SUMMARY OF PRODUCT CHARACTERISTICS

1.1 (Invented) Name of the medicinal product

AFRICEF SB

1.2 Strength

Ceftriaxone & Sulbactam for Injection 1.5 gm

Each vial contains:

Ceftriaxone Sodium USP equivalent to Ceftriaxone....1000 mg

Sulbactam Sodium USP equivalent to Sulbactam.....500 mg

1.3 Pharmaceutical Form

Dry Powder for Injection

2. Qualitative and Quantitative Formula

Batch Size: (30.00 Kg)

3. Pharmaceutical form

A white to off white crystalline powder

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Infections caused by pathogens sensitive to Ceftriaxone Injection, e.g.:

- sepsis
- meningitis
- abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts)
- infections of the bones, joints, soft tissue, skin and of wounds
- infections in patients with impaired defence mechanisms
- renal and urinary tract infections
- respiratory tract infections, particularly pneumonia, and ear, nose and throat infections
- genital infections, including gonorrhoea.

Perioperative prophylaxis of infections.

For pre-operative prophylaxis of surgical site infections.

Posology and method of administration:

The recommended adult dosage is 1.5 g (1 g Ceftriaxone as the sodium salt plus 0.5 g sulbactam as the sodium salt) to 3 g (2 g Ceftriaxone as the sodium salt plus 1 g sulbactam as the sodium salt) every six hours. This 1.5 to 3 g range represents the total of Ceftriaxone content plus the sulbactam content and corresponds to a range of 1 g Ceftriaxone /0.5 g sulbactam to 2 g Ceftriaxone /1 g sulbactam. The total dose of sulbactam should not exceed 4 grams per day.

Neonates, infants and children up to 12 years

The following dosage schedules are recommended for once daily administration. Neonates (up to 14 days): 20 to 50 mg/kg bodyweight once daily. The daily dose should not exceed 50 mg/kg. It is not necessary to differentiate between premature and term infants. Infants and children (15 days to 12 years): 20 to 80 mg/kg once daily. For children with bodyweights of 50 kg or more, the usual adult dosage should be used. Intravenous doses of NLT 50 mg/kg bodyweight should be given by infusion over at least 30 minutes.

Method of administration

Ceftriaxone & Sulbactam for injection can be administered by both I.V & I.M route.

4.3 Contraindications:

Ceftriaxone Injection is contraindicated in patients with known hypersensitivity to cephalosporin antibiotics. In patients hypersensitive to penicillin, consider the possibility of allergic cross-reactions.

The use of sulbactam is contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins.

4.4 Special warnings and precautions for use:

Warnings Serious or occasionally fatal anaphylactic reactions have been reported in patients receiving beta-lactam antibiotics. These reactions are more likely to occur in individuals with a history of hypersensitivity reactions to multiple allergens. Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad spectrum antibiotics), therefore it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use. General Transient elevations of BUN and serum creatinine have been observed, at recommended doses, the nephrotoxic potential of ceftriaxone is same as other cephalosporins. Since Ceftriaxone is excreted both via renal and bile patients with renal failure normally require no adjustment in dosage when usual doses of Ceftriaxone are

administered. Dosage adjustments are not necessary in patients with hepatic dysfunction; however in patients with both renal failure and hepatic dysfunction, dosage should not exceed more than 2 g daily with close monitoring of serum concentrations.

4.5 Interaction with other medicinal products and other forms of interaction

No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diurectics.

Ceftriaxone and chloramphenicol have been shown to be antagonistic in in vitro studies.

In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals.

Coombs test may show false-positive results during Ceftriaxone therapy.

4.8 Adverse Drug Reactions

Gastrointestinal: Diarrhoea, nausea & vomiting (less frequent), stomatitis, and glossitis.

Hepatic: Elevations of SGOT/SGPT.

Hematological: Eosinophilia, thrombocytopenia, leukopenia, granulocytopenia, hematoma or bleeding. Hemolytic anemia is observed less frequently.

Agranulocytosis (< 500/mm3) has been reported occasionally at a total cumulative dose exceeding 20 g.

Skin reactions: Exanthema, allergic dermatitis, pruritis, urticaria, edema, erythema multiforme. Other side effects such as headache, dizziness, increase in serum creatinine, mycosis of the genital tract, oliguria, fever, and shivering have been observed.

Anaphylactic shock may occur which requires immediate counter-measures.

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group

Ceftriaxone: Antibiotic

Sulbactam Sodium: Beta Lactamase inhibitor

ATC code

Ceftriaxone Sodium: J01DD04

Sulbactam Sodium: J01CG01

Mode of action:

The bactericidal activity is due to the Ceftriaxone component and the ability of Ceftriaxone to interfere with the biosynthesis of the peptidoglycan component of the bacterial cell wall by binding to and inactivating penicillin-binding proteins(PBPs). Ceftriaxone induces filamentation in Escherichia coli and Pseudomonas aeruginosa, it binds primarily to PBP 3 which is responsible for formation of cross-wall or septum of dividing bacilli. Ceftriaxone has a high degree of stability against the beta-lactamases, both penicillinases and cephalosporinases produced by both gram -ve and gram +ve bacteria but not against chromosomally and plasmid mediated ESBL's produced by some strains of Klebsiella, Escherichia coli, Enterobacter spp and Serratia spp.

