SUMMARY OF PRODUCT CHARACTERISTICS
ATHEMAX (α-β ARTEETHER INJECTION 150 MG/2ML)

1. NAME OF THE MEDICINAL PRODUCT:

ATHEMAX (α-β ARTEETHER INJECTION 150 MG/2ML)

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

COMPOSITION:

Each 2 ml contains:

α, β Arteether	150 mg
Ethyl oleate BP	Q.S.

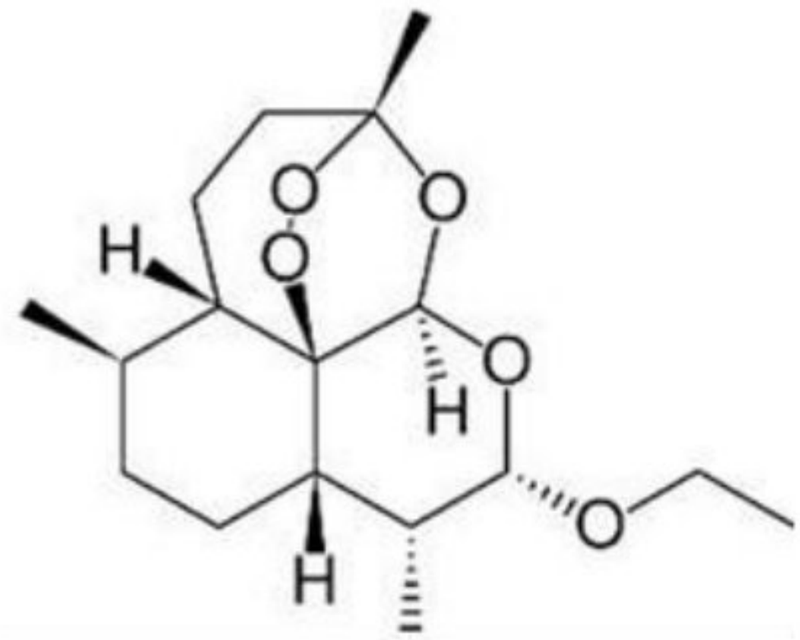
CHEMICAL NAME AND THE STRUCTURAL FORMULA OF EACH ACTIVE INGREDIENT:-

α, β ARTEETHER

Chemical Name:

(3R,5aS,6R,8aS,9R,10S,12R,12aR)-10-ethoxydecahydro- 3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin

Chemical Structure:



Molecular Formula: $C_{17}H_{28}O_5$

Molecular Weight: 312.40 gm/mol

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NAME AND QUANTITY OF EACH INGREDIENT:

UNIT DOSE

Ingredients	Qty./ ml In mg	Use/Function
Active Ingredient		
α, β Arteether I.H.S.	75.00	Anti-malarial
In Active Ingredients		
Ethyl oleate BP	1.1 ml	Vehicle
Benzyl alcohol BP	0.04 ml	Preservative
Tocopheryl acetate BP	Q.S.	To improve absorption

Reference:
BP = British Pharmacopoeia
IHS = In-house specification

3. PHARMACEUTICAL FORMS:
Light yellow coloured clear solution

CLINICAL PARTICULARS:

4. INDICATIONS FOR USE:

ATHEMAX is indicated for use in Sever P. falciparum malaria including cerebral malaria and as a second line treatment in chloroquine resistant malaria. No cross resistance detected with chloroquine.

5. CONTRAINDICATIONS:
α, β arteether injection is contraindicated in patients hypersensitive to artemisinin derivatives.

6. SPECIAL PRECAUTIONS FOR USE:
The product must be used only via the intramuscular route. The use of tuberculin syringes is recommended for administration, particularly in young children.

The loading dose should be equally divided and injected anteriorly into both thighs with each subsequent dose injected into alternating thighs.

The use of α, β Arteether for the treatment of severe malaria in patients with pre-existing renal or liver failure has not been studied.

7. ADVERSE EFFECTS
Neurotoxicity is the common side effect associated with all artemisinin compounds in high doses.

Neurotoxicity in manifests as gait disturbances, loss of spinal cord pain responses, incoordination, respiratory depression, convulsions and cardio respiratory arrest.

