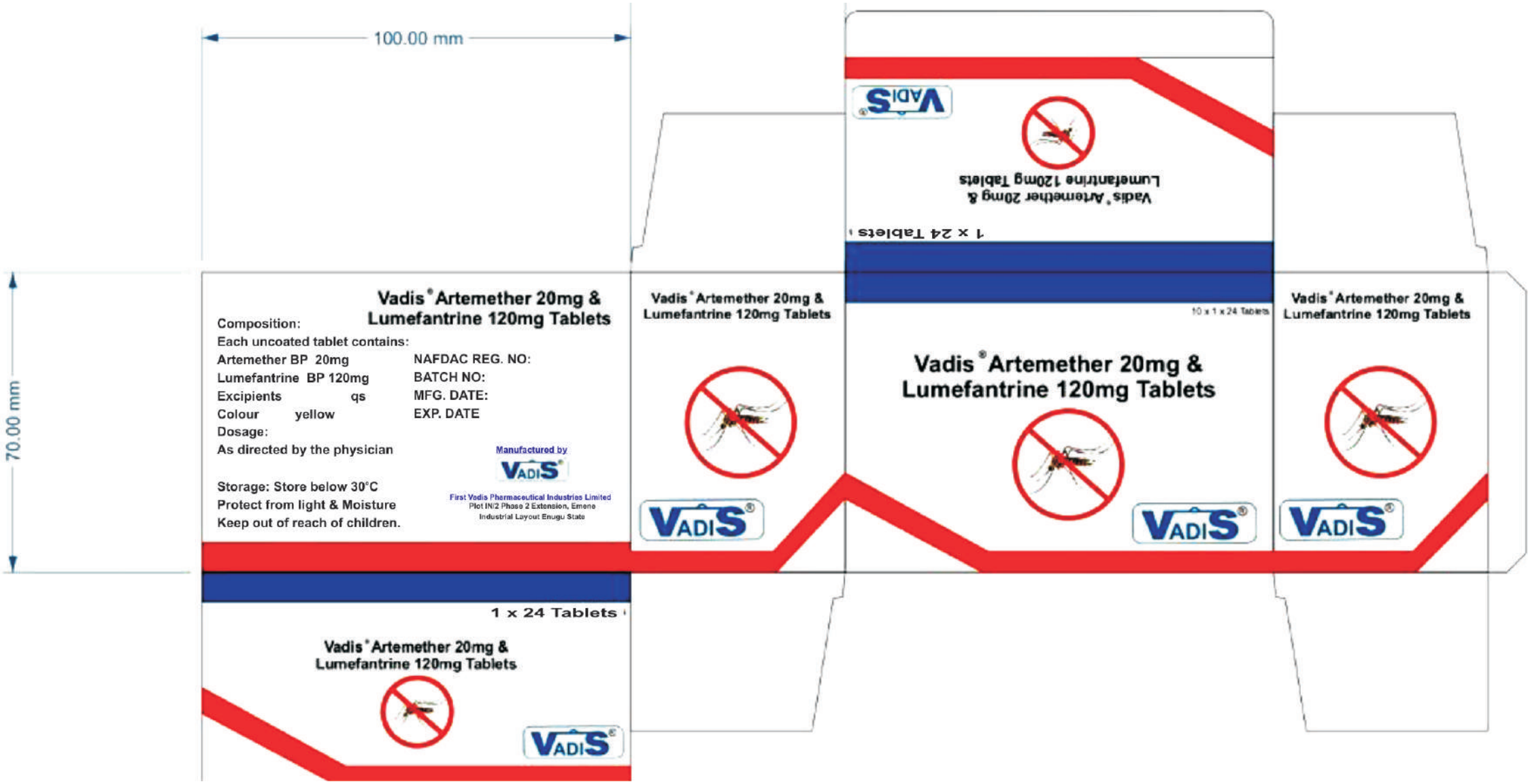
100.00 mm
70.00 mm
Vadis® Artemether 20mg & Lumefantrine 120mg Tablets
Composition:
Each uncoated tablet contains:
Artemether BP 20mg
Lumefantrine BP 120mg
Excipients qs
Colour yellow
Dosage:
As directed by the physician
NAFDAC REG. NO:
BATCH NO:
MFG. DATE:
EXP. DATE
Manufactured by
VADIS®
First Vadis Pharmaceutical Industries Limited
Plot IN/2 Phase 2 Extension, Emene
Industrial Layout Enugu State
Storage: Store below 30°C
Protect from light & Moisture
Keep out of reach of children.
1 x 24 Tablets
Vadis® Artemether 20mg & Lumefantrine 120mg Tablets
VADIS®
Vadis® Artemether 20mg & Lumefantrine 120mg Tablets
VADIS®
10 x 1 x 24 Tablets
Vadis® Artemether 20mg & Lumefantrine 120mg Tablets
VADIS®
Vadis® Artemether 20mg & Lumefantrine 120mg Tablets