Sulbactam irreversibly blocks the destruction of beta-lactam ring of Ceftriaxone by these wide variety of ESBLs and chromosomally mediated beta-lactamases by attaching to these enzymes and acting as a suicide substrate that forms a stable intermediate, rendering the enzyme inactive. Sulbactam is a broader-spectrum beta-lactamase inhibitor. Sulbactam does not induce chromosomal beta-lactamases like clavulanic acid, nor does it select for derepressed beta- lactamase-producing bacteria. Thus the full potential of Ceftriaxone against Klebsiella, pseudomonas, Eschericia coli spp is restored by addition of Sulbatam.

5.2 Pharmacokinetic properties

Following intramuscular administration, peak serum concentrations of Ceftriaxone and Sulbactam are seen between 15 minutes to 2 hrs. The maximum plasma conc of Ceftriaxone after a single IM dsoe of 1.0 g is about 81mg/L and is reached 2-3 hrs after the dose while that of Sulbactam sodium is 6-24 mg/L and is reached approximately 1 hr after the dose. Hence effective amount of beta-lactamases are destroyed by the time peak concentration of Ceftriaxone is reached allowing full potential of action of Ceftriaxone against ESBL producing Klebsiella, E coli spp.

Serum concentrations have been shown to be proportional to the amount of dose administered. The area under curve (AUC) after IM administration is equivalent to that after IV administration of an equivalent dose, indicating 100% bioavailability of intramuscularly administered Ceftriaxone sodium.

On intravenous administration Ceftriaxone sodium diffuses into the tissue fluid where if given in the recommended doses bactericidal concentrations are maintained for upto 24 hrs. Ceftriaxone is highly bound to human serum protein by about 83-90%.

Distribution

The volume of distribution of Ceftriaxone sodium is 7-12 L and that of Sulbactam is 18-27.6 L. Ceftriaxone sodium penetrates well into the extravascular spaces, tissue fluid and the synovial fluid of inflamed joints. The concentrations in most extracellular foci reach or exceed several times the MIC of most pathogens for at least 24 hours after a single administration. Ceftriaxone sodium reaches therapeutically effective concentrations in patients with bacterial meningitis which are at least ten-fold the MICs of common pathogens such as, Enterobacteriaceae, H.influenzae, Meningococci, Pneumococci and Group B Streptococci. Ceftriaxone crosses placenta and is distributed in the amniotic fluid. It is also distributed in the milk.

Metabolism and excretion

Ceftriaxone is not metabolised in the body and is eliminated unchanged via two pathways, urine and bile. 40-50% of parenterally administered dose is excreted into the urine within 48 hours as active drug. Thus, high concentrations are attained in urine, whatever is not excreted via kidney is excreted through bile. Metabolism of sulbactam is less than 25%. 70-80% of Sulbactam is excreted by the kidney biliary excretion is minimal and. renal excretion is blocked by probenecid. Sulbactam and Ceftriaxone can be removed by hemodialysis. Impaired renal function and Hepatic insufficiency: Ceftriaxone is excreted via both renal and biliary pathways therefore patients with renal failure normally require no adjustments of dose however concentration of the drug should be monitored in such patients and if there is evidence of drug accumulation then dosage adjustments should be made accordingly. Dosage adjustments are not necessary in patients with hepatic dysfunction, however in patients with both hepatic dysfunction and significant renal failure, dosage should not exceed more than 2 gm daily with close monitoring of serum concentrations.

5.3 Preclinical safety data

Clinical studies of the combination of sulbactam plus beta-lactam antibiotics or penicillins have revealed no major hematologic, renal, hepatic, or central nervous system reactions. Diarrhea has not been a major problem after intravenous use. Incidence of side-

effects due to Ceftriaxone is as follows: G.I. effects- 2-3%, cutaneous reactions 1-3%, haemotological 1-2%, miscellaneous

1.5-3%.

6. Pharmaceutical particulars

6.1 List of Excipients

Product is sterile dry powder for injection. Does not contains any added Excipients.

6.2 Incompatibilities

Do not use any other solutions other than those mentioned in "direction for use.

6.3 Shelf life

Unopened – 24 Months

For reconstituted solution, Chemical and Physical in-use stability has been demonstrated for 4 hours at 25°C and for 8 hours at 2-8°C. From a microbiological point of view, once opened, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 8 hours at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Unopened: Do not store above 25°C. Keep the vials in the outer carton.

After reconstitution: Store at 2-8°C.

.

6.5 Nature and contents of container

CEFTRIAXONE & SULBACTAM FOR INJECTION 1.5 is packed in 10 ml transparent glass Vial USP Type III stoppered with grey bromo butyl rubber stopper and sealed with red flip off seal packed in printed carton along with package insert.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

MEDAFRIQ PHARMA LTD

P.O BOX 243-00623, NAIROBI, KENYA

8. MARKETING AUTHORISATION NUMBER(S)

H2022/CTD8289/16073

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17.02.2023

10. DATE OF REVISION OF THE TEXT

17.02.2023