SUMMARY OF PRODUCT CHARACTERISTICS

1.NAME OF THE MEDICINAL PRODUCT

Artemether and Lumefantrine Tablets 80/480 mg
Artemether and Lumefantrine Tablets 20/120mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

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

Each uncoated tablet contains:
Artemether Ph.Int. 20mg
Lumefantrine 120 mg
Excipients.....q.s.

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Artemether and lumefantrine combination therapy is indicated for the treatment of acute uncomplicated malaria caused by Plasmodium falciparum, including malaria acquired in chloroquine-resistant areas. May also be used to treat uncomplicated malaria when the Plasmodium species has not been identified. Indicated for use in adults and children greater than 5 kg.

4.2 Dosage and administration:

TABLETS for oral administration.
To increase absorption, Artemether and lumefantrine should be taken with food or a milky drink. If patients are unable to tolerate food, should be administered, but the systemic exposure may be reduced. Patients who vomit within 1 hour of taking the medication should repeat the dose.
For administration to small children and infants, the tablet/s may be crushed.

Adults and children weighing 35 kg and above(Atemether 80mg and lumefantrine 480mg)
For patients 12 years of age and above and 35 kg body weight and above, a course of treatment comprises six doses of six tablets i.e. total of 6 tablets, given over a period of 60 hours as follows: the first dose of one tablet, given at the time of initial diagnosis, should be followed by five further doses of one tablet given at 8, 24, 36, 48 and 60 hours thereafter.

Adults and children weighing 35 kg and above(Atemether 20mg and lumefantrine 120mg)

For patients 12 years of age and above and 35 kg body weight and above, a course of treatment comprises six doses of four tablets i.e. total of 24 tablets, given over a period of 60 hours as follows: the first dose of four tablets, given at the time of initial diagnosis, should be followed by five further doses of four tablets given at 8, 24, 36, 48 and 60 hours thereafter.

Children and infants weighing 5 kg to less than 35 kg

A six-dose regimen is recommended with 1 to 3 tablets per dose, depending on bodyweight:

5 to less than 15 kg bodyweight: the first dose of one tablet, given at the time of initial diagnosis, should be followed by five further doses of one tablet given at 8, 24, 36, 48 and 60 hours thereafter.

15 to less than 25 kg bodyweight: the first dose of two tablets, given at the time of initial diagnosis, should be followed by five further doses of two tablets given at 8, 24, 36, 48 and 60 hours thereafter.

25 to less than 35 kg bodyweight: the first dose of three tablets, given at the time of initial diagnosis, should be followed by five further doses of three tablets given at 8, 24, 36, 48 and 60 hours thereafter.

4.3 Contraindications:

Artemether/lumefantrine caplet is contraindicated in individuals hypersensitive to artemether and lumefantrine. Therefore, there are no strict contra-indications for the use of Artemether in children.

4.4 Special Warnings and Precautions for Use

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. It is recommended that this drug is only administered if the expected benefits outweigh the potential risks. Artemether/lumefantrine caplet should not be taken during breastfeeding. 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 treatment.

4.5 Interaction with other Medicinal products and other forms of Interaction

Interaction with other antimalarial drugs

Data on safety and efficacy are limited, and Artemether and lumefantrine should therefore not be given concurrently with other antimalarials unless there is no other treatment option.

If Artemether and lumefantrine is given following administration of mefloquine or quinine, close monitoring of food intake (for mefloquine) or of the ECG (for quinine) is advised. The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with Artemether and lumefantrine. In patients previously treated with halofantrine, Artemether and lumefantrine should not be administered earlier than one month after the last halofantrine dose. Mefloquine

A drug interaction study with Artemether and lumefantrine in man involved administration of a 6dose regimen over 60 hours in healthy volunteers which was commenced at 12 hours after completion of a 3-dose regimen of mefloquine or placebo. Plasma mefloquine concentrations from the time of addition of Artemether and lumefantrine were not affected compared with a group which received mefloquine followed by placebo.

Pre-treatment with mefloquine had no effect on plasma concentrations of artemether or the artemether/dihydroartemisinin ratio but there was a significant reduction in plasma levels of lumefantrine, possibly due to lower absorption secondary to a mefloquine-induced decrease in bile production. Patients should be encouraged to eat at dosing times to compensate for the decrease in bioavailability.

Quinine

A drug interaction study in healthy male volunteers showed that the plasma concentrations of lumefantrine and quinine were not affected when i.v. quinine (10 mg/kg BW over 2 hours) was given sequentially 2 hours after the last (sixth) dose of Artemether and lumefantrine (so as to produce concurrent plasma peak levels of lumefantrine and quinine). Plasma concentrations of artemether and dihydroartemisinin (DHA) appeared to be lower. In this study, administration of Artemether and lumefantrine to 14 subjects had no effect on QTc interval. Infusion of quinine alone in 14 other subjects caused a transient prolongation of QTc interval, which was consistent with the known cardiotoxicity of quinine. This effect was slightly, but significantly, greater when quinine was infused after Artemether and lumefantrine in 14 additional subjects. It would thus appear that the inherent risk of QTc prolongation associated with i.v. quinine was enhanced by prior administration of Artemether and lumefantrine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is insufficient data from the use of artemether and lumefantrine in pregnant women. Based on animal data, Artemether and lumefantrine is suspected to cause serious birth defects when administered during the first trimester of pregnancy. Reproductive studies with artemether have shown evidence of post-implantation losses and teratogenicity in rats and rabbits. Other artemisinin derivatives have also demonstrated teratogenic potential with an increased risk during early gestation

Safety data from an observational pregnancy study of approximately 500 pregnant women who were exposed to Artemether and lumefantrine (including a third of patients who were exposed in the first trimester), and published data of another over 500 pregnant women who were exposed to artemether-lumefantrine (including over 50 patients who were exposed in the first trimester), as well as published data of over 1,000 pregnant women who were exposed to artemisinin derivatives, did not show an increase in adverse pregnancy outcomes or teratogenic effects over background rates.

