SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Combipack of Artesunate for Injection 60 mg, Sodium Bicarbonate Injection BP 5.0% w/v & Sodium Chloride Injection BP 0.9% w/v

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative Declaration

Each Combipack contains:

(A) One vial of Artesunate for Injection

Each vial Contains:

Artesunate (Sterile) ..... 60 mg

(B) One ampoule of 1 ml Sodium Bicarbonate Injection BP .... % w/v

(C) One ampoule of 5 ml Sodium Chloride Injection BP..... 0.9% w/v.

2.2 Quantitative Declaration

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dry powder for injection

Appearance: White to off white colour powder.

Distribution Category: POM.

4. CLINICAL PARTICULARS

4.1 Indications

Artesunate for Injection 60 mg is indicated for the treatment of severe malaria caused by Plasmodium falciparum, in adults and children.

4.2 Posology and Method of Administration

Adults and children:

Artesunate injection is administered at a dose of 2.4 mg of artesunate/kg body weight, by intravenous (I.V.) or intramuscular (I.M.) injection, at 0, 12 and 24 hours, then once daily until oral treatment can be substituted.

Administration:

The powder for injection is difficult to dissolve and care should be taken to ensure that it is completely dissolved before parenteral administration.

The formulation should be used immediately after reconstitution. If the solution is cloudy or precipitate is present, the parenteral solution should be discarded. Do not use water for injection for reconstitution of the artesunate powder or for dilution of the resulting solution prior to injection.

For Artesunate for Injection 60 mg

The powder for injection should be reconstituted with 1 ml of sodium bicarbonate 5.0% w/v, shake vigorously till the solution becomes clear.

Appearance After Reconstitution: A clear Solution.

For I.V. Use: Add 5 ml of sodium chloride 0.9% w/v and mix again to prepare final concentration of 10 mg/ml for I.V. use. The required amount of drug for I.V. use should be administered slowly over a period of 2-3 minutes.

For I.M. Use: Add 2 ml of sodium chloride 0.9% w/v and mix again to prepare final concentration of 20 mg/ml for I.M. use.

4.3 Contraindications

It is contraindicated in patients with hypersensitivity to artesunate or other artemisinin derivatives.

4.4 Special Warnings and Special Precautions for Use

Non-falciparum malaria:

Artesunate has not been evaluated in the treatment of severe malaria due to Plasmodium vivax, Plasmodium malariae or Plasmodium ovale.

In cerebral malaria and complicated malaria, general supporting therapy is usually required.

Renal/hepatic impairment:

Dose adjustment is not necessary in patients with hepatic or renal impairment.

Pregnancy:

There has been limited clinical experience with the use of artesunate in pregnancy. In animal studies, artesunate has been associated with foetal toxicity during the first trimester of pregnancy. To date, clinical data regarding safety in the first trimester have not indicated an increased risk of foetal harm. Treatment with artesunate should not be withheld during the first trimester if it is potentially life-saving for the mother.

Lactation:

The active metabolite of artesunate is excreted at low levels in breast milk. The drug levels are not expected to cause any adverse effects in breastfed infants. The amount of drug present in breast milk does not protect the infant from malaria.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Few clinical drug-drug interaction studies have been performed; however, no clinically significant interactions have been identified.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: There has been limited clinical experience with the use of artesunate in pregnancy. In animal studies, artesunate has been associated with foetal toxicity during the first trimester of pregnancy. To date, clinical data regarding safety in the first trimester have not indicated an increased risk of foetal harm. Treatment with artesunate should not be withheld during the first trimester if it is potentially life-saving for the mother.

Lactation: The active metabolite of artesunate is excreted at low levels in breast milk. The drug levels are not expected to cause any adverse effects in breastfed infants. The amount of drug present in breast milk does not protect the infant from malaria.

4.7 Effects on Ability to Drive and Use Machines

Patients receiving Artesunate for injection should be warned that dizziness may occur, in which case they should not drive or use machines.

4.8 Undesirable Effects

Blood and lymphatic systems disorders: Neutropenia and anaemia (both occasionally severe), thrombocytopenia, pure red cell aplasia, post-treatment anaemia, mild and transient decrease in reticulocyte count.

