1. NAME OF THE MEDICINAL PRODUCT

Artket-LM 80/480 (Artemether & Lumefantrine 80/480 mg) Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Artemether	80 mg
Lumefantrine	480 mg
Excipients	q.s.

3. PHARMACEUTICAL FORM

Oral Solid Dosage Form

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

Consideration should be given to official guidance regarding the appropriate use of antimalarial agents.

4.2 Posology and Method of Administration *Posology*

To increase absorption, Artemether & Lumefantrine Tablets 80/480 mg should be taken with food or a milky drink. If patients are unable to tolerate food, Artemether & Lumefantrine Tablets 80/480 mg should be administered, but the systemic exposure may be reduced. Patients who vomit within 1 hour of taking the medication should repeat the dose.

For administration to small children and infants, the tablet/s may be crushed.

Adults and children weighing 35 kg and above:

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.

Children and infants weighing 5 kg to less than 35 kg:

A six-dose regimen is recommended with 1 to 3 tablets per dose, depending on bodyweight:
5 to less than 15 kg bodyweight: the first dose of one tablet, given at the time of initial diagnosis, should be followed by five further doses of one tablet given at 8, 24, 36, 48 and 60 hours thereafter.
15 to less than 25 kg bodyweight: the first dose of two tablets, given at the time of initial diagnosis, should be followed by five further doses of two tablets given at 8, 24, 36, 48 and 60 hours thereafter.
25 to less than 35 kg bodyweight: the first dose of three tablets, given at the time of initial diagnosis, should be followed by five further doses of three tablets given at 8, 24, 36, 48 and 60 hours thereafter.

Elderly:
Although no studies have been carried out in the elderly, no special precautions or dosage adjustments are considered necessary in such patients.

Renal impairment:
No specific studies have been carried out in these groups of patients. However, there is no significant renal excretion of Lumefantrine, Artemether and Dihydroartemisinin in humans; therefore, no dose adjustment for the use of Artemether & Lumefantrine Tablets 80/480 mg in patients with renal impairment is advised.
Caution is advised when administering Artemether & Lumefantrine Tablets 80/480 mg to patients with severe renal impairment. In these patients, ECG and blood potassium monitoring is advised.

Hepatic impairment:
No specific studies have been carried out in these groups of patients. Therefore, no specific dose adjustment recommendations can be made for patients with hepatic impairment.
Caution is advised when administering Artemether & Lumefantrine Tablets 80/480 mg to patients with severe hepatic impairment.

New infections:
Data for a limited number of patients in a malaria endemic area show that new infections can be treated with a second course of Artemether & Lumefantrine Tablets 80/480 mg. In the absence of carcinogenicity study data, and due to lack of clinical experience, more than two courses of Artemether & Lumefantrine Tablets 80/480 mg cannot be recommended.

Method of administration For
Oral administration.

4.3 Contra-indications

Artemether & Lumefantrine Tablets 80/480 mg 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 metabolised by the cytochrome enzyme CYP2D6 (e.g. 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 taking drugs that are known to prolong the QTc interval. These drugs include:

− Antiarrhythmics of classes IA and III,

− Neuroleptics, antidepressive agents,

- Certain antibiotics including some agents of the following classes: macrolides, fluoroquinolones, imidazole and triazole antifungal agents, - certain non-sedating antihistamines (terfenadine, astemizole), Cisapride.
- Patients with a history of symptomatic cardiac arythmias or with clinically relevant bradycardia or with congestive cardiac failure accompanied by reduced left ventricle ejection fraction.
- Patients with disturbances of electrolyte balance e.g. hypokalemia or hypomagnesemia

4.4 Special Warnings and Special Precautions for Use

Artemether & Lumefantrine Tablets 80/480 mg must not be used in the first trimester of pregnancy in situations where other suitable and effective antimalarial are available.

Artemether & Lumefantrine Tablets 80/480 mg 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, Artemether & Lumefantrine Tablets 80/480 mg should not be given concurrently with any other antimalarial agent unless there is no other treatment option.

If a patient deteriorates whilst taking Artemether & Lumefantrine Tablets 80/480 mg, 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 Artemether & Lumefantrine Tablets 80/480 mg.

If quinine is given after Artemether & Lumefantrine Tablets 80/480 mg, close monitoring of the ECG is advised.

