SHAL'ARTEM

(Artemether and Lumefantrine Dispersible Tablets)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1.1 Product name: SHAL'ARTEM (Artemether and Lumefantrine Dispersible Tablets)

1.2 Dosage Strength:

Each dispersible tablet contains:

Artemether……20 mg

Lumefantrine……..120 mg

1.3 Dosage Form: Oral Dispersible Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ingredient	Quantity per tablet (mg)	Standard batch Quantity In kg	Category
Artemether IH	20.0	4.5	Antimalarial
Lumefantrine IH	120.0	27.0	Antimalarial
Microcrystalline Cellulose BP	44.8	10.080	Diluent
Croscarmellose Sodium BP	10.00	2.25	Disintegrating Agent
Hypromellose BP (E-5)	10.00	2.25	Binding Agent
Polysorbate 80 BP	0.200	0.045	Dispersing Agent
Isopropyl Alcohol BP	85.0	19.125	Binding Solvent
Crospovidone BP (XL)	25.00	5.625	Disintegrating Agent
Microcrystalline Cellulose BP (Grade 102)	50.00	11.250	Diluent
Purified Talc BP	7.00	1.575	Glidant
Colloidal Anhydrous Silica BP (Aerosil)	3.00	0.675	Glidant
Aspartame USP	6.00	1.350	Sweetening Agent
Saccharine Sodium BP	6.00	1.350	Sweetening Agent
Flavour BTM DM 7020A (Bitter Taste Masking flavor)	4.00	0.90	Bitter Taste Masking Flavor
Flavour Cherry	5.00	1.125	Flavor
Magnesium Stearate BP	9.00	2.025	Lubricant

Definitions: BP: British Pharmacopoeia
USP: United State Pharmacopoeia
IH: In-House Specifications

3. PHARMACEUTICAL FORM

Dispersible Tablets

Yellow coloured, Circular, flat faced, bevelled edged tablets plain on both sides

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Shal'Artem Dispersible Tablets contains two substances called artemether and lumefantrine. They belong to a group of medicines called anti-malarials, which interfere with the energy production in the malarial parasite ultimately results in the death of it.

Shal'Artem Dispersible Tablets is used for the treatment of malaria infections caused by a parasite called "Plasmodium falciparum" (when it is not cured by chloroquine and sulfadoxine-pyrimethamine combination).

4.2 Posology and method of administration

Children weight 5 kg to less than 15 kg: Take 10 ml of water in glass then put the dispersible tablet for one dose in it and stir gently and give immediately to patient. Pour 10 ml of water again into the glass and give immediately to the patient.

A standard 3-day treatment schedule, with a total of 6 doses, is recommended as follows.

Day 1		Day 2		[
First dose	Second dose	Third dose	Fourth dose	Fifth dose
At 0 hour	After 8 hours	Morning	Evening	Morning

Shal'Artem Dispersible Tablets should be taken with food or drinks having high quantity of fat such as milk.

If vomiting occurs within one hour of taking Shal'Artem Dispersible Tablets a repeat dose should be taken

Shal'Artem Dispersible Tablets should be cautiously used if patient has severe kidney and liver dysfunctions.

If you take more amount of Shal'Artem Dispersible Tablets than you should Contact your health care provider immediately and say exactly how much you have taken. Your health care provider will advise you what to do. It is important to contact your health care provider even if you feel well.

4.3 Contraindications

Shal'Artem Dispersible Tablets is contraindicated in:

• are allergic to any of the constituents of Shal'Artem Dispersible Tablets.

• have abnormality in the rhythm of heartbeats (slow or fast heartbeats) or severe heart disease.

• have an impairment in the electrolyte (potassium and magnesium) levels in blood.

• have a severe type of malaria infection.

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 adverse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

4.5 Interaction with other medicinal products

Please inform health care provider if taking or have recently taken any of the following medicines:
Mefloquine, quinine, halofantrine and the other drugs used in treatment of malaria.

