Summary of Product Characteristics (SmPC)

1. NAME OF MEDICINAL PRODUCTS

La-Tesen Tablet - Combi

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Artemether 40mg and Lumefantrine 240mg.

2. PHARMACEUTICAL FORM

A yellow round concave tablet with AFRAB inscribed on one side and a marked line on the other.

3. CLINICAL PARTICULARS

4.1 Therapeutic Indications

La-tesen© Tablets is indicated for the treatment of malarial caused by all forms of Plasmodium.

4.2 Posology and method of administration

4.2.1 Posology

Body Weight	**Day 1**		**Day 2**		**Day 3**	
TABLETS Artemether 20mg + Lumefantrine 120mg	**0 Hrs**	**8 Hrs after**	**Morning**	**Evening**	**Morning**	**Evening**
5<25kg(≥1-3yrs)	1	1	1	1	1	1
15<25kg(≥3-8yrs)	2	2	2	2	2	2
25<35kg(≥9-14yrs)	3	3	3	3	3	3
35kg and above (Adult)	4	4	4	4	4	4
TABLETS Artemether 40mg + Lumefantrine 240mg	**0 Hrs**	**8 Hrs after**	**Morning**	**Evening**	**Morning**	**Evening**
15<25kg(≥3-8yrs)	1	1	1	1	1	1
25<35kg(≥9-14yrs)	1½	1½	1½	1½	1½	1½
35kg and above (Adult)	2	2	2	2	2	2
CAPLETS (DS)	**0 Hrs**	**8 Hrs after**	**Morning**	**Evening**	**Morning**	**Evening**
Adults	1	1	1	1	1	1

0r as directed by the Doctor.

4.2.2 Method of Administration

Oral administration only

4.3 Contraindications

La-tesen© is contraindicated in individuals hypersentive to Arthemether and Lumefantrine. In 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, with clinically with relevant bradycardia or with severe cardiac disease.

La-tesen© is also in contraindicated in pregnancy especially the first trimester but in view of the high risk of malarial during pregnancy for mother and foetus, it may be considered essential as in the case of cerebral malaria, to treat a pregnant woman. Breast-feeding women should not take La-tesen©.

4.4 Special warning and precaution for use

La-tesen tablets is not recommended during the first trimester of pregnancy in situations where other suitable and effective anti-malarial are available.

4.5 Interactions with other medicinal products and other forms of interaction

Interaction with drugs that are known to prolong the QTc interval

La-tesen is contraindicated with concomitant use of drugs (they may cause prolonged QTc interval and Torsade de pointes) such as: antiarrhythmics of classes IA and III, neuroleptics and antidepressant agents, certain antibiotics including macrolides, fluoroquinolones, imidazole and triazole antifungal agents.

Interaction with strong inducers of CYP3A4 such as rifampicin

Oral administration of rifampicin (600mg daily), strong CYP3A4 inducer, with La-tesen tablets in six HIV-1 and tuberculosis coinfected adults without malaria resulted in significant decrease caplet administration, unless critical to use a judged by the prescriber.

Interaction with other anti-malarial drugs

Data on safety and efficacy are limited, and La-tesen tablets should therefore not be given concurrently with other anti-malarials unless there is no other treatment option.

4.6 Pregnancy and Lactation

Women using oral, transdermal patch, or other systemic hormonal contraceptives should be advised to use an additional non-hormonal method of birth control for about one month.

Pregnancy

A meta-analysis of observational studies including over 500 artemether-lumefantrine exposed women in their firdt trimester of pregnancy assessed adverse pregnancy outcomes. The data showed that compared to quinine, artesinin treatment, including artemether-lumefantrine, was not associated with an increased risk of miscarriage, still-birth or congenital anomalies.

However, due to the limitations of these studies, the risk of adverse pregnancy outcomes for artemether-lumefantrine exposed women in early pregnancy cannot be excluded.

Safety data from pregnancy studies including over 1200 pregnant women who were exposed to artemether-lumefantrine during the second or third trimester did not show an increased in adverse pregnancy outcomes or teratogenic effects over background rates.

Studies in animals have shown reproductive toxicity.

Latesen tablet treatment is not recommended during the first trimester of pregnancy in situations where other suitable and effective anti-malarials are available. However, it should not be withheld in life-threatening situations, where no other effective anti-malarials are available. During the second and third trimester, La-tesen tablet treatment should be considered if the expected benefit to the mother outweighs he risk to the foetus.

Breast-feeding
Animal data suggest excretion into breast milk but no data are available in humans. Women taking La-tesen tablets should not breast-feed during their treatment. Due to the long elimination half-life of lumefantrine (2 to 6 days), it is recommended that breast-feeding should not resume until at least one week after the last dose of La-tesen tablets unless potential benefits and child outweigh the risks of La-tesen tablets treatment.

Fertility
There is no information on the effects of La-tesen tablet on human fertility

4.7 Effect on ability to drive and use machines
Patients should be warned that dizziness may occur,
in which case they should not drive or use machines.

4.8 Undesirable Effects
La-tesen© generally well tolerated by children and adults, with most adverse effects being of mild to moderate severity and duration. Many of the reported events are likely to be related to the underlying malarial and I or to an unsatisfactory response to the treatment rather than to La-tesen. Other common side effects include nausea, headache, dizziness, fever, cough, weakness, loss of appetite and muscle pain.

4.9 Overdose
In cases of suspected over dosage symptomatic and supportive therapy should be given as appropriate, which should include ECG and blood potassium monitoring**.**

5.0 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamics Properties
La-tesen© contains a fixed ratio ratio of 1:6 parts of Artemether and Lumefantrine respectively. Artemether is a sesquiterpene lactone derived from the naturally occurring substance Artemisinin Lumefantrine is a synthethic racemic fluorine mixture. Both components of La-tesen© have their own action site in the malaria parasite. The presence of the end peroxide bridge in Artemether

appears to be essential for anti-malarial activity. Morphological changes of the parasitic membranes induced by Artemether have been described, being the result of free-radical action. Lumefantine interferes more in the polymerization processes. Other in-vitro test suggest that both caused a mark diminution of nucleic acid synthesis. Inhibition of protein synthesis as the basic mechanism of action is suggested in studies which showed morphological changes in ribosomes as well as in the endoplasmic recticulum.

5.2 Pharmacokinetic properties
Orally administered Artemether is rapidly absorbed reaching therapeutic levels within 60-90 minutes. Artemether is metabolized in the liver to the demethylated derivate dihydroartemisinin. The eliminationis rapid,with a T1/2 of 2-4 hours. Dihydroartemisinin, being a potent anti-malarial itself, has a T1/2 of about 2-4 hours. The degree of binding to plasma proteins varied markedly according to the species studied. The binding of Artemether with plasma proteins in man is 50%. Radioactivity distribution of Artemether was found to be equal between cells and plasma. The absorption of Lumefantrine is highly influenced by lipids and food intake. Therefore patients should be encouraged to take the medication with some fatty food as soon as it can be tolerated.

5.3 Preclinical safety data
None stated.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Avicel 102, Hydroxyl propyl methyl cellulose,Tween 80,Crospovidone,Aerosil 200,Magnesium stearate,Talcum powder

6.2 Incompactibilities
Not Applicable

6.3 Shelf Life
3 years

6.4 Special precaution for Storage
Store below 30^0C

6.5 Nature and contents of container
Alu/PVC Blister pack of 1 x 12

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

7. Marketing authorization holder
Afrab-Chem Limited, 22, Abimbola Street, Isolo Estate, Isolo