If Artemether & Lumefantrine Tablets 80/480 mg is given after mefloquine, close monitoring of food intake is advice.

In patients previously treated with halofantrine, Artemether & Lumefantrine Tablets 80/480 mg should not be administered earlier than one month after the last halofantrine dose.

Artemether & Lumefantrine Tablets 80/480 mg is not indicated for, and has not been evaluated in, the treatment of malaria due to P. vivax, P. malariae or P. ovale, although some patients in clinical studies had coinfection with P. falciparum and P. vivax at baseline. Artemether & Lumefantrine

Tablets 80/480 mg is active against blood stages of Plasmodium vivax, but is not active against hypnozoites.

Artemether & Lumefantrine Tablets 80/480 mg is not indicated and has not been evaluated for prophylaxis.
Like other antimalarials (e.g. halofantrine, quinine and quinidine) Artemether & Lumefantrine Tablets 80/480 mg has the potential to cause QT prolongation.

In the adult/adolescent population included in clinical trials, 8 patients (0.8%) receiving
Artemether & Lumefantrine Tablets 80/480 mg experienced a QTcB >500 msec and 3 patients (0.4%) a QTcF >500 msec. Prolongation of QTcF interval >30 msec was observed in 36% of patients.
In the infant/children population included in clinical trials, 3 patients (0.2%) experienced a QTcB >500 msec. No patient had QTcF >500 msec. Prolongation of QTcF intervals >30 msec was observed in 34% of children weighing 5-10 kg, 31% of children weighing 10-15 kg and 24% of children weighing 15-25 kg, and 32% of children weighing 25-35 kg.

Caution is recommended when combining Artemether & Lumefantrine Tablets 80/480 mg with drugs exhibiting variable patterns of inhibition, induction or competition for CYP3A4 as the therapeutic effects of some drugs could be altered.

Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

Caution is advised when administering Artemether & Lumefantrine Tablets 80/480 mg to patients with severe renal, hepatic or cardiac problems.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction Interaction with other antimalarials:

A drug interaction study with Artemether & Lumefantrine Tablets 80/480 mg in man involved administration of a 6-dose regimen over 60 hours in healthy volunteers which was commenced at 12 hours after completion of a 3-dose regimen of mefloquine or placebo. Plasma mefloquine concentrations from the time of addition of Artemether & Lumefantrine Tablets 80/480 mg were not affected compared with a group which received mefloquine followed by placebo.

Pre-treatment with mefloquine had no effect on plasma concentrations of Artemether or the Artemether/dihydroartemisinin ratio but there was a significant reduction in plasma levels of Lumefantrine, possibly due to lower absorption secondary to a mefloquine-induced decrease in bile production. Patients should be encouraged to eat at dosing times to compensate for the decrease in bioavailability.

A drug interaction study in healthy male volunteers showed that the plasma concentrations of Lumefantrine and quinine were not affected when i.v. quinine (10 mg/kg BW over 2 hours) was given sequentially 2 hours after the last (sixth) dose of Artemether & Lumefantrine Tablets 80/480 mg (so as to produce concurrent plasma peak levels of Lumefantrine and quinine). Plasma concentrations of Artemether and dihydroartemisinin (DHA) appeared to be lower. In this study, administration of Artemether & Lumefantrine Tablets 80/480 mg to 14 subjects had no effect on QTc interval. Infusion of quinine alone in 14 other subjects caused a transient prolongation of QTc interval, which was consistent with the known cardiotoxicity of quinine. This effect was slightly, but significantly, greater when quinine was infused after Artemether & Lumefantrine Tablets 80/480 mg in 14 additional subjects. It would thus appear that the inherent risk of QTc prolongation associated with i.v. quinine was enhanced by prior administration of Artemether & Lumefantrine Tablets 80/480 mg.

Interaction with CYP450 3A4 inhibitors (ketoconazole):
Both Artemether and Lumefantrine are metabolised predominantly by the cytochrome enzyme CYP3A4, and do not inhibit this enzyme at therapeutic concentrations. The concurrent oral administration of ketoconazole with Artemether & Lumefantrine Tablets 80/480 mg led to a modest increase (≤ 2-fold) 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. Based on this study, dose adjustment of Artemether & Lumefantrine Tablets 80/480 mg is considered unnecessary in falciparum malaria patients when administered in association with ketoconazole or other potent CYP3A4 inhibitors.

