SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product
ARTE-L (Artemether and Lumefantrine Tablets)

2. Qualitative and quantitative composition
Each uncoated tablet contains:
Artemether .....20 mg
Lumefantrine..... 120 mg
Excipients q.s.

Sr. No.	Ingredients
1	Artemether
2	Lumefantrine
3	Microcrystalline Cellulose
4	Calcium Hydrogen Phosphate Dihydrate
5	Maize Starch (For Mixing)
6	Povidone (P.V.P.K - 30)
7	Isopropyl Alcohol
8	Magnesium Stearate
9	Purified Talc
10	Colloidal Anhydrous silica (Aerosil)
11	Sodium Starch Glycolate (Type A)
12	Maize Starch (For Drying)

3. Pharmaceutical form
Tablets

Yellow colour, circular, flat uncoated tablets having break line on one side and plain on another side.

4. Clinical particulars

4.1 Therapeutic indications
ARTE-L is indicated for the treatment of acute uncomplicated *Plasmodium falciparum* malaria.

4.2 Posology and method of administration

Tablets for oral administration. To increase absorption, ARTE-L should be taken with food or a milky drink. 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 3-day treatment schedule with a total of 6 doses is recommended as below:
5 kg to less than 15 kg bodyweight: One tablet as an initial dose, 1 tablet again after 8 hours and then 1 tablet twice daily (morning and evening) for the following two days (total course of 6 tablets).
15 kg to less than 25 kg bodyweight: Two tablets as an initial dose, 2 tablets again after 8 hours and then 2 tablets twice daily (morning and evening) for the following two days (total course of 12 tablets).
25 kg to less than 35 kg bodyweight: Three tablets as an initial dose, 3 tablets again after 8 hours and then 3 tablets twice daily (morning and evening) for the following two days (total course of 18 tablets).

4.3 Contraindications

Artemether & Lumefantrine Tablets are contraindicated in:
Patients with known hypersensitivity to the active substances or to any of the excipients.
Patients with disturbances of electrolyte balance e.g. hypokalemia or hypomagnesemia.

4.4 Special warnings and precautions for use
Artemether & Lumefantrine Tablets 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.
If a patient deteriorates whilst taking Artemether & Lumefantrine Tablets, 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.

If Artemether & Lumefantrine Tablets is given following administration of mefloquine or quinine, close monitoring of food intake (for mefloquine) or of the ECG (for quinine) is advised.
The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with Artemether & Lumefantrine Tablets. In patients previously treated with halofantrine, Artemether & Lumefantrine Tablets should not be administered earlier than one month after the last halofantrine dose.
Artemether & Lumefantrine Tablets is not indicated and has not been evaluated for prophylaxis.
Artemether & Lumefantrine Tablets should be used cautiously in patients on ARTs since decreased Artemether, DHA, and/or Lumefantrine concentrations may result in a decrease of antimalarial efficacy of Artemether & Lumefantrine Tablets.
Caution is recommended when combining Artemether & Lumefantrine Tablets 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 Artemether & Lumefantrine Tablets.
Patients using oral, transdermal patch, or other systemic hormonal contraceptives should be advised to use an additional non-hormonal method of birth control.
Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.
In patients with severe hepatic impairment, a clinically relevant increase of exposure to Artemether and Lumefantrine and/or their metabolites cannot be ruled out. Therefore caution should be exercised in dosing patients with severe hepatic impairment.
Renal impairment: No specific studies have been carried out in this group of patients. There is no significant renal excretion of Lumefantrine, Artemether and Dihydroartemisinin in studies conducted in healthy volunteers and clinical experience is limited. No dose adjustment for the use of Artemether & Lumefantrine Tablets in patients with renal impairment is recommended. Caution is advised when administering Artemether & Lumefantrine Tablets to patients with severe renal impairment. In this case, patient's ECG and blood potassium monitoring is advised.
Hepatic impairment: No specific studies have been carried out in this group of patients. No dose adjustment is recommended for patients with mild to moderate hepatic impairment. Caution is advised when administering Artemether & Lumefantrine Tablets to patients with severe hepatic impairment. In these patients, ECG and blood potassium monitoring is advised.
Elderly: There is no information suggesting that the dosage in patients over 65 years of age should be different than in younger adults.
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.
In the absence of carcinogenicity study data, and due to lack of clinical experience, more than two courses of Artemether & Lumefantrine Tablets cannot be recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Strong CYP3A4 Inducers: Co-administration of strong inducers of CYP3A4 such as Rifampin, Carbamazepine, Phenytoin and St. John's wort with Artemether & Lumefantrine Tablets can result in decreased concentrations of Artemether and/or Lumefantrine and loss of antimalarial efficacy.

