Artecxin™

(Artemether + Lumefantrine)

Highnoon

COMPOSITION

1. **Artecxin Dispersible Tablet:**
   Each dispersible tablet contains:
   Artemether 20mg
   Lumefantrine 120mg
2. **Artecxin Forte Dispersible Tablet:**
   Each dispersible tablet contains:
   Artemether 40mg
   Lumefantrine 240mg
3. **Artecxin Plus Dispersible Tablet:**
   Each dispersible tablet contains:
   Artemether 80mg
   Lumefantrine 480mg

DESCRIPTION

Artemether is a semisynthetic chiral acetal derivative from artemisinin, a bicydic sesquiterpene lactone endoperoxide isolated from the plant Artemisia annua.
Lumefantrine is a dichlorobenzylidine derivatives given orally with artemmether. Lumefantrine is a racemic mixture of a synthetic fluorene derivative.

Artecxin range comprises a fixed combination of artemether and lumefantrine (one part of the artemether and six part of lumefantrine), which acts as a blood schizontocide. Artemether has quick onset of action while Lumefantrine has longer duration of action.

PHARMACOLOGICAL PROPERTIES

Pharmacokinetics:
Artemether is absorbed fairly rapidly 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 concentration about 6 to 8 hours after administration. Food enhances the absorption of both artemether and lumefantrine. Patients should therefore be encouraged to take the medication with a normal diet as soon as food can be tolerated. 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% to 76%). Protein binding to human plasma protein is linear. Artemether is rapidly and extensively metabolised to the biologically active main metabolite dihydroartemisinin (demethylation), predominantly through the enzyme CYP3A4/5.
Lumefantrine is N-debutylated, mainly by CYP3A4, in liver. Artemether and dihydroartemisinin are rapidly cleared from plasma with an elimination half- life of about 2 hours. Bioavailability of Lumefantrine after oral doses is variable; absorption begins a lag time of up to 2 hours and bioavailability is substantially increased when given with food, particularly meals high in fat. Peak plasma concentration occurs after 6 to 8 hours. Lumefantrine is almost completely protein bound. It is considered to be metabolized mainly in the liver and is excreted in the faeces. The elimination half-life is reported to be between 4 to 6 days in patients with malaria.

INDICATIONS

- It is indicated for treatment of acute uncomplicated falciparum malarial treatment of chloroquine resistant non falciparum malaria.
- It is indicated in uncomplicated falciparum malaria.

DOSAGE AND ADMINISTRATION

The dispersible tablet(s) composing 1 dose should be completely dispersed in a small amount of water (approximately 10 mL per tablet for 20/120 mg, approximately 20 mL per tablet for 40/240 & 80/480 respectively). Stir gently and administer immediately to the patient. Rinse the glass with an additional small amount of water (approximately 10 mL) and give immediately to the patient.
The dose should be followed by food or drinks rich in fat such as milk. Patients with acute malaria are frequently averse to food. Patients should be encouraged to resume normal eating.
Artecxin should be administered twice a day for 3 days (total, six doses). The first two doses, should ideally, be given 8 hours apart and then twice daily (morning and evening) for the following two days.
The number of tablets per dose for children / adult is determined by bodyweight, as shown in the chart below.

Body weight (kg)	Dose (mg) of artemether + lumefantrine given twice daily for 3 days
5 to < 15	20 + 120
15 to < 25	40 + 240
25 to < 35	60 + 360
≥ 35	80 + 480

Note: The dosage in children / adult be adjusted as advised by the physician.
Target dose range: A total dose of 5 – 24 mg/kg body weight of artemether and 29 – 144 mg/kg body weight of lumefantrine.
Dosage in patients with mild to moderate renal or hepatic impairment:
No dose adjustment is advised in patients with renal impairment. No specific dose adjustment recommendations can also be made for patients with hepatic impairment.
New and recrudescent infections:
Data for a limited number of patients with Artemether Lumefantrine combination show that new and recrudescent infections can be treated with a second course of the medication.