Interaction with CYP450 enzymes:
Studies in humans have demonstrated that artemisinins have some capacity to induce CYP3A4 and CYP2C19 and inhibit CYP2D6 and CYP1A2. Although the magnitude of the changes was generally low it is possible that these effects could alter the therapeutic response of drugs that are predominantly metabolised by these enzymes.

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 Artemether & Lumefantrine Tablets 80/480 mg with drugs that are metabolised by this iso-enzyme is contraindicated. In vitro studies indicated that Lumefantrine metabolism is inhibited by halofantrine and quinine.

Interaction with protease inhibitor anti-retroviral drugs:
Due to variable patterns of inhibition, induction or competition for CYP3A4 with protease inhibitor anti-retroviral drugs, use of such drugs, especially combinations of them, concomitantly with Artemether & Lumefantrine Tablets 80/480 mg, requires clinical surveillance and monitoring of clinical response/undesirable effects.

Other interactions:
Administration of Artemether & Lumefantrine Tablets 80/480 mg is contra-indicated in patients taking drugs that are known to prolong the QTc interval.

In patients previously treated with halofantrine, Artemether & Lumefantrine Tablets 80/480 mg should be dosed at least one month after the last halofantrine dose.

Due to the limited data on safety and efficacy, Artemether & Lumefantrine Tablets 80/480 mg should not be given concurrently with any other antimalarial agent.

In addition, due to the propensity of some antimalarial agents to prolong the QTc interval, caution is advised when administering Artemether & Lumefantrine Tablets 80/480 mg to patients in whom there may still be detectable concentrations of these drugs in the plasma following prior treatments.

4.6 Pregnancy and Lactation **Pregnancy**

There is insufficient data from the use of Artemether and Lumefantrine in pregnant women. Based on animal data, Artemether & Lumefantrine Tablets 80/480 mg is suspected to cause serious birth defects when administered during the first trimester of pregnancy Reproductive studies with Artemether have shown evidence of post-implantation losses and teratogenicity in rats and rabbits. Other artemisinin derivatives have also demonstrated teratogenic potential with an increased risk during early gestation Artemether & Lumefantrine Tablets 80/480 mg treatment must not be used during the first trimester of pregnancy in situations where other suitable and effective antimalarial 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, treatment should only 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 Artemether & Lumefantrine Tablets 80/480 mg should not breast-feed during their treatment. Due to the long elimination half-life of Lumefantrine (4 to 6 days), it is recommended that breastfeeding should not resume until at least one week after the last dose of Artemether & Lumefantrine Tablets 80/480 mg unless potential benefits to the mother and child outweigh the risks of Artemether & Lumefantrine Tablets 80/480 mg treatment.

4.7 Effects on Ability to Drive and Use Machines

Patients receiving Artemether & Lumefantrine Tablets 80/480 mg should be warned that dizziness or fatigue/asthenia may occur in which case they should not drive or use machines.

4.8 Undesirable Effects

The safety of Artemether & Lumefantrine Tablets 80/480 mg has been evaluated in 20 clinical trials with more than 3500 patients. A total of 1810 adults and adolescents above 12 years of age as well as 1788 infants and children of 12 years of age and below have received Artemether & Lumefantrine Tablets 80/480 mg in clinical trials.
Adverse reactions reported from clinical studies and post-marketing experience are listed below according to system organ class.
Adverse reactions are ranked under headings of frequency using the MedDRA frequency convention:

Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000); Not known (cannot be estimated from available data).

Cardiac disorders
Very common: Palpitations
Common: Electrocardiogram QT prolonged
Nervous system disorders
Very common: Headache, Dizziness
Common: Paraesthesia
Uncommon: Ataxia, hypoaesthesia, Clonus, somnolence
Respiratory, thoracic and mediastinal disorders
Common: Cough
Gastrointestinal disorders
Very common: Vomiting, Abdominal pain, Nausea, Diarrhoea
Skin and subcutaneous tissue disorders
Common: Rash, Pruritus
Not known: Urticaria, angioedema
Musculoskeletal and connective tissue disorders
Very common: Arthralgia, Myalgia
Metabolism and nutrition disorders
Very common: Anorexia
General disorders and administration site conditions
Very common: Asthenia, Fatigue
Common: Gait disturbance
Immune system disorders
Not known: Hypersensitivity
Hepatobiliary disorders
Uncommon: Liver function tests increased
Psychiatric disorders
Very common: Sleep disorders
Common: Insomnia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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, Artemisinin and derivatives, combination. **ATC Code:** P01 BF01.

