Leaflet for Bioart Dispersible Tablet

Date: 20-07-24
Date: 22-07-24
Date: 24-07-24
Date: 29-07-24

Size: 76 x 178 mm

BIOART
(Artemether + Lumefantrine)
20mg / 120mg Tablet

بائیوآرٹ
(آرٹیمیتھر + لومیفینٹرین) ۲۰ ملی گرام + ۱۲۰ ملی گرام

BIOART-DS
(Artemether + Lumefantrine)
40mg / 240mg Tablet

بائیوآرٹ ۔ ڈی ایس
(آرٹیمیتھر + لومیفینٹرین) ۴۰ ملی گرام + ۲۴۰ ملی گرام

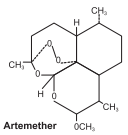
BIOART Forte
(Artemether + Lumefantrine)
80mg / 480mg Tablet

بائیوآرٹ ۔فورٹ
(آرٹیمیتھر + لومیفینٹرین) ۸۰ ملی گرام + ۴۸۰ ملی گرام

DESCRIPTION:
BIOART is a new treatment of malaria. It is the fixed combination of Artemether (Methyl-ether derivative of Artemisinin) & Lumefantrine (fluorene derivative belonging to aminoalcohol class).

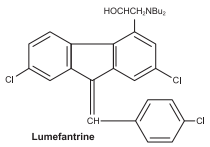
Chemical Structure

Artemether molecular formula is $C_{16}H_{26}O_5$ and the structural formula is:



Artemether

Lumefantrine molecular formula is $C_{30}H_{32}Cl_3NO$ and the structural formula is:



Lumefantrine

COMPOSITION:
BIOART Dispersible Tablets:
Each Dispersible Tablet Contains:
Artemether 20mg
Lumefantrine 120mg
(Product Complies with Shrooq's Specs.)

BIOART DS Dispersible Tablets:
Each Dispersible Tablet Contains:
Artemether 40mg
Lumefantrine 240mg
(Product Complies with Shrooq's Specs.)

BIOART FORTE Dispersible Tablets:
Each Dispersible Tablet Contains:
Artemether 80mg
Lumefantrine 480mg
(Product Complies with Shrooq's Specs.)

CLINICAL PHARMACOLOGY:
Mechanism of Action:
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 hemoglobin breakdown, to the nontoxic hemozoin, malarial pigment. Lumefantrine is thought to interfere with the polymerization 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. The antimalarial activity of the combination of lumefantrine and artemether is greater than that of either substance alone.

PHARMACOKINETICS:
Absorption: Artemether is absorbed fairly rapidly with peak plasma concentrations reaching 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 6-8 hours after dosing. Food enhances the absorption of both Artemether+Lumefantrine. In order to improve bioavailability patients should be encouraged to take the drug with food. **Distribution:** Artemether and Lumefantrine are both highly bound to human serum proteins in vitro (95.4% and 99.7%, respectively). The artemisinin metabolite dihydroartemisinin is also bound to human serum proteins (47% - 76%). **Metabolism:** Artemether is rapidly and extensively metabolized (substantial first pass metabolism) by human liver microsomal enzyme mainly by CYP3A4/5 to the biologically active metabolite dihydroartemisinin. Lumefantrine is N-butylated, mainly by CYP3A4 in human liver microsomes. **Elimination:** Artemether and dihydroartemisinin are rapidly cleared from plasma with an elimination half-life of 2 hours. Lumefantrine is eliminated very slowly with a terminal half-life of 2-3 days in healthy person and 4-6 days in patients with falciparum malaria.

INDICATIONS:
BIOART is indicated for treatment of adults and children with acute, uncomplicated infections due to Plasmodium falciparum or mixed infections including P. falciparum. It is effective against drug sensitive and drug-resistant strains of P. falciparum. It is also recommended for malaria infection acquired in areas where the parasites may be resistant to other antimalarials.

DOSAGE & ADMINISTRATION:
Patients with acute malaria are frequently averse to food. The dose may be encouraged to resume normal eating as soon as food can be tolerated since this improves absorption of artemether and lumefantrine. In the event of vomiting within 1 hour of administration a repeat dose should be taken. 6-dose regimen should be given for 3 days as oral treatment 1st dose at the time of initial diagnosis & than at 8, 24, 36, 48, 60hrs.

BIOART (Artemether+Lumefantrine) should be taken with food or milk.

	Dosage – Body Weight	
BIOART Tablets 20/120	05kg to 14kg	1 BID for 3-Days
BIOART DS Tablets 40/240	15kg to 24kg	1 BID for 3-Days
	25kg to 34kg	1.5 BID for 3-Days
BIOART Forte Tablets 80/480	Adults & Over 35kg	1 BID for 3-Days

SPECIAL POPULATIONS:
Infants weighing less than 5 kg
The safety and efficacy have not been established in infants weighing less than 5kg and no dosing recommendations can be made.