Nervous system disorders: Dizziness, light-headedness, headache, insomnia, tinnitus, peripheral neuropathy.

Respiratory disorders: Cough, nasal symptoms.

Gastrointestinal disorders: Altered taste, nausea, vomiting, abdominal pain or cramps, diarrhoea, raised serum amylase, pancreatitis.

Hepatobiliary disorders: Transient rises in liver transaminases (AST, ALT), hepatitis.

Skin and subcutaneous tissue disorders: Rash, alopecia.

Musculoskeletal and connective tissue disorders: Arthralgia, muscle disorders.

General disorders and administration site conditions: Fatigue, malaise, fever, pain at injection site.

Immune system disorders: Hypersensitivity.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Health care professionals are asked to report any suspected adverse reactions via the https://pv.pharmacyboardkenya.org

4.9 Overdose

Experience of acute overdose with artesunate is limited. The overdose of artesunate is associated with pancytopenia, melena, seizures, multiorgan failure and death. Treatment of overdose should consist of general supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group: Anti-Malarial

ATC Code: P01BE03

Artesunate is a hemisuccinate derivative of dihydroartemisinin, which is itself formed by the reduction of artemisinin. The mechanism of action of the artemisinins likely involves cleavage of the internal endoperoxide bridge through reaction with haeme within the infected erythrocyte, thereby generating free radicals which alkylate vital parasite proteins. However, artemisinins have also been reported to inhibit an essential parasite calcium adenosine triphosphatase.

The artemisinins are distinguished from other antimalarials by their ability to kill all erythrocytic stages of the malaria parasite, including the relatively inactive ring stage and late schizonts, as well as the gametocytes responsible for malaria transmission. Artesunate and the artemisinins are the most rapid acting of the antimalarials, and they have also been shown to enhance splenic clearance of infected erythrocytes by reducing cytoadherence.

5.2 Pharmacokinetic Properties

Absorption: After intravenous injection artesunate is very rapidly biotransformed to its active metabolite, dihydroartemisinin (DHA). Consequently, artesunate half-life (t½) is estimated to be less than 5 minutes. Artesunate is rapidly absorbed following intramuscular injection, and peak plasma levels are generally achieved within 30 minutes of administration.

Distribution: Dihydroartemisinin (DHA) has been shown to substantially accumulate in P. falciparum infected erythrocytes. Plasma protein binding of dihydroartemisinin is determined to be 93% in patients and 88% in healthy volunteers.

Metabolism and Elimination: Artesunate is extensively and rapidly hydrolysed by plasma esterases, with possible minimal contribution by CYP2A6. The main metabolite, dihydroartemisinin, accounts for most of the in vivo antimalarial activity of IV administration. DHA is further metabolized in the liver via glucuronidation and is excreted in the urine; α-dihydroartemisinin-β-glucuronide has been identified as the major urinary product in patients with falciparum malaria.

5.3 Preclinical Safety Data

Not Applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium Bicarbonate, Sodium Chloride, Water for Injection.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months.

6.4 Special Precautions for Storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and Contents of Container

7.5 ml clear glass USP type-I vial having 20 mm grey butyl rubber stopper & 20 mm blue F/O seal. Such one vial is packed in a printed blister pack with 1 ml sodium bicarbonate injection & 5 ml sodium chloride injection; such one blister is packed in a printed carton with packaging insert.

6.6 Special Precautions for Disposal and Other Handling

The powder for injection should be reconstituted with 1 ml of sodium bicarbonate 5.0% w/v, shake vigorously till the solution becomes clear. Appearance After Reconstitution: A clear Solution.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

7.1 Name and Address of Marketing Authorisation Holder

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Tal.-Kalol,

Dist.- Gandhinagar, Gujarat State, India.

Telephone no.: +91-079-41078096

Email: hiren@lincolnpharma.com

Website: www.lincolnpharma.com

8. MARKETING AUTHORISATION NUMBER

H2019/CTD3920/1486ER

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

29.08.2019

10. DATE OF REVISION OF THE TEXT

February 2024