forte are 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 toArtemether 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, Shal'Artem / Shal'Artem Forte should be administered atleast one month after the last halofantrine dose. Due to limited data on safety and efficacy, the combination should not be given concurrently with other antimalarials 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.

Taking other medicines (drug-drug interactions)

Please tell your health care provider if you take or have recently taken: any other medicine to treat or prevent malaria, medicines for your heart, antipsychotic medicines (to treat disorders of mind), antidepressants (to alleviate mood disorder), antibiotics, antifungal medicines, medicines to treat HIV infection, birth control pill.

Shal'Artem/ Shal'Artem Forte with food and drink (drug-food interactions)

Shal'Artem/ Shal'Artem Forte should be taken with food or a milky drink.

4.6 Pregnancy and lactation

Shal'Artem Forte are contraindicated during the first trimester of pregnancy. During the second and

third trimester, treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus. Breast-feeding women should not take Shal'Artem / Shal'Artem Forte. Due to the long elimination half-life of Lumefantrine (4 to 6 days), it is recommended that breast-feeding should not resume before day 28 after discontinuation of Artemether and Lumefantrine combination unless potential benefits to mother and child outweigh the risk of the combination treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed with Paracetamol. Based on the pharmacodynamic properties and the side effects of paracetamol, no influence on the reactivity and the ability to drive or use machines is expected.

4.8 Undesirable effects

Common adverse events reported with Artemether and Lumefantrine combination included headache, dizziness, sleep disorder, abdominal pain, anorexia, diarrhoea, 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.

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. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 properties

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 metabolized 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

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose, maize starch, colloidal anhydrous silica, purified talc, magnesium stearate, triacetin, ethylcellulose, hypromellose, sodium starch glycolate and hydroxyl propyl cellulose, Yellow Iron Oxide USP, Lake Quinoline Yellow, Titanium Dioxide BP, Methylene Chloride

6.2 Incompatibilities

None known.

6.3 Shelf life

3 Years

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 container

PVC Film / Printed Aluminium Foil blister.
Shal'Artem Forte Tablet is packed in blister of 6 Tablets. 1 Such filled blister is packed in a printed carton along with a leaflet. 5 such inner cartons are packed in 1 outer carton.

6.6 Special precautions for disposal and other handling

Do not store above 30°C. Protect from sunlight. Keep out of reach of children.

7. MARKETING AUTHORISATION HOLDER

M/s SHALINA HEALTHCARE DMCC
30th Floor, Almas Towers,
Jumeirah Lakes Towers Dubai-UAE.
Telephone: +971 4 4309111
Telefax: +971 4 4309112
Website: www.shalina.com
E-Mail: regulatory@shalina.com

8. MARKETING AUTHORISATION IN OTHER COUNTRIES

Product is registered in Republic of Guinea, Democratic Republic of Congo, Nigeria, Kenya, Central African Republic, Zambia, Niger, Ivory Coast.

9. DATE OF REVISION OF TEXT

Every two years.

10. LEGAL CATERGORY

OTC (Over the Counter)