Artemether and lumefantrine treatment must not be used during the first trimester of pregnancy in situations where other suitable and effective antimalarials are available. However, it should not be withheld in life-threatening situations, where no other effective antimalarials are available. During the second and third trimester, treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus. Women of childbearing potential

Women using oral, transdermal patch, or other systemic hormonal contraceptives should be advised to use an additional non-hormonal method of birth control for about one month

Lactation

Animal data suggest excretion into breast milk but no data are available in humans. Women taking Artemether and lumefantrine should not breast-feed during their treatment. Due to the long elimination half-life of lumefantrine (2 to 6 days), it is recommended that breast-feeding should

not resume until at least one week after the last dose of Artemether and lumefantrine unless potential benefits to the mother and child outweigh the risks of treatment.

Fertility

There is no information on the effects of Artemether and lumefantrine on human fertility

4.7 Effects on Ability to Drive and Use Machines:

None

4.8 Undesirable Effects

With Artemether virtually no side effects 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 ECG changes has been noticed. At high doses transient abdominal pain, tinnitus and diarrhea have been described but a causal relationship is unclear. Some antimalarials as halofantrine and quinine can influence the ECG pattern Attention should be made to patients previously treated with those antimalarials. A reasonable period should be taken in account before to start a treatment with lumefantrine combinations. For those patients physicians will be prescribed Artemismin derivatives in mono therapy in cause of severe paludism. Sometimes it could be possible that the following common side effect occur; rash, check this with you doctor. Other common side effects may occur as trouble of sleeping, nausea, vomiting, diarrhea, coughing. They need medical attention when persisting.

4.9 Overdose

In cases of suspected over dosage symptomatic and supportive therapy should be given as appropriate, which should include ECG and blood potassium monitoring.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: antimalarials, blood schizontocide, ATC code: P01 BF01.

Pharmacodynamic effects

Artemether and lumefantrine comprises a fixed ratio of 1:6 parts of artemether and lumefantrine, respectively. The site of antiparasitic action of both components is the food vacuole of the malarial parasite, where they are thought to interfere with the conversion of haem, a toxic intermediate produced during haemoglobin breakdown, to the nontoxic haemozoin, 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. Both artemether and lumefantrine have a secondary action involving inhibition of nucleic acid- and protein synthesis within the malarial parasite.

Treatment of Acute Uncomplicated P. falciparum Malaria

The efficacy of Artemether and lumefantrine Tablets was evaluated for the treatment of acute, uncomplicated malaria (defined as symptomatic P. falciparum malaria without signs and symptoms of severe malaria or evidence of vital organ dysfunction) in five 6-dose regimen studies and one study comparing the 6-dose regimen with the 4-dose regimen. Baseline parasite density ranged from 500/μL - 200,000/μL (0.01% to 4% parasitemia) in the majority of patients. Studies

were conducted in otherwise healthy, partially immune or non-immune adults and children (≥5kg body weight) with uncomplicated malaria in Thailand, sub-Saharan Africa, Europe, and South America.

Efficacy endpoints consisted of:

- 28-day cure rate, proportion of patients with clearance of asexual parasites within 7 days without recrudescence by day 28
- parasite clearance time (PCT), defined as time from first dose until first total and continued disappearance of asexual parasite which continues for a further 48 hours
- fever clearance time (FCT), defined as time from first dose until the first time body temperaturefell below 37.5°C and remained below 37.5°C for at least a further 48 hours (only for patients with temperature >37.5°C at baseline)

5.3 Preclinical safety data

There is no preclinical data available that is of relevance to the prescriber

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS:

Artemether Ph. Int., Lumefantrine IHS, Microcrystalline Cellulose BP, Maize Starch BP, Starch paste BP, Sodium lauryl Sulphate BP, Sodium Starch Glycolate BP, Colloidal Silicon Dioxide BP, Magnesium Stearate BP, Purified Water BP, Hypromellose BP,Isopropyl Alcohol BP, Methylene Dichloride BP,Titanium Dioxide BP, Purified Talc BP, Polyetheylne Glycol 6000 BP, Iron Oxide Yellow Lake, Quinoline Yellow Lake IH

6.2 Shelf Life

36 Months

6.3 Special Precautions for Storage

Protect from light.

6.4 Nature and Contents of Container

1 X 6 TABLETS ALU - PVC BLISTER PACK

1X24 TABLETS ALU-PVC BLISTER PACK

6.5 Special Precautions for Disposal and Other Handling

No special requirements

7. MARKETING AUTHORISATION HOLDER

SMART WAY PHARMA LTD

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AGUDA, LAGOS.