Mechanism of action

Artemether involves an interaction with ferriprotoporphyrin IX ("heme"), or ferrous ions, in the acidic parasite food vacuole, which results in the generation of cytotoxic radical species. The generally accepted mechanism of action of peroxide antimalarials involves interaction of the peroxide-containing drug with heme, a hemoglobin degradation byproduct, derived from proteolysis of hemoglobin. This interaction is believed to result in the formation of a range of potentially toxic oxygen and carbon-centered radicals.

The exact mechanism by which Lumefantrine exerts its antimalarial effect is unknown. However, available data suggest that Lumefantrine inhibits the formation of β-hematin by forming a complex with hemin and inhibits nucleic acid and protein synthesis.

5.2 Pharmacokinetic Properties 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 Artemether & Lumefantrine Tablets 80/480 mg, 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 Artemether & Lumefantrine Tablets 80/480 mg 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 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%).

Metabolism:
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 Artemether & Lumefantrine Tablets 80/480 mg, 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. The clinical evidence of induction is consistent with the in vitro data.
Lumefantrine is N-debutylated, mainly by CYP3A4, in human liver microsomes. In vivo in animals (dogs and rats), glucuronidation of Lumefantrine takes place directly and after oxidative biotransformation. In humans, the exposure to Lumefantrine increases with repeated administration of Artemether & Lumefantrine Tablets 80/480 mg over the 3-day treatment period, consistent with the slow elimination of the compound .Systemic exposure to the metabolite desbutyl-lumefantrine, for which the in vitro antiparasitic effect is 5 to 8 fold higher than that for Lumefantrine, was less than 1% of the exposure to the parent drug. Desbutyl-lumefantrine data is not available specifically for an African population. In vitro, Lumefantrine significantly inhibits the activity of CYP2D6 at therapeutic plasma concentrations.

Elimination:
Artemether and Dihydroartemisinin are rapidly cleared from plasma with a terminal 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. Demographic characteristics such as sex and weight appear to have no clinically relevant effects on the pharmacokinetics of Artemether & Lumefantrine Tablets 80/480 mg.
Limited urinary excretion data are available for humans. In 16 healthy volunteers, neither

Lumefantrine nor Artemether was found in urine after administration of Artemether & Lumefantrine Tablets 80/480 mg, and only traces of Dihydroartemisinin were detected (urinary excretion of Dihydroartemisinin amounted to less than 0.01% of the Artemether dose).
In animals (rats and dogs), no unchanged Artemether was detected in faeces and urine due to its rapid and extensive first-pass metabolism, but numerous metabolites (partly identified) have been detected in faeces, bile and urine. Lumefantrine was excreted unchanged in faeces and with traces only in urine. Metabolites of Lumefantrine were eliminated in bile/faeces.

Pharmacokinetics in special patient populations:
In paediatric malaria patients, mean Cmax (CV%) of Artemether (observed after first dose of Artemether & Lumefantrine Tablets 80/480 mg) were 223 (139%), 198 (90%) and 174 ng/mL (83%) for body weight groups 5-<15, 15-<25 and 25-<35 kg, respectively, compared to 186 ng/mL (67%) in adult malaria patients. The associated mean Cmax of DHA were 54.7 (108%), 79.8 (101%) and 65.3 ng/mL (36%), respectively compared to 101 ng/mL (57%) in adult malaria patients. AUC of Lumefantrine (population mean, covering the six doses of Artemether & Lumefantrine Tablets 80/480 mg) were 577, 699 and 1150 µg•h/mL for paediatric malaria patients in body weight groups 5-<15, 15-<25 and 25<35 kg, respectively, compared to a mean AUC of 758 µg•h/mL (87%) in adult malaria patients. The elimination half-lives of Artemether and Lumefantrine in children are unknown.
No specific pharmacokinetic studies have been performed either in patients with hepatic or renal insufficiency or elderly patients. Based on the pharmacokinetic data in 16 healthy subjects showing no or insignificant renal excretion of Lumefantrine, Artemether and Dihydroartemisinin, no dose adjustment for the use of Artemether & Lumefantrine Tablets 80/480 mg in patients with renal impairment is advised.