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of medicinal product

Artemether 20 mg and Lumefantrine 120 mg Tablets

2. Composition:

Each uncoated tablet contains:

Artemether	20 mg
Lumefantrine	120 mg
Excipients	Q.S.

3. Pharmaceutical Form:

Solid Oral

4. Clinical Particulars

4.1 Indication

It is indicated for the treatment of acute uncomplicated Plasmodium falciparum malaria in adults, children and infants of 5 kg and above.

4.2 Posology and Administration

For patients 12 years of age and above and 35 kg body weight and above, a course of treatment comprises six doses of four tablets i.e. total of 24 tablets, given over a period of 60 hours as follows: the first dose of four tablets, given at the time of initial diagnosis, should be followed by five further doses of four tablets given at 8, 24, 36, 48 and 60 hours thereafter.

4.3 Contraindication

Hypersensitivity to the active substance(s) or to any of the excipients listed.

4.4 Special Warning & precautions for use

It is not recommended during the first trimester of pregnancy in situations where other suitable and effective antimalarials are available.
It has not been evaluated for the treatment of severe malaria, including cases of cerebral malaria or other severe manifestations such as pulmonary oedema or renal failure.
Due to limited data on safety and efficacy, It should not be given concurrently with any other antimalarial agent unless there is no other treatment option.
If a patient deteriorates whilst taking It, alternative treatment for malaria should be started without delay. In such cases, monitoring of the ECG is recommended and steps should be taken to correct any electrolyte disturbances.
The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with It.
If quinine is given after It, close monitoring of the ECG is advised.

If It is given after mefloquine, close monitoring of food intake is advised.
In patients previously treated with halofantrine, It should not be administered earlier than one month after the last halofantrine dose.
Caution is recommended when combining It with drugs exhibiting variable patterns of inhibition, moderate induction or competition for CYP3A4 as the therapeutic effects of some drugs could be altered. Drugs that have a mixed inhibitory/induction effect on CYP3A4, especially anti-retroviral drugs such as HIV protease inhibitors and non-nucleoside reverse transcriptase inhibitors should be used with caution in patients taking tablet.
Caution is recommended when combining It with hormonal contraceptives.
It may reduce the effectiveness of hormonal contraceptives. Therefore, patients 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.
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

Interaction with drugs that are known to prolong the QTc interval
It 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 some agents of the following classes: macrolides, fluoroquinolones, imidazole, and triazole antifungal agents, certain non-sedating antihistamins (terfenadine, astemizole), cisapride, flecainide
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 It 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 It Tablets (6-dose regimen over 3 days) in six HIV-1 and tuberculosis coinfected adults without malaria resulted in significant decreases in exposure to artemether (89%), DHA (85%) and lumefantrine (68%) when compared to exposure values after It alone. Concomitant use of strong inducers of CYP3A4 such as rifampin, carbamazepine, phenytoin, St. John's Wort is contraindicated with It.
Inducers should not be administered at least one month after It administration, unless critical to use as judged by the prescriber.
When tablet is co-administered with moderate inducers of CYP3A4, it may result in decreased concentrations of artemether and/or lumefantrine and loss of antimalarial efficacy.

4.6 Fertility, Pregnancy and lactation

the risk of adverse pregnancy outcomes for artemether-lumefantrine exposed women in early pregnancy cannot be excluded. treatment is not recommended during the first trimester of pregnancy in situations where other suitable and effective antimalarials are available.