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Other side effects are Nausea, dizziness and depressed GIT activity. Clinical, neurological, electro-cardiographic and biochemical abnormality were seen.

In the multicentric trails of α, β Arteether involving 478 patients suffering from P. falciparum malaria, no significant side effects were observed.

8. USES DURING PREGNANCY, LACTATION:

Pregnancy

Since no clinical data is available for the use of α, β Arteether during pregnancy, it should be used with caution in pregnant women, if the potential benefitis justify the potential risk to the foetus.

Nursing Mother

It is not known whether α, β Arteether is excreted in human milk, because many drugs are excreted in human milk caution should be exercised while using α, β Arteether.

9. DRUG INTERACTIONS:

Does not interfere with the action of other commonly used drugs for treatment of P. falciparum malaria eg. Quinine and can be administered along with these drugs for the treatment of severe form of malaria.
(Except for other Artemisinin derivatives like Artesunate and Artemether).

10. DOSAGES AND ADMINISTRATION:

α / β arteether is for intramuscular use only

Adult – 150 mg i.e. 1 ampoule of α, β arteether once daily for 3 consecutive days or as directed by the physician.

Children - 3mg/Kg per day administered by intramuscular injection over a 3-day period or as directed by the physician.

The injection must be given under aseptic conditions, deep intramuscularly in the upper external quadrant of the buttock. No other drug should be mixed in the same syringe.

11. OVERDOSAGES:

The pre-clinical studies of α, β Arteether have shown that LD50 value is more than 1000 mg/kg, whereas the maximum dose injected in adult is about 2.5 mg/kg per day. This confirms that the safety window for the dose administered is very wide. Hence this study concludes that α, β Arteether is well tolerate even when overdose is administered.

12. PHARMACOLOGY:

α, β arteether is a fast acting blood schizonticidal agent for P. falciparum malaria at the erythrocytic stage.

α, β arteether is concentrated in parasitized erythrocytes. The functional group responsible for antimalarial activity of α / β arteether is endoperoxide bridge. Iron from the digested haemoglobin of the parasite's victim reduces this bridge, releasing a highly reactive free radical iron oxo species which causes lysis of the parasitic cell.

Lysis of parasitic cell membrane occurs. Damage includes swelling and deformity of food vacuoles membrane, nuclear membrane, endoplasmic reticulum and formation of autophagic vacuoles.

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It is also proposed that α / β arteether inhibits the protein synthesis and alters the ribosomal organization and endoplasmic reticulum.

α, β Arteether also acts on the membranes of the parasites through lipid peroxidation.

13. PHARMACOKINETICS:

Main metabolite of α, β Arteether is dihydroartemisinin. The half-life of dihydroartemisinin is more than 20 hours. The elimination of the drug is through hepatic metabolism and gets eliminated at a low rate as compared to other artemisinin derivatives.

After intramuscular injection, drugs are released slowly into the systemic circulation. Peak plasma concentrations are generally attained between 3-12 hrs. following drug administration. The plasma elimination half- life is determined by the slow release from the injection site and varies dependent on muscle tone and activity. It is generally around 20-24 hrs.
The steady state area under the curve (AUC) (over 24 hours after the last dose) increases linearly with dose.
There are no indications for gender differences in the pharmacokinetics of α, β Arteether.

Prior to excretion, the majority of α, β Arteether is metabolized. The most important route is an oxidative dealkylation by CYP3A4 to dihydroartemisinin and the biliary excretion of glucronidated dihydroartemisinin with the faeces. A minor part (20-30%) may be excreted in the urine as dihydroartemisinin glucoronidine. Since dihydroartemisinin has a short half-life of only a few hours, the temporal pattern of its plasma concentration is probably determined by its rate of formation from the parent compound.

14. STORAGE:

Store in a cool place below 25°c protect from light.

Do not use later than the date of expiry.
KEEP OUT OF REACH OF CHILDREN.

15. SHELF-LIFE:

30 MONTHS

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