Summary of Product Characteristics (SmPC)

1. NAME OF MEDICINAL PRODUCT
La-tesen DS caplet

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each caplet contains Artemether 80mg and Lumefantrine 480mg

2. PHARMACEUTICAL FORM
A yellow caplet with AFRAB inscribed on one side and a maked line on the other.

3. CLINICAL PARTICULARS
4.1 Therapeutic indications
La-tesen® DS Caplet is indicated for the treatment of malaria 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	
Caplet	0 Hrs	8 Hrs after	Morning	Evening	Morning	Evening
Adult	1	1	1	1	1	1

Or as directed by the Doctor.

4.2.2 Method of administration
La-tesen DS caplet is administered orally

4.3 Contraindications
La-tesen ® is contraindicated in individuals hypersensitive to Artemether 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 relevant bradycardia or with severe cardiac disease. '
La-tesen® is also contraindicated in pregnancy especially the first trimester but in view of the high risk of malaria 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 warnings and precaution for use
Latesen Caplet is not recommended during the first trimester of pregnancy in situations where other suitable and effective antimalarials are available

4.5 Interaction with other medicinal product and other forms of interaction
Interaction with drugs that are known to prolong the QTc interval

Latesen 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 s macrolides, fluoroquinolones, imidazole, and triazole antifungal agents.

Interaction with drugs metabolized by CYP2D6

Lumefantrine was found to inhibit CYP2D6 in vitro. This may be of particular clinical relevance for compounds with a low therapeutic index. Co-administration of Latesen with drugs that are metabolised by this iso-enzyme is contraindicated (e.g. neuroleptics, metoprolol, and tricyclic antidepressants such as imipramine, amitriptyline, clomipramine) is contraindicated .

Interaction with strong inducers of CYP3A4 such as rifampin
Oral administration of rifampin (600 mg daily), a strong CYP3A4 inducer, with Latesen caplet in six HIV-1 and tuberculosis coinfected adults without malaria resulted in significant decreases in exposure to artemether (89%), Inducers should not be administered at least one month after Latesen caplet administration, unless critical to use as judged by the prescriber.

Interaction with other antimalarial drugs

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

4.6 Pregnancy and Lactation
Women of childbearing potential

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 first trimester of pregnancy assessed adverse pregnancy outcomes. The data showed that compared to quinine, artemisinin treatment, including artemether- lumefantrine, was not associated with an increased risk of miscarriage, stillbirth 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 increase in adverse pregnancy outcomes or teratogenic effects over background rates.
Studies in animals have shown reproductive toxicity .

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

Breast-feeding
Animal data suggest excretion into breast milk but no data are available in humans. Women taking Latesen caplet 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 Latesen caplet unless potential benefits to the mother and child outweigh the risks of Latesen caplet treatment.
Fertility
There is no information on the effects of Latesen caplet on human fertility.

4.7 Effects 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®is 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 malaria and I or to an unsatisfactory response to the treatment rather than to LA•TESEN®.Other common side effects include nausea, head ache, dizziness, fever, cough, weakness, loss of appetite and muscle pain

4.9 Overdose
In cases 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 Pharmacodynamics Properties
LA-TESEN® contains a fixed 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 synthetic racemic fluorine mixture. Both components of LA-TESEN®have their own action site in the malarial para ite. The presence of the end peroxide bridge in Artemether appears to be essential for antimalarial activity. Morphological changes of the parasitic membranes induced by Artemether have been described, being the result of free-radical action. Lumefantrine interferes more in the polymerization processes. Other in vitro test suggest that both cause a marked diminutionof 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 reticulum.

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 elimination is 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 protein in man is about 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.

5.3Preclinical safety data
None stated

6. PHARMACEUTICAL PARTICULARS

6.1List of excipients
Povidon PVP (K-30) Corn Starch
Microcrystalline cellulose 102
Aerosil 200
Sodium Lauryl
Sulphate Methyl
Paraben Magnesim
Stearate Sodium
Starch Glycollate
Crospovidone
Talcum powder
Propyl paraben

6.2 Incompatibilities
Not Applicable.

6.3Shelf life
3years

6.4 Special precautions for storage

Store below $30^{O}C$

6.5 Nature and contents of container
Alu/PVC Blister pack of 1 x 6 caplets

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

7. Marketing authorisation holder
Afrab-Chem Limited,
22, Abimbola street, Isolo Industrial Estate, Isolo Lagos.