®

ULTIMARPLUS SUSPENSION

(Artemether 180mg + Lumefantrine 1080 mg Suspension)

COMPOSITION:
One bottle of 60 ml for reconstitution containing Artemether 180 mg and Lumefantrine 1080 mg.

INDICATIONS:

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ULTIMARPLUS Suspension an artemisinin-based combination therapy (ACT) is indicated for the treatment of malaria in children caused by all forms of plasmodium including severe malaria caused by multiple drug resistant strains of P. Falciparum.

DOSAGE AND ADMINISTRATION:

Body weight/kg	**DAILY DOSE (ML)**					
	1ST DAY		**2ND DAY**		**3RD DAY**	
	0 hr	8 hrs	24 hrs	36 hrs	48hrs	60 hrs
5kg to less than 15kg (6 months – 3 years)	7 ml	7ml	7ml	7ml	7ml	7ml
15kg to less than 25kg (4 years – 8 years)	13 ml	13ml	13ml	13ml	13ml	13ml

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ULTIMARPLUS suspension is designed for use in children up to 15 kg.
To make up the suspension take the following steps:
- Open the bottle after breaking the seal and add purified water up to the 60 ml mark on the bottle.
- Shake the bottle very well until a uniform suspension is achieved. It may be necessary to make up the volume to 60 ml by adding a little more water. This suspension is stable for 14 days.

To administer shake the bottle first before following the dose indicated in table above. Generally, 4 mg artemether/kg body weight in combination with lumefantrine is administered once daily on 3 consecutive days and each daily dose should be administered in one go. Vomiting within 1 hour requires repeating the dose.A full course therapy of 3 days is important in order to avoid recrudescence.

PHARMACOLOGICAL PROPERTIES:

PHARMACOKINETICS: Artemether administered orally is absorbed rapidly reaching therapeutic levels within 60-90 minutes. Peak plasma concentration is achieved in about 2 hours after dosing.Artemether is rapidly and extensively metabolised in the liver to the biologically active main metabolite dihydroartemisinin.Artemether and dihydroartemisinin are bound to human plasma protein and this binding is linear.The elimination of artemether and dihydroartemisinin from plasma is rapid with an elimination half-life of about 2 hours.
Lumefantrine (a highly lipophilic compound) absorption starts after a lag-time of about 2 hours with peak plasma concentration in about 6 to 8 hours after administration.Lumefantrine is

eliminated very slowly with a terminal half-life of 2 to 3 days in healthy individuals and 4 to 6 days in patients with falciparum malaria.
Food enhances the absorption of both artemether and lumefantrine therefore patients are encouraged to take the medication with fatty food if possible.
PHARMACODYNAMICS: ULTIMARPLUS suspension act as blood schizontocides and is associated with more rapid gametocyte clearance. Its site of antiparasitic effect is the food vacuole of the malaria parasite, where it is thought to interfere with the conversion of haem, a toxic intermediate produced during haemoglobin breakdown, to the non-toxic haemozin 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.Ultimarplus has a secondary action involving inhibition of nucleic acid and protein synthesis within the malaria parasite. Data from in-vitro and in-vivo studies show that Ultimarplus did not induce resistance.

CONTRAINDICATIONS:
Ultimarplus suspension is formulated specifically for paediatric use therefore there are no strict contra-indications for the use of artemether in children.Utimarplus suspension is contraindicated in individuals hypersensitive to any of the ingredients. Patients who are taking drugs known to prolong the QT interval such as certain antibiotics (macrolides, fluoroquinolones, and imidazole) or family history of cardiac arrhythmias are advised to be cautious.

DRUG INTERACTIONS:
No particular detrimental drug-drug interaction was observed. However since grapefruit juice inhibits the metabolism of some antimalarias it is not advisable to drink grapefruit juice while taking Ultimarplus.

SIDE EFFECTS/ADVERSE REACTIONS:
Ultimarplus suspension is well tolerated by infants and children. Patients previously treated with antimalarials which can influence the ECG pattern e.g. halofantrine and quinine, should be given a reasonable period of time before starting treatment with Ultimarplus suspension.
Common side effects which may occur include: dizziness, anorexia, nausea, vomiting, diarrhoea, coughing, and rashes.

PRECAUTIONS/WARNINGS:
Ultimarplus suspension is not recommended for prophylaxis. Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

STORAGE:
Ultimarplus bottles for suspension should be stored below 30ºC away from light and humidity. Powders for suspension are stable for two years if kept in a closed bottle. Ultimarplus suspension should not be used after the date marked "EXP" on the pack.
Keep out of reach and sight of children.