LINZ

For Medical Professionals only

Herme Tablet

(Artemether + Lumefantrine)

HermeDS Tablet

(Artemether + Lumefantrine)

HermeFlash Tablet

(Artemether + Lumefantrine)

Herme Injection 80mg

(Artemether)

Description:

Herme provides an important addition to the armamentarium against malaria in the form of a safe and effective combination therapy. To date, it is the only fixed dose artemisinin-based combination therapy (ACT) combining artemether,an artemisinin derivative, and lumefantrine, a synthetic antimalarial drug. Artemisinin is a compound derived from the sweet wormwood plant and has been used for centuries in traditional Chinese medicine to treat fever.

Composition:

Herme Tablets: Each tablet contains:

Artemether M.S..... 20 mg, Lumefantrine U.S.P. .....120 mg.

Herme DS Tablets: Each tablet contains:

Artemether M.S..... 40 mg, Lumefantrine U.S.P. .....240 mg.

Herme Flash Tablets: Each dispersible tablet contains:

Artemether M.S..... 20 mg, Lumefantrine U.S.P. .....120 mg.

Herme Injection 80mg: Each ml contains:

Artemether M.S..... 80mg.

Pharmacodynamics:

Herme has a fixed ratio of 1:6 parts of Artemether and Lumefantrine, respectively. The antiparasitic action of both components is the site of food vacuole of the malarial parasites, where they are thought to interfere with the conversion of haem, a toxic intermediate produced during hemoglobin breakdown, to the non-toxic haemozoin, malaria 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.

Pharmacokinetics:

Absorption

Artemether is absorbed fairly rapidly with peak plasma concentrations reached 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 to 8 hours after administration. Food enhances the absorption of both Artemether and Lumefantrine: in healthy volunteers the relative bioavailability of Artemether was increased more than two-fold and that of Lumefantrine sixteen-fold compared with fasted conditions when **Herme** was taken after a high-fat meal. The food interaction data indicate that

absorption of Lumefantrine under fasted conditions is very poor (assuming 100 % absorption after a high-fat meal, the amount absorbed under fasted conditions would be <10% of the dose). Patients should therefore be encouraged to take the medication with a normal diet as soon as food can be tolerated.

Distribution

Artemether and Lumefantrine are both highly protein bound (95.4% and 99.7%, respectively). Dihydroartemisinin is also bound to human serum proteins (47% to 76%). Protein binding to human plasma protein is linear.

Metabolism

Artemether is rapidly and extensively metabolized by human liver microsomes (mostly through the enzyme CYP3A4/5) to the biologically active main metabolite - dihydroartemisinin. Lumefantrine is also metabolized predominantly by the enzyme CYP3A4 in human liver microsomes.

Elimination and excretion

Artemether was rapidly cleared from plasma with an elimination half-life of approximately 2 hours. Lumefantrine is cleared more slowly with an elimination half-life of approximately 2-3 days in healthy patients, and 4-6 days in patients with *falciparum* malaria.

In healthy volunteers, neither Lumefantrine nor Artemether was found in urine after administration of **Herme**, and urinary excretion of DHA amounted to less than 0.01% of the Artemether dose.

Indications:

Herme is indicated for the treatment of:

1) Standby emergency treatment of adults, children and infants with acute, uncomplicated infections due to *Plasmodium falciparum* or mixed infections including *Plasmodium falciparum*.

2) Because **Herme** is effective against both drug-sensitive and drug-resistant *P. falciparum*. it is also recommended for malaria infections acquired in areas where the parasites may be resistant to other antimalarials.

Contraindications:

Herme (as other Artemether + Lumefantrine combination) is contraindicated in:

· Patients with hypersensitivity to Artemether, Lumefantrine or to any of the excipients.

· Patients with severe malaria including cerebral malaria, or malaria with pulmonary edema or renal failure.

· First trimester of pregnancy. During the second and third trimester, treatment should only be considered if the expected benefit to the mother overweighs the risk to the foetus.

· During breast-feeding.

· 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 symptomatic 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 metabolized by the cytochrome enzyme CYP2D6 (e.g. flecainide, metoprolol, imipramine, amitriptyline, clomipramine).

Side effects:

Following clinical studies, the following adverse effects were reported:

Gastrointestinal (abdominal pain, anorexia, nausea, vomiting, diarrhea) and of the central nervous system (headache, dizziness and sleep disturbance). There is no evidence of serious or persistent neurotoxicity. However, a few patients presented with symptoms such as abnormal gait (4 patients), nystagmus (1 adult), ataxia (3 adults), decreased hearing (4 adults) and paraesthesia (15 adults). Pruritus and rash were reported by less than 2% of patients. Over 90% of the reported adverse events, which could also have been attributed to malaria, were rated mild to moderate in intensity. Artemether+Lumefantrine combination did not lead to any clinical relevant alterations of the laboratory parameters.