CONTRAINDICATIONS

- Patients hypersensitive to artemether, lumefantrine or to any of the excipients.
- Family history of congenital QT prolongation.
- History of arrythmias.
- History of clinically relevant bradycardia.
- History of congestive heart failure accompanied by reduced left ventricular ejection fraction.

WARNINGS AND PRECAUTIONS

- Avoid use in patients with known QT prolongation, those with hypokalemia or hypomagnesaemia, and those taking other drugs that prolong the QT interval.
- Antimalarials should not be given concomitantly, unless there is no other treatment option, due to limited safety data.
- QT prolonging drugs, including quinine and quinidine, should be used cautiously following the combination (artemether and lumefantrine). Substrates, inhibitors, or inducers of CYP3A4, including antiretroviral medications, should be used cautiously with the combination (artemether and lumefantrine), due to a potential loss of efficacy of the concomitant drug or additive QT prolongation.
- Avoid use acute porphyria.
- Avoid use in electrolyte disturbance.
- Caution should be exercised in patient with severe hepatic or renal impairment.

ADVERSE REACTIONS

Abdominal pain, appetite decreased, arthralgia, asthenia, cough, diarrhea, dizziness, gait abnormal, headache, movement disorder, myalgia, palpitations, QT interval prolongation, sensation abnormal, skin reaction, sleep disturbance, drowsiness, angioedema, gastrointestinal disturbance (nausea, vomiting, diarrhea and abdominal pain), anorexia, pruritus, rash, fatigue, severe hemolytic anemia, porphyria, anorexia, pruritus, rash, tinnitus, neutropenia, elevated liver enzyme values, arrhythmia, conjunctivitis, eosinophilia, leukocytosis, neutropenia, thrombocytopenia, cardiac conduction disorder, hepatic disorder, hypochromia, increase risk of infection, lymphadenopathy, rhinorrhea, seizures, splenomegaly, stomatitis, and fatigue.

DRUG INTERACTIONS

- CYP3A4 Inhibitors: Use cautiously due to potential for QT prolongation.
- Drugs which caused prolonged QT interval (Mefloquine, Quinine and Halofantrine): If used immediately before treatment, monitor for decreased efficacy of the combination (artemether and lumefantrine) and encourage food consumption.
- Hormonal Contraceptives: Effectiveness may be reduced; use an additional method of birth control.
- Anti-Retroviral: Use cautiously due to potential for QT prolongation, loss of anti-viral efficacy, or loss of antimalarial efficacy of the combination (artemether and lumefantrine).
- CYP2D6 Substrates: The combination is also considered contra-indicated in patients taking any drugs that are metabolized by the cytochrome enzyme CYP2D6, particularly those with cardiac effects (including amitriptyline, clomipramine, flecainide, imipramine, and metoprolol).

PREGNANCY & LACTATION

- **Pregnancy:** There are no adequate data from the use of Artemether and Lumefantrine in pregnant women. Artemether and Lumefantrine treatment should only be considered if the expected benefits to the mother outweigh the risk to the fetus.
- **Nursing Mothers:** It should not be given to a nursing woman as it is excreted in the breast milk.
- **Pediatric Use:** Studied in children 2 months of age and older with a bodyweight of 5 kg and greater.
- **Geriatric Use:** Not studied in geriatric patients.
- Patients receiving Artemether & Lumefantrine combination should be warned that dizziness or fatigue/asthenia might occur in which case they should not drive or use machines.

OVERDOSAGE

In cases of suspected over dosage, symptomatic and supportive therapy should be given as appropriate. ECG and electrolytes (e.g. potassium) should be monitored.

DOSAGE AND INSTRUCTIONS

To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION

1. **Artecxin Dispersible Tablets:**
   Alu. Alu. Blister Pack of 2 x 8's.
2. **Artecxin Forte Dispersible Tablets:**
   Alu. Alu. Blister Pack of 2 x 4's.
3. **Artecxin Plus Dispersible Tablets:**
   Alu. Alu. Blister Pack of 2 x 8's.

آرٹیکسِن™

(آرٹیمیتھر + لومیفینٹرین)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
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