4.6 Fertility, pregnancy and lactation

Shal'Artem Dispersible Tablets must not be used during the first 3 months of pregnancy if it is possible for a doctor to give an alternative medicine first. In the later stages of pregnancy, you should take this medicine only if clearly necessary and in consultation with your doctor.
You should not breast-feed if you are taking or have taken this medicine at least 1 week before.

4.7 Effects on ability to drive and use machines

Driving and use of machinery are not recommended because Shal'Artem Dispersible Tablets may cause impairment in balance

4.8 Adverse Reactions

Shal'Artem Dispersible Tablets are well-tolerated in majority of patients. It may cause following side effects.

• Nausea, vomiting, diarrhea, stomach pain and loss of appetite are common.

• Other side effects are headache, giddiness (loss of balance), pain in joints and muscles, tiredness, itching, rashes and disturbance in sleep and gait.

• Allergic reactions are rare.

• In children less than 5 years old it may cause personality disorders.

4.9 Symptoms of Over dosage & Treatment

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

Pharmacotherapeutic group: Artemisinin and derivatives**, ATC code:** P01BE52.

Mechanism of action

The site of antiparasitic action of both components is the food vacuole of the malaria parasite. Lumefantrine is thought to interfere with the polymerization process that brings about the conversion of haem, a toxic intermediate produced during haemoglobin breakdown, to the non-toxic haemozoin, malaria pigment. Artemether, on the other hand, may generate toxic, reactive metabolites as a result of the interaction between its endoperoxide bridge and haem iron. Both artemether and lumefantrine have a secondary action involving inhibition of nucleic acid and protein synthesis.

Pharmacodynamic effects:

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 properties

Absorption

Artemether is absorbed fairly rapidly, with peak plasma concentrations attained approx. 2 hours after administration. Absorption of lumefantrine, a highly lipophilic compound, starts after a lag-time of up To 2 hours, with peak plasma concentration about 6–8 hours after administration. Food enhances the absorption of both artemether and lumefantrine: In healthy volunteers given a high-fat meal, the relative bioavailability of artemether was increased more

than two-fold, and that of lumefantrine sixteen-fold compared with fasted conditions. Food has also been shown to increase the absorption of lumefantrine in patients with malaria, although to a lesser extent (approximately two-fold), most probably due to the lower fat content of the food ingested by acutely ill patients. Food interaction data indicate that absorption of lumefantrine under fasted conditions is very poor (probably less than 10% of the dose). Patients should therefore be strongly encouraged to take the medication with a normal diet as soon as food can be tolerated.

Distribution:

Artemether and lumefantrine are both highly bound to human serum proteins in vitro (95.4% and 99.7%, respectively). DHA is also bound to human serum proteins (47%–76%). Protein binding to human plasma protein is linear

Biotransformation:

Artemether is rapidly and extensively metabolized (substantial first-pass metabolism).

In vitro data show that human liver microsomes metabolize artemether to the biologically active main metabolite DHA (demethylation), predominantly by way of CYP3A4/5.

Elimination:

Artemether and DHA are rapidly cleared from plasma with an elimination half-life of about 2 hours. 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.

Pharmacokinetics in special patient groups

No specific pharmacokinetic studies have been performed in patients with hepatic or renal impairment.

Systemic exposure to artemether, DHA, and lumefantrine in paediatric malaria patients

(≥5 to <35 kg body weight) dosed on a mg/kg body weight basis is comparable to that measured in adult malaria patients on the recommended dosing regimen.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Lauryl Sulphate BP, Microcrystalline Cellulose BP, Croscarmellose Sodium BP, Hypromellose BP, Polysorbate 80 BP, Crospovidone BP, Colloidal Anhydrous Silica BP, Purified Talc BP, Magnesium Stearate BP, Aspartame USP, Saccharin Sodium BP. Flavour: Cherry and bitter taste masking flavour.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 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 container

Shal'Artem Dispersible Tablets is available in strip pack of 06 tablets. Such 1 blister is packed in a printed carton along with leaflet.

7. MARKETING AUTHORISATION HOLDER

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