Precautions:

Administration of Artemether + Lumefantrine with drugs that are metabolized by the cytochrome enzyme CYP2D6 (e.g. flecainide, metoprolol, imipramine, amitriptyline, clomipramine) should be avoided. Co-administration of Artemether + Lumefantrine should be with caution in patients taking drugs that are known to prolong the QTc interval such as anti-arrhythmic of class IA and III, neuroleptics, antidepressant agents, certain antibiotics including same agents of macrolides. Pregnant women (especially during 1st trimester) and nursing mother should not be prescribed Artemether + Lumefantrine.

Overdosage:

In case of suspected over dosage, symptomatic and supportive therapy should be given as appropriate.

Dosage & administration:

For adults and children following dosing schedule should be adopted, depending on their weights:

Herme Tablet 20/120 mg

Body weight (kg)	0 hrs	After 8-12 hrs	After 12 hrs	After 12 hrs	After 12 hrs	After 12 hrs
<15	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.

HermeDS Tablet 40/240 mg

Body weight (kg)	0 hrs	After 8-12 hrs	After 12 hrs	After 12 hrs	After 12 hrs	After 12 hrs
15-24	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.
25-34	1 1/2 Tabs.	1 1/2 Tabs.	1 1/2 Tabs.	1 1/2 Tabs.	1 1/2 Tabs.	1 1/2 Tabs.
>34	2 Tabs.	2 Tabs.	2 Tabs.	2 Tabs.	2 Tabs.	2 Tabs.

HermeFlash Tablet 20/120 mg

Body weight (kg)	0 hrs	After 8-12 hrs	After 12 hrs	After 12 hrs	After 12 hrs	After 12 hrs
<15	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.	1 Tab.

Herme Injection:

In severe malaria for adult usual starting dose is 2 ampoules of 80mg given i.m on day 1, followed by 1 ampoule of 80mg for 2nd to 5th day. Herme injection for children, 3.2 mg/kg by the intramuscular route as a loading dose on the first day, followed by 1.6mg/kg for 2nd to 5th day.

W.H.O Recommendation 2006:"The regimen can be expressed more simply for ease of use at the program level as follows: the second dose on the first day should be given any time between 8h to 12h after the first dose. Dosage on the second and third day is twice a day (morning & evening)."

Treatment in non-immune children and multi-drug resistant areas:

(Most tourists and business travelers, considered to be non-immune):

A thorough 3-day course is recommended for the treatment of non-immune children and in areas of multi-drug-resistant malaria, with 1-4 **Herme** 20/120mg tablets and ½ - 2 of **Herme** DS 40/240mg tablets (depending on bodyweight), given as a single dose at the time of initial diagnosis, again after 8 hours and twice daily on each of the following days (entire course comprises 6, 12, 18 and 24 **Herme** 20/120mg tablets or 3,6,9 or 12 of **Herme** DS 40/240mg tablets depending on bodyweight).

Stand-by emergency treatment:

A thorough 3-day course is recommended for stand-by emergency treatment, with 1-4 **Herme** 20/120mg tablets or ½ -2 **Herme** DS 40/240mg tablets (depending on bodyweight), given as a single dose at the time of start of symptoms, again after 8 hours and then twice daily on each of the following two days (entire course comprises 6, 12, 18 and 24 **Herme** 20/120mg tablets or 3,6,9 or 12 **Herme-DS** 40/240mg tablets depending on bodyweight).

Dosage in hepatic and renal impairment:

No special precautions or dosage adjustments are considered in mild to moderate hepatic or renal impairment. Moreover, the side effect profile did not differ in patients with and those without hepatic impairment. Most patients with acute malaria present with some degree of relative hepatic impairment.

Elderly patients:

No special precautions or dosage adjustments are required.

Presentation:

Herme (Artemether 20mg + Lumefantrine 120mg) tablets are available in Alu-Alu pack of 16's.

Herme-DS (Artemether 40mg + Lumefantrine 240mg) tablets are available in Alu-Alu pack of 8's.

Herme Flash (Artemether M.S. 20mg + Lumefantrine U.S.P. 120mg) tablets are available in Alu-Alu pack of 16's.

Herme Injection (Artemether) 80mg/ml Pack of 5's.

Storage:
Protect from light & moisture, store at room temperature.

Keep out of the reach of children.

WARNING: To be sold on the prescription of registered medical practitioner only.

ہدایات :

روشنی اور نمی سے محفوظ کمرے کے درجہ حرارت میں رکھیں۔

بچوں کی پہنچ سے دُور رکھیں۔

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

انتباہ : صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لئے۔

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ISO 9001:2015 Certified Company