Arenax Plus® Forte

Artemether 80 mg + Lumefantrine 480 mg

swipha
swiss pharma nigeria Ltd.

COMPOSITION
Each Tablet contains:
Artemether - 80 mg
Lumefantrine - 480 mg

INDICATIONS AND USE
Arenax Plus® Forte is a fixed combination of artemether and lumefantrine which acts as a blood schizonticide. It is indicated for treatment of adults with 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.

CLINICAL PHARMACOLOGY
The site of antiparasitic action of both components is the food vacuole of the malaria parasite where they are thought to interfere with the conversion of haem, a toxic intermediate produced during haemoglobin breakdown, to the non-toxic malaria pigment (haemozoin).
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 secondary action involving inhibition of nucleic acid and protein synthesis within the malarial parasite. The antimalarial activity of the combination of lumefantrine and artemether in Arenax Plus® Forte is greater than that of either substance alone.

Artemether is rapidly absorbed with peak plasma concentrations reached about 2 hours after dosing. The absorption of lumefantrine starts after a lag-time of up to 2 hours with peak plasma concentration about 6 to 8 hours after administration. A high- fat meal enhances the absorption of both artemether and lumefantrine.
Artemether is rapidly and extensively metabolised. Human liver microsomes metabolize artemether to the biologically active main metabolite dihydroartemisinin (by demethylation) predominantly through the enzyme CYP3A4/5. Lumefantrine is N-debutylated mainly by CYP3A4, in human liver microsomes.
Artemether undergoes extensive first-pass metabolism and is mainly eliminated by the liver. It has an elimination half life of 2 hours whereas, lumefantrine which is also eliminated by metabolism has a half-life of 4-6 days in patients infected with *falciparum* malaria.

CONTRAINDICATIONS
Arenax Plus® Forte is contraindicated in patients with hypersensitivity to artemether, lumefantrine or to any excipients of Arenax Plus® Forte.
Patients with a family history of congenital prolongation of the QTc interval or sudden death or with any other clinical condition known to prolong the QTc interval such as patients with a history of systemic cardiac arrhythmias, with clinically relevant bradycardia or with severe cardiac disease. Patients with known disturbances of electrolyte balance e. g hypokalaemia or hypomagnesaemia. Patients taking any drug which is metabolised by the cytochrome enzyme CYP2D6 (e.g flecainide, metoprolol, imipramine, amitriptyline, clomipramine).

Patients taking drugs that are known to prolong the QTc interval such as antiarrhythmics of classes IA and III, neuroleptics, antidepressive agents, certain antibiotics including some agents of the following classes: macrolides, fluoroquinolones, imidazole and triazole antifungal agents, certain non-sedating antihistamines (terfenadine, astemizole), cisapride.

INTERACTIONS
Data on safety and efficacy are limited and Arenax Plus® Forte should therefore not be given concurrently with other antimalarials unless there is no other treatment option.
The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with Arenax Plus® Forte.
In patients previously treated with halofantrine, Arenax Plus® Forte should not be administered earlier than one month after the last halofantrine dose.

PREGNANCY AND LACTATION
Pregnancy
The safe use of artemether and lumefantrine during pregnancy has not been established. Reproductive toxicity studies in rats and rabbits have shown no evidence of teratogenicity for the combination or for the individual components, lumefantrine and artemether, though artemisinins are known to be embryotoxic in animals.
Artemether/Lumefantrine was not embryotoxic in rats at doses of $\leq$ 25 mg/kg; however artemether alone showed materno-feto and embryotoxicity at doses $\geq$ 10mg/kg in rats and $\leq$ 30mg/kg in rabbits.
It is advisable not to use drugs during pregnancy but in view of the high risk of malaria during pregnancy for mother and foetus, the responsible physician may consider it essential, as in the case of cerebral malaria, to treat a pregnant woman.

Artemisinin derivatives like artemether are the fastest acting schizonticides and rapid clearance of parasites is essential.
Arenax Plus® Forte treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus.

Lactation
Animal data suggest excretion into breast milk but no data are available in humans. Breast feeding women should not take Arenax Plus® Forte due to the long elimination half-life of lumefantrine (4 to 6 days) . Itis recommended that breast feeding should not resume before day 28 unless potential benefits to mother and child outweigh the risk of Arenax Plus® Forte treatment.

SPECIAL WARNINGS AND PRECAUTIONS
Dizziness or fatigue/asthenia might occur in patients receiving Arenax Plus® Forte. Arenax Plus® Forte has not been studied for efficacy and safety in patients with severe hepatic or renal insufficiency and therefore no recommendations can be made for these group of patients.

MEDICINE: KEEP OUT OF REACH OF CHILDREN

Arenax Plus® Forte has not been evaluated for prophylaxis and is therefore not indicated.
Arenax Plus® Forte has not been evaluated for the treatment of Cerebral malaria or other severe manifestations of complicated malaria including pulmonary oedema or renal failure.
Arenax Plus® Forte is not indicated for and has not been evaluated in the treatment of malaria due to *P.vivax*, *P.malariae* or *P. ovale*, although some patients in clinical studies have co-infection with *P. falciparum* and *P. vivax* at baseline.
Arenax Plus® Forte is active against blood stages of *Plasmodium vivax*, but is not active against hypnozoites. Therefore, sequential treatment with primaquine should be used to achieve hypnozoite eradication in cases of co-infection with *Plasmodium vivax*.
Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.

ADVERSE REACTIONS
Arenax Plus® Forte is generally very well tolerated by adults,with most adverse events being of mild to moderate severity and duration. Many of the reported events are likely to be related to the underlying malaria and/or to an unsatisfactory response to the treatment rather than to Arenax Plus® Forte.

DOSAGE AND ADMINISTRATION
This regimen is recommended for adults of body weight above 34kg or more than 14 years of age.

Days	Day 1		Day 2		Day 3	
Time	Start	8 hours Later	Morning	Evening	Morning	Evening
Number of Tablets	1	1	1	1	1	1

STORAGE CONDITION
Store below 30°C.
Protect from moisture and light.
This medicine should always be kept in its original package.

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