CYP3A4 Inhibitors: Both artemether and lumefantrine are metabolised predominantly by the cytochrome enzyme CYP3A4, but do not inhibit this enzyme at therapeutic concentrations.
Antiretroviral drugs: Artemether & Lumefantrine Tablets should be used cautiously in patients on antiretroviral drugs because decreased Artemether, DHA, and/or Lumefantrine concentrations may result in a decrease of antimalarial efficacy of Artemether & Lumefantrine Tablets, and increased Lumefantrine concentrations may cause QT prolongation.
Other anti-malarial drugs: Data on safety and efficacy are limited, and Artemether & Lumefantrine Tablets should therefore not be given concurrently with other antimalarials (mefloquine or quinine, halofantrine) unless there is no other treatment option.
Hormonal Contraceptives: Artemether has been reported to weakly induce, in humans, the activity of CYP2C19, CYP2B6, and CYP3A. Therefore, Artemether & Lumefantrine Tablets may potentially reduce the effectiveness of hormonal contraceptives.
CYP2D6 Substrates: Many of the drugs metabolized by CYP2D6 can prolong the QT interval and should not be administered with Artemether & Lumefantrine Tablets due to the potential additive effect on the QT interval (e.g., Metoprolol, Flecainide, Imipramine, Amitriptyline, Clomipramine).
Interaction with Drugs that are known to prolong the QT Interval: Artemether & Lumefantrine Tablets is to be used with caution when co-administered with drugs that may cause prolonged QT interval 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 antihistaminics (terfenadine, astemizole), cisapride, flecainide.

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 is suspected to cause serious birth defects when administered during the first trimester of pregnancy.
Artemether & Lumefantrine Tablets treatment must not be used 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, treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus.
Lactation: Women taking Artemether & Lumefantrine Tablets should not breast-feed during their treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Patients receiving Artemether and Lumefantrine Tablets should be warned that dizziness, fatigue or asthenia may occur, in which case their ability to drive or operate machines may be impaired.

4.8 Undesirable effects

The most common adverse reactions in adults (>30%) are headache, anorexia, dizziness, asthenia, arthralgia and myalgia. The most common adverse reactions in children (>12%) are pyrexia, cough, vomiting, anorexia and headache.

4.9 Overdose

In cases of suspected overdosage, symptomatic and supportive therapy, which would include ECG and blood electrolyte monitoring, should be given as appropriate

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group:
Artemether and Lumefantrine: Antimalarials (Artemisinin and derivatives, combinations)
ATC Code: P01BF01
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.

5.2 Pharmacokinetic properties

Absorption: Artemether is absorbed with peak plasma concentrations reached about 2 hours after dosing. Absorption of Lumefantrine, a highly lipophilic compound, starts after a lag-time of up to 2 hours, with peak plasma concentrations about 6 to 8 hours after administration.
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 (DHA) has been attributed to endoperoxide moiety and is further converted to inactive metabolites.
Lumefantrine is N-debutylated, mainly by CYP3A4, in human liver microsomes. Available data suggest Lumefantrine inhibit the formation of β-hematin by forming a complex with hemin.
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. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:
Microcrystalline Cellulose BP, Calcium Hydrogen Phosphate Dihydrate BP, Maize Starch BP, Povidone BP, Isopropyl Alcohol BP, Magnesium Stearate BP, Purified Talc BP, Colloidal Anhydrous Silica (Aerosil) BP, Sodium Starch Glycolate (Type A) BP.

6.2 Incompatibilities:
No available data.

6.3 Shelf life:
24 Months

6.4 Special precautions for storage:
Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container
1 Alu/PVC Blister containing 8 tablets, such 3 blisters are packed in Primary carton along with pack insert.

7. MARKETING AUTHORISATION HOLDER:
AKRITI PHARMACEUTICALS PVT. LTD

205, "Thane MINT", Indiabulls, Behind Hiranandani Meadows, Near Hyde Park,

off B.N.Pai Road, Thane (W)-400 610, Maharashtra, India

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS
3341/3290/NMR/2017
06299/08062/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24.07.2017
Jul 25, 2021

10. DATE OF REVISION OF THE TEXT
Not Applicable