5.3 Preclinical Safety Data General toxicity:

The main changes observed in repeat-dose toxicity studies were associated with the expected pharmacological action on erythrocytes, accompanied by responsive secondary haematopoiesis.

Mutagenicity:
No evidence of mutagenicity was detected in in vitro or in vivo tests with an Artemether: Lumefantrine combination (consisting of 1 part Artemether: 6 parts Lumefantrine). In the micronucleus test myelotoxicity was seen at all dose levels (500, 1,000 and 2,000 mg/kg), but recovery was almost complete 48 hours after dosing.

Carcinogenicity:
Carcinogenicity studies with the Artemether/Lumefantrine combination were not conducted.

Reproductive toxicity studies:

Reproductive toxicity studies performed with the Artemether/Lumefantrine combination caused maternal toxicity and increased post-implantation loss in rats and rabbits at doses 50 mg/kg/day (corresponding to approximately 7 mg/kg/day Artemether) and 175 mg/kg/day (corresponding to 25 mg/kg/day Artemether) respectively. These effects were not observed at lower doses.
Lumefantrine alone caused no sign of reproductive or development toxicity at doses up to 1,000 mg/kg/day in rats and rabbits.
Embryotoxicity has been observed in rat and rabbit reproductive toxicity studies conducted with Artemether, a derivative of artemisinin. Artemisinins (e.g. artesunate) are known to be embryotoxic in animals.
Artemether caused increases in post-implantation loss and teratogenicity (characterised as a low incidence of cardiovascular and skeletal malformations) in rats at 19.4 mg/kg, and in rabbits at 30 mg/kg. Maternal toxicity was also observed in rabbits at 30 mg/kg/day. No other adverse effects were observed at lower doses in rabbits. The no observed effect dose was 3 mg/kg/day in rats and 25 mg/kg/day in rabbits.
The embryotoxic Artemether dose, 20 mg/kg/day in the rat, yields Artemether and dihydroartemisinin exposures similar to those achieved in humans.
Artesunate, a structurally related compound, also caused increases in post-implantation loss and teratogenicity (low incidence of cardiovascular and skeletal malformations) in rats at 6 mg/kg and in the lowest dose tested in the rabbits, 5 mg/kg/day

Cardiovascular Pharmacology:
In toxicity studies in dogs at doses > 600 mg/kg/day only, there was some evidence of prolongation of the QTc interval, at higher doses than intended for use in man. In an in vitro assay of HERG channels, Lumefantrine and the main metabolite desbutyl-lumefantrine showed some inhibitory potential in one of the currents responsible for cardiac repolarization. From the estimated IC50 values, the order of potency of HERG current block was halofantrine (IC50 = 0.04 μM) > chloroquine (2.5 μM) > mefloquine (2.6 μM) > desbutyl-lumefantrine (5.5 μM) > Lumefantrine (8.1 μM). Clinical studies show, that prolongation of QTcF can occur with standard dosing of Artemether/Lumefantrine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Povidone	USP
Hypromellose	USP
Microcrystalline Cellulose	USP
Tartrazine Lake	IH
Isopropyl Alcohol	USP
Colloidal Silicon Dioxide	USP
Croscarmellose Sodium	USP
Magnesium Stearate	USP

6.2 Incompatibilities None Known

6.3 Shelf Life
36 Months

6.4 Special Precautions for Storage
Store at a temperature not exceeding 30°C in dry place. Protect from light.

6.5 Nature and Contents of Container
1x6 Alu-PVC blister is packed in a carton along with leaflet.

6.6 Special precautions for disposal and other handling None

7. MARKETING AUTHORISATION HOLDER

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#17 Afram Street Asylum Down Accra, P.O. Box AN 10822, Accra-North, Ghana.

MANUFACTURING SITE ADDRESS
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8. MARKETING AUTHORISATION NUMBER

FDA/SD.243-030364

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

3/1/2024

10. DATE OF REVISION OF THE TEXT

08/2025