Geriatric patients (65 years or above)
There is no information suggesting that the dosage in patients over 65 years of age should be different than in younger adults.

Renal impairment
No specific studies have been carried out in this group of patients. There was no significant renal excretion of lumefantrine, artemether and dihydroartemisinin (DHA) in studies conducted in healthy volunteers

and clinical experience is limited. No dose adjustment in patients with renal impairment is recommended.

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 should be exercised in dosing patients with severe hepatic impairment (see section WARNINGS AND PRECAUTIONS). Most patients with acute malaria present with some degree of related hepatic impairment. The adverse event profile did not differ in patients with and those without hepatic impairment. Moreover, baseline abnormalities in liver function tests improved in nearly all patients after treatment.

CONTRAINDICATIONS AND PRECAUTIONS:

Hypersensitivity: Hypersensitivity to any of the ingredients or the excipients; patients with severe malaria according to WHO specifications; patients with a family history of prolongation of the QT interval or sudden death or cardiac arrhythmias or severe cardiac disease; patients with known history of electrolyte imbalance; patients taking drugs metabolized by the cytochrome enzyme CYP2D6; Patients taking drugs that are known to prolong the QT interval such as antiarrhythmics of classes IA and III, neuroleptics.

Adverse Reactions: Artemether+Lumefantrine is generally well tolerated. Many of the adverse experiences are due to the disease rather than to drug itself.

Very Common: Palpitations, headache, dizziness, abdominal pain, anorexia, vomiting, nausea, arthralgia, mylagia, asthenia, fatigue and sleep disorders.

Common: Amnesia, paraesthesia, diarrhea, pruritus, rash, cough, electrocardiogram QT prolongation, gait disturbances and insomia.

Uncommon: Liver function test increased, clonus, hypoesthesia and ataxia and somnolence.

Rare: Hypersensitivity

DRUG INTERACTIONS:

Interaction with other antimalarials

Mefloquine: Pre-treatment with mefloquine has no effect on plasma concentrations of artemether or the artemether/dihydroartemisinin ratio but there was a significant reduction in plasma levels of lumefantrine. Patients should be encouraged to eat at dosing times to compensate for the decrease in bioavailability.

Quinine: Infusion of quinine alone caused a transient prolongation of the QTc interval, which was consistent with its known cardiotoxicity. Thus, prior administration of Artemether+Lumefantrine combination appears to enhance the inherent risk of QTc prolongation from IV quinine.

Interaction with CYP450 3A4 inhibitors (Ketoconazole): The concurrent oral administration of ketoconazole with Artemether+Lumefantrine combination led to a modest increase (< 2-fold) in artemether, DHA, and lumefantrine exposure in healthy subjects. Dose adjustment ofArtemether + Lumefantrine is considered unnecessary in falciparum malaria patients when administered in association with ketoconazole or other potent CYP3A4 inhibitors.

Halofantrine: In vitro studies indicated that lumefantrine metabolism is inhibited by halofantrine. In patients previously treated with halofantrine, Artemether+Lumefantrine combination should be dosed at least one month after the last halofantrine dose.

PREGNANCY:

During the second and third trimester, treatment with Artemether+Lumefantrine combination tablets should only be considered if the expected benefit to the mother outweighs the risk to the fetus.

NURSING MOTHERS:

Due to the long elimination half-life of lumefantrine (4 to 6 days), it is recommended that breast-feeding should not resume until at least one week after the last dose of artemether and lumefantrine combination unless potential benefits to the mother and child outweigh the risks of artemether + lumefantrine combination treatment.

OVERDOSAGE:

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

PRESENTATION:

BIOART 20/120mg Dispersible Tablets are available in Alu-Alu Blister pack of 16's.

BIOART DS 40/240 Dispersible Tablets are available in Alu-Alu Blister pack of 8's.

BIOART Forte 80/480 Dispersible Tablets are available in Alu-Alu Blister pack of 6's.

How to use Dispersible Tablets: Dissolve each tablet in half glass of plain water & drink.

Dosage:

As directed by the physician.

INSTRUCTIONS:

Store at 25°C (excursions permitted between 15°C-30°C).
Protect from direct sunlight & moisture.
Keep all medicines out of the reach of children.
To be sold on prescription of a Registered Medical Practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں۔ (درجہ حرارت کی حد ۱۵ تا ۳۰ ڈگری سینٹی گریڈ ہے)
دھوپ اور نمی سے بچائیں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔ تفصیلی معلومات کے لئے ڈبے میں موجود پرچہ کا مطالعہ کریں۔

Manufactured By:
SHROOQ PHARMACEUTICALS (PVT) LTD.
21-Km. Feroz Pur Road, Lahore-Pakistan.

Marketed By:
CENRJY Pharmaceuticals