SUMMARY OF PRODUCT CHARACTERISTICS

1-Name of the Medicinal Product:

1.1 Product Name
Luter Tablet 80/480 mg

1.2 Strength
Artemether 80 mg and Lumefantrine 480 mg

1.3 Pharmaceutical Dosage Form
Tablet

2-Quality and Quantitative Composition:

ACTIVE INGREDIENTS	PER TABLET (MG)
Artemether	80.00
Lumefantrine	480.00

For excipients, see 6.1

3-Pharmaceutical Form:

Oblong, yellow film-coated tablet, deep convex faces, “HD” embossed on the same face.

4-Clinical Particulars:

4.1 Therapeutic indications
For treatment of uncomplicated falciparum malaria.

Posology and method of administration
For oral administration.

Adults and children weighing 35 kg and above: A course of treatment comprises six doses of 80 mg Artemether and 480 mg Lumefantrine at the time of initial diagnosis, 8, 24, 36, 48, 60 hours thereafter.

Children weighing 15 to less than 25 kg: A course of treatment comprises six doses of 40 mg Artemether and 240 mg Lumefantrine at the time of initial diagnosis, 8, 24, 36, 48, 60 hours thereafter.

Note: The information given here is limited. For further information, consult your doctor or pharmacist

4.2 Contraindications
LUTER is contraindicated in:

- Patients with known hypersensitivity to the active substances or to any of the excipients.
- Patients with severe malaria according to WHO definition.
- Patients who are taking any drug which is metabolized by the cytochrome enzyme CYP2D6, for examples are flecainide, metoprolol, imipramine, amitryptyline, clomipramine.
- Patients with a family history of sudden death or of congenital prolongation of the QTc interval on electrocardiograms, or with any other clinical condition known to prolong the QTc interval.
- Patients with a history of symptomatic cardiac arrhythmias or with clinically relevant bradycardia or with congestive cardiac failure accompanied by reduced left eventricle ejection fraction.
- Patients with disturbances of electrolyte balance such as hypokalemia or hypomagnesemia.
- Patients taking drugs that are known to prolong the QTc interval. These drugs include antiarrythmics of classes IA and III, neuroleptics, antidepressive agents, certain antibiotics including some agents of the macrolides, fluoroquinolones, imidazole and triazole classes, certain non-sedating antihistamines (terfenadine, astemizole), cisapride.

4.4 Special warning and precautions for use

- Caution is advised when administering LUTER to patients with severe renal, hepatic or cardiac problems. In these patients, ECG and blood potassium monitoring is advised.
- If patient deteriorates when taking LUTER, alternative treatment for malaria should be started without delay.
- LUTER should not be administered earlier than one month after the last halofantrine dose.
- LUTER has the potential to cause QT prolongation.
- Patients who remain averse to food during treatment should be monitored closely as the risk of recrudescence may be greater.

4.5 Interaction with other medicinal products and other forms of Interactions

- The concurrent oral administration of ketoconazole with LUTER led to a modest increase in Artemether, DHA, and Lumefantrine exposure in healthy adult subjects. This increase in exposure to the antimalarial combination was not associated with increased side effects or changes in electrocardiographic parameters. Thus, dose adjustment of LUTER is considered unnecessary in falciparum malaria patients when administered in association with ketoconazole or other potent CYP3A4 inhibitors.
- Artemisinins have some capacity to induce CYP3A4 and CYP2C19 and inhibit CYP2D6 and CYP1A2. This may alter therapeutic response of drugs that are predominantly metabolized by these enzymes.
- Lumefantrine was found to inhibit CYP2D6 in vitro. Co-administration of LUTER with drugs that are metabolized by this isoenzyme is contraindicated. Lumefantrine metabolism is inhibited by halofantrine quinine.
- Use of protease inhibitor anti-retroviral drugs with LUTER requires clinical surveillance and monitoring of clinical response / undesirable effects due to variable patterns of inhibition, induction or competition for CYP3A4.
- Administration of LUTER is contra-indicated in patients taking drugs that are known to prolong the QTc interval.

- LUTER should not be given concurrently with any other antimalarial agent. If quinine is given after LUTER, close monitoring of ECG is advised.

4.6 Pregnancy and lactation

- Do not consume LUTER in the first trimester of pregnancy in situations where other suitable and effective anti-malarials are available.
- Women taking LUTER should not breastfeed during the treatment. It is recommended that breastfeeding should not resume until at least one week after the last dose of LUTER

4.7 Effects on ability to drive and use machine

NOT APPLICABLE.

4.8 Undesirable effects

- Headache, dizziness, sleep disturbance, palpitations, gastrointestinal disturbances, anorexia, pruritus, rash, cough, arthralgia, myalgia and fatigue.

4.9 Overdose

Treatment of overdosage: In case of suspected overdosage, symptomatic and supportive therapy should be given as appropriate, which should include ECG and blood potassium monitoring.

5-Pharmacological Properties:

5.1 Pharmacodynamic Properties

Artemether is an artemisinin derivative which has largely replaced artemisinin in practice. It is a potent and rapidly acting blood schizontocide active against Plasmodium vivax and against both chloroquine-sensitive and chloroquine resistant strains of *P. falciparum.*

Lumefantrine is a blood schizontocide with a relatively slow onset of action but it has a longer duration of action than Artemether

5.2 Pharmacokinetic properties

Peak plasma concentrations have been achieved in about 3 hours after oral doses of Artemether. Artemisinin derivatives are all rapidly hydrolysed to the active metabolite dihydroartemisinin. Reported elimination half-life has been about 4 hours to 11 hours after oral Artemether.

Bioavailability of Lumefantrine after oral doses is variable; absorption begins after a lag-time of up to 2 hours and bioavailability is substantially increased when given with food, particularly meals high in fat. Peak plasma concentrations occur after about 6 to 8 hours. Lumefantrine is almost completely protein bound. It is considered to be metabolized mainly in the liver and is excreted in the faeces. The elimination half-life is reported to be between 4 to 6 days in patients with malaria.

6-Pharmaceutical Particulars:

6.1 List of excipients

Isopropyl alcohol

Polyvinylpyrrolidone
Polyvinylpolypyrrolidone
Cornstarch
Microcrystalline cellulose
Talc
Colloidal silicon dioxide
Magnesium stearate
Iron oxide yellow
Quinoline yellow lake
Opadry

6.2 Incompatibilities
NOT APPLICABLE

6.3 Shelf life
3 years from date of manufacture.

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container

Immediate Container/Packaging
Blister packaging

Type : Push-through blister pack; the package consists of a transparent thermoformable plastic material and a heat-sealable lacquered backing material.
Material : Thermoformable plastic material: Polyvinyl Chloride (PVC)
Backing Material : Aluminium Foil

6.6 Special precaution for disposal
Not Applicable

7- Registrant

Marketing Authorization Holder:

Name : HOVID Bhd.
Address : 121, Jalan Tunku Abdul Rahman,
(Jalan Kuala Kangsar)
30010 Ipoh, Perak, Malaysia

Production site: HOVID BHD.,
Lot 56442, 7 ½miles, Jalan Ipoh/Chemor,
31200 Chemor, Perak, Malaysia.

8-Date of revision of the text:

May 2023

9-Dosimetry (If applicable):

Not Applicable

10-Instruction for preparation of Radiopharmaceuticals (If Applicable):

Not Applicable