4.7 Effects on ability to drive and use machines

Patients receiving tablet should be warned that dizziness or fatigue/asthenia may occur in which case they should not drive or use machines.

4.8 Undesirable effects

Respiratory, dizziness, nausea, vomiting and cutaneous hypersensitivity reactions have been observed in isolated cases.

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 Pharmacodynamic properties

Pharmacotherapeutic group: antimalarials, blood schizontocide, ATC code: P01BF01.
It comprises a fixed ratio of 1:6 parts of artemether and lumefantrine, respectively. The site of antiparasitic action of both components 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 nontoxic haemozoin, malaria pigment. Lumefantrine is thought to interfere with the polymerisation process, while artemether generates reactive metabolites as a result of the interaction between its peroxide bridge and haem iron. Both artemether and lumefantrine have a secondary action involving inhibition of nucleic acid- and protein synthesis within the malarial parasite. It has been reported to have potent activity in terms of clearing gametocytes.

5.2 Pharmacokinetic properties

Pharmacokinetic characterisation of Riamet is limited by the lack of an intravenous formulation, and the very high inter-and intra-subject variability of artemether and lumefantrine plasma concentrations and derived pharmacokinetic parameters (AUC, Cmax).

Absorption

Artemether is absorbed fairly rapidly and dihydroartemisinin, the active metabolite of artemether, appears rapidly in the systemic circulation with peak plasma concentrations of both compounds reached about 2 hours after dosing. Mean Cmax and AUC values of artemether ranged between 60.0-104 ng/mL and 146-338 ng·h/mL, respectively, in fed healthy adults after a single dose of Riamet, 80 mg artemether/480 mg lumefantrine. Mean Cmax and AUC values of dihydroartemisinin ranged between 49.7-104 ng/mL and 169-308 ng·h/mL, respectively. Absorption of lumefantrine, a highly lipophilic compound, starts after a lag-time of up to 2 hours, with peak plasma concentration (mean between 5.10-9.80 µg/mL) about 6-8 hours after dosing. Mean AUC values of lumefantrine ranged between 108 and 243 µg·h/mL. Food enhances the absorption of both artemether and lumefantrine: in healthy volunteers the relative bioavailability of artemether was increased more than two-fold, and that of lumefantrine sixteen-fold compared with fasted conditions when Riamet was taken after a high-fat meal.

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. The food interaction data indicate that absorption of lumefantrine under fasted conditions is very poor (assuming 100% absorption after a high-fat meal, the amount absorbed under fasted conditions would be <10% of the

dose). Patients should therefore be 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). Dihydroartemisinin is also bound to human serum proteins (47-76%).

Biotransformation

Artemether is rapidly and extensively metabolised (substantial first-pass metabolism) both in vitro and in humans. Human liver microsomes metabolise artemether to the biologically active main metabolite dihydroartemisinin (demethylation), predominantly through the isoenzyme CYP3A4/5. This metabolite has also been detected in humans in vivo.

Dihydroartemisinin is further converted to inactive metabolites.

The pharmacokinetics of artemether in adults is time-dependent. During repeated administration of Riamet, plasma artemether levels decreased significantly, while levels of the active metabolite (dihydroartemisinin) increased, although not to a statistically significant degree. The ratio of day 3/day 1 AUC for artemether was between 0.19 and 0.44, and was between 1.06 and 2.50 for dihydroartemisinin. This suggests that there was induction of the enzyme responsible for the metabolism of artemether. Artemether and dihydroartemisinin were reported to have a mild inducing effect on CYP3A4 activity.

Elimination

Artemether and dihydroartemisinin are rapidly cleared from plasma with a terminal half-life of about 2 hours. Lumefantrine is eliminated very slowly with an elimination half-life of 2 to 6 days.

6. Shelf Life
36 months

7. Special precaution for Storage

Do not store above 30°C.

8. Nature and contents of container
Tablets are available in blister packed in carton along with insert.

9. Marketing Holder

First Vadis Pharmaceutical Industries Limited
Plot IN/2 Phase 2 Extension, Emene Industrial Layout Enugu state

10. Manufacturer

First Vadis Pharmaceutical Industries Limited
Plot IN/2 Phase 2 Extension, Emene Industrial Layout Enugu state