ARTEMETRIN® TABLET

Each tablet contains:
Artemether 80mg
Lumefantrine 480mg
Excipients.... q.s.

PROPERTIES
Artemether is the most active derivate of the Artemisinines, a new class of antimalarial drugs derived from Artemisinin. The latter compound is extracted from the artemisia annua and Artemether is prepared semi-synthetically.
Lumefantrine is a synthetic aryl amino alcohol similar to mefloquine and halofantrine.

INDICATIONS:
Artemetrin(R) Tablet is indicated for the treatment of malaria, caused by all forms of plasmodium including severe malaria, caused by multiple drug resistant strains of p. Falciparum.

PHARMACOLOGICAL PROPERTIES:
Pharmacodynamics:
Artemetrin(R) has its own action site in the malarial parasite. The presence of the new endoperioxide bridge in Artemether (generating single oxygen and free radicals: which are very cytotoxic to the plasmodia) appears to be essential for anti-malaria acitivity.
Morphological changes of the parasitic membranes included by Artemether have been described, being the result of free-radical action.
Lumefantrine interferes more in the polymerization processes.
Other in vitro test suggest that both causes marked diminution of nucleic acid synthesis.
Inhibition of protein synthesis as the basic mechanism of action is suggested in studies which showed morphological changes in ribosom as well as in the ensoplasmic reticulum.
Although Artemether acts essentially as a blood schizonticide, Artemetrine did clear Gametocides in comprarative clinical trials.

PHARMACOKINETICS:
Orally administered Artemether is rapidly absorbed reaching therapentic levels in 60-90 minutes. Artemether is metabolized in the liver to the demethylated derivate Ditydroatemisinin (DHA). The elimination is rapid, with a T½ of about 2 - 4 hours. Dihydroartemisinin, being a potent antimalarial itself, has a T½ of about 24 hours.
The degree of binding of Artemether to plasmaprotein in man is about 50%.
Radioactivity distribution of Artemether as found to be equal between cells and plasma.
The absorption of lumefantrine is highly influenced by lipids and food intake (from 10% by fasting to 100% at normal diet) therefore patients should be encouraged to take the medication with some fatty food as soon as it can be tolerated. Lumefantrine is N-debutylated in human liver microsomes. The metabolite has 5 to 8 fold higher antiparasitic effects than lumefantrine. Lumefantrine is found to be highly protein bound (95%). The elimination half life in malaria attested patients will be 4 to 6 days. Lumefantrine and its metabolities are found in bile and faeces.

PHARMACEUTICAL PRECAUTIONS AND CONTRA-INDICATIONS:
Artemether is contraindicated in individuals hypersensitive to Artemether and lumefantrine. Therefore, there are no strict contra- indications for the use of Artemether in children. Nevertheless, no correlation has been found between QtC interval prolongation and plasma concentrations of lumefantrine. Caution is advised for patients who are taking drugs that are known to prolong the QTC interval, such as certain antibiotics (macrolides, fluoroquinolones, imidazole) or who are predisposed to cardiac arrhythmias. It is advisable not to use drugs during pregnancy for mother and foetus, the physician may consider it essential (as in case of cerebral malaria) to treat a pregnant woman. Artemisinin derivatives (Like Artemether) are the fastest acting schizontocides and rapid clearance of parasites essential. Since Artemetrin(R) has been designed for use in children it is unlikely that this problem will arise Artemetrin(R) should not be taken during breast - feeding. Due to the long elimination half-life of lumefantrine, it is recommended that breast -feeding should not start until at least one week after stopping an Artemether /lumefantrine combination therapy.

DRUG INTERACTIONS:
Specific negative drug-drug interactions were not seen. Artemether potentiates the antimalarial activity of other antimalarials.
As grapefruit juice retards the metabolism of some antimalarials, it would be better not drink grapefruit juice while taking Artemetrin.(R)

SIDE EFFECTS:
with Artemether virtually no side effect have been seen. Laboratory abnormalities such as slight rise in transaminases and a decrease in reticulocyte count are rare and transient. A lowering of sinus frequency without causing EGG changes has been noticed. At high doses transient abdominal pain, tinnites and diarrhoea have been described but a causal relationship is unclear. Some antimalarials such as halofantrine and quinine can influence the EGG pattern. Attention should be made to patients previously treated with these antimalarials. A reasonable period should be taken into account before starting treatment with lumefantrine combinations. For these patients physicians will prescribe Artemisinin derivatives in mono therapy in case of several paludism. Sometimes it is possible that a common side effect such as rash could occur. Report this to your doctor. Other common side effects may occur such as trouble of sleeping, nausea, vomiting, diarrheoa, coughing. These need medical attention when persistent.

RESISTANCE AND RECRUDESCENCE:
Resistance of plasmodia to artemether has not been observed. It is also unlikely to occur in view of the specific mechanism of action which is very cytotoxic for plasmodia (opening of a peroxide bridge). An apparent resistance is sometimes seen but is mainly due to multiple broods of plasmodia developing at different times in the same patient. It controlled studies recrudescence does not exceed 10%. In case of recrudescence (renal or apparent) a new complete treatment for three days is advisable.
DOSAGE: One tablet to be taken twice daily for three days. As for adult.

ARTEMETRIN (R)

Weight in kg	Total Tablet	REGIME DE DOSAGE					
		Day -1		Day -2		Day -3	
		0 hr	8 hr	24hr	36hr	48hr	60hr
Adult	6	1	1	1	1	1	1

BREASTFEEDING: Data on excretion in breast milk are not available for humans.

SHELF LIFE: 2 Years from the date of manufacturing.

DISPENSING CATEGORY: Prescription only medicine.

PRESENTATIONS:
ARTEMETRIN (R) 80 / 480 Each packet contains blisters of 1 x 6 tablets.

Storage condition: store below 30°c

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