SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

INN Name: Amodiaquine and Artesunate Granules

Trade mark name : ANATE（Children）

2. Qualitative and quantitative composition

Each Amodiaquine Granules contains Amodiaquine base 150mg and each Artesunate Granules contains Artesunate 50mg

3. Pharmaceutical form

Granules

4. Clinical particulars

4.1 Therapeutic indications

It is indicated for treatment of uncomplicated malarial attacks, including multi drug resistant strains of P.falciparum.

4.2 Posology and method of administration

Under one year-Each paediatric sachet containing Artesunate 25mg and Amodiaquine base 75mg should be dissolved in 10ml clean water and taken daily for 3 days.

1-6 years-Each childer sachet containing Artesunate 50mg and Amodiaquine Hydrochloride base 150mg should be dissolved in 30 ml clean water and taken daily for 3 days.

7-13 years- One tablet of each white tablet(Artesunate 100mg) and one tablet of each yellow tablet (Amodiaquine hydrochloride equivalent to Amodiaquine base 300mg)daily for 3 days.

14 years and above- One tablet of each white tablet(Artesunate 100mg) and one tablet of each yellow tablet (Amodiaquine hydrochloride equivalent to Amodiaquine base 300mg) in the morning and evening daily for 3 days.

4.3 Contraindication

Linking to Amodiaquine: ANATE must not be used in the following cases namely: hypersensitivity to one of the constituents, history of fever disease or blood impairment during an anterior treatment with amodiaquine and retinopathy (in the event of frequent treatment). Do not use this medicine during the pregnancy and the lactation.

Linking to Artesunate: For now no recorded contraindication is reported, however, this drug must not be used in case of hypersensitivity to one of the constituents.

4.4 Special warnings and precautions for use

Do not exceed the recommended dose without seeking further medical advise.

Keep this medicine out of the reach of children.

4.5 Interaction with other medical products and other forms of interaction
None known.

4.6 Pregnancy and lactation

Use in Pregnancy: Use of the product is not recommended during the organogenesis period except if, in the doctor is opinion, the benefits outweigh the risks as seen with cerebral malaris. Administration of the drug during the first trimester must be avoided.
Breast-feeding: Artesunate is not known to cross into maternal milk.

4.7 Effects on ability to drive and use machines

There have been no reports of negative drug interactions to date. For the combination with Amodiaquine Hydrochloride, these was a significant improvement of the cure rates at different stages of the clinical tests.

4.8 Undesirable effects

Undesirable effects of Artesunate are generally rare at the therapeutic recommended dose. In rare cases, however, slight changes to haematology values have been seen, including a reduction in the number of reticulocytes as well as a slight increase in transaminase. These signs, however, do not generally give rise to any noticeable clinical

manifestations. In rare cases, a slight but transient reduction in sinus heats has been observed. Abdominal cramps and mild diarrhoea have been reported at elevated doses.

Since amodiaquine may concentrate in the liver, the drug should be used with caution in patients with hepatic diseases or alcoholism, and patients receiving hepatotoxic drugs.

After the intake of Amodiaquine neurological effects such as lethargy and drowsiness have been reported at therapeutic doses. Also patients can experience involuntary movements.

Patients with hypersensitivity to Amodiaquine can develop hepatitis. Nausea, vomiting and diarrhoea have also been reported. Ina number of case it has been seen that Amodiaquine causes agranulocytosis and other blood dyscrasias.

4.9 Overdose

You should stop the treament and consult immediately a doctor or a pharmacist in case of headache, dizziness, visual diaturbances, convulsion. These symptoms usua indicate an overdosage.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Artesunate The plasma concentration-time curve when Artesunate was given orally to human beings followed a one-compartment open model. The mean time to peak was 53 minutes, peak level was 1.94Ч g/ml and the elimination half-life t½ß was 41.33 minutes.

The plasma concentration-time curve when Artesunate was given i.v. followed a two compartment model. The mean last phase elimination half-life was 38 minutes.

Excretion in the urine reached a maximum after 30-60minutes .

Amodiaquine readily absorbed from the GI tract and is rapidly converted in the liver to the active metabolite desethylamodiaquine.

5.2 Pharmacokinetic properties

Blood Concentration: After an oral dose of 10mg/kg, plasma concentrations of 300-560 ng/ml are attained in 4 hours; therapeutic concentrations are attained 1-2 hours after dosing.

Distribution: Widely distributed throughout the tissues; high concentrations are found in the liver, spleen, kidneys, and lungs with smaller amounts in the brain and cerebrospinal fluid; in the blood, higher concentrations are found in red cells than in the plasma.

Excretion: Slowly excreted in the urine but the rate may be increased if the urinary pH is decreased.

For interchangeable multi-source pharmaceutical products (generics), bioequivalence data shall be required. 2 This shall include a comparative study with the innovator product.

5.3 Preclinical safety data

Particulars referring to the tests which have been performed on animals/humans regarding the efficiency of the drug and the purpose(s) for which it will be promoted, with special reference to the dosage and method of administration (pharmacological trial)

Clinical evaluation of therapeutic regimens is required to validate clinical efficacy of this promising drug (Oduola et al 1998). Artemisinin has a quick onset of action thereby, stoping the parasites from developing and cytoadherence is not reached. Drug disposition of Artemisinin after oral administration has been determined, using a one-compartment model with separate pharmacokinetic estimates for children and adults. The population estimates for Artemisinin clearance and distribution volume, respectively, were 432 Lh-1 and 1600 L for adults and 14.4 Lh-1 kg-1 and 37.9 Lkg-1 for children, with an inter-subject variability (collectively for both age groups) of 45% and 104%, respectively. The oral bioavailability was estimated to decrease from Day 1 to Day 5 by a factor of 6.9, a value found to be similar for children and adults (Sidhu et al. 1998). Half-lives of Artemisinin is 4hrs, artesunate, 45 min and artemether, 4-11 hrs (Batty et al 1998). Findings like this have advocated the dosing of Artemisinin to children according to bodyweight and to adults according to a standard dose.

6. Pharmaceutical particulars

6.1 List of excipients

Powdered sugar, Carboxymethyl starch sodium , Disodium Edetate, Acesulfame Po tassium, 95% Ethanol, Purified Water, Pulverous Orange flavor, Aspartame.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not exceed the expired date indicated on the outside packaging. Keep it in the original packed and store below 30°C.

6.5 Nature and contents of container

PET/LDPE laminating film bag
(3+3) link-sachet/box, 240boxes/carton.

6.6 Special precautions for disposal and other handing

If a reaction suggesting sensitivity or severe irritation occurs, use of the medication should be discontinued. If the degree of local irritation warrants, patients should be directed to use the medication less frequently, to discontinue use temporarily, or to discontinue use altogether. ANATE should not come into contact with the eyes, mouth, nostrils or mucous membranes. If product enters the eye, wash immediately with warm water.

7. Registrant

Applicant: ARSTRA PHARMA LTD

Address: No 1 Adesoye Street Mende, Maryland， Lagos, Nigeria.

E-mail: arstrapharma@gmail.com

Contact person : Henry hudoka

Tel: +234 803 308 1835

8. Manufacturer

Manufacturer name: Front Pharmaceutical PLC

Physical address: Xuancheng Economic and Technical Development Zone, Anhui, China

Tel: 86-0563-2625199

Fax: 86-0563-2625199

E-mail: export@frontpharma.com

9. Date of revision of the text

July 2021

10. DOSIMETRY (IF APPLICABLE)

N/A

11. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

N/A