NATIONAL AGENCY FOR FOOD & DRUG ADMINISTRATION & CONTROL (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

Product Name

FRESHBORN CEFTRIAXONE AND SULBACTAM POWDER FOR INJECTION

(Ceftriaxone & Sulbactam for Injection
& Sterilised Water for Injections BP
& Lidocaine injection BP 1%)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

FRESHBORN CEFTRIAXONE AND SULBACTAM POWDER FOR INJECTION
(Ceftriaxone & Sulbactam for Injection & Sterilised Water for Injections BP
& Lidocaine injection BP 1%)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the Medicinal Product

Ceftriaxone & Sulbactam for Injection 1.5 gm

2. Qualitative and Quantitative Composition

Each combipack contains:

1. Each vial contains:
   Sterile Ceftriaxone Sodium USP eq. to anhydrous Ceftriaxone 1 gm
   Sterile Sulbactam Sodium USP equivalent to Sulbactam 500 mg
2. One ampoule of Sterilised Water for Injections BP 10 ml
3. One ampoule of Lidocaine Injection BP 1 % 5 ml

3. Pharmaceutical Form

Dry Injection

4. Clinical Particulars

4.1 Therapeutic indications

Ceftriaxone & Sulbactam for Injection is indicated in infections caused by Ceftriaxone sodium- sensitive pathogens and may be used in the clinical settings in:

- Sepsis
- Meningitis
- Abdominal Infections (e.g. Peritonitis, Infections of the Biliary tract)
- Infections of the Bones, Joints, Soft Tissue, Skin and of Wounds
- Renal and Urinary Tract Infections
- Respiratory Tract infections, particularly Pneumonia, and Ear, Nose and Throat Infections
- Genital infections, including gonorrhea.

Ceftriaxone & Sulbactam for Injection may also be used for Peri-operative Prophylaxis of Infections. A single dose given Preoperatively may reduce chances of Postoperative Infection

4.2 Posology and method of administration

Dosage and Administration

For IM/IV use only.

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

NEONATES, INFANTS AND CHILDREN UPTO 12 YEARS:

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

4.3 Contraindications

Ceftriaxone & Sulbactam for Injection is contraindicated in patients with known allergy to Cephalosporin group of antibiotics. Hypersensitivity to penicillin may pre-dispose the patient to the possibility of allergic cross-reactions.

Pregnancy and lactation:

Reproductive studies on ceftriaxone have been performed in mice and rats at very high doses. No evidence of embryotoxicity, fetotoxicity or teratogenicity was observed. However, in absence of adequate and well- controlled studies in pregnant women, and since reproductive animal studies may not always reflect human response, this drug should be used during pregnancy only if clearly needed. As ceftriaxone is secreted in the breast-milk, albeit at low concentrations, caution should be exercised in nursing mothers.

Mutagenicity/ Carcinogenicity/ Fertility:

In vitro tests show that Ceftriaxone is not mutagenic. No animal studies have been carried out to check the carcinogenic potential of Ceftriaxone. When given at high doses compared to the human clinical dose, Ceftriaxone did not show any adverse effect on fertility in rats.

4.4 Special warning and special precaution for use

The following side effects, reported to occur during Ceftriaxone therapy, may be seen with the combination as well:

- 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/mm^3) 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.

Local reactions:

- Pain, induration, and tenderness may be encountered in a small number of patients.
- Inflammatory reactions in the vein wall may also occur after IV administration. These may be minimized by slow injection, given over 2 to 5 minutes.

4.5 Interaction with other medicinal products and form of interaction

Limited information is available on the acute toxicity of Ceftriaxone & Sulbactam for Injection. Hemodialysis does not remove the drug from system effectively. Hence, the treatment for Ceftriaxone & Sulbactam for Injection overdose is essentially supportive and symptomatic.

No specific antidote is available for the treatment of overdose.

4.6 Pregnancy and lactation

Use in Pregnancy

Category B

Reproductive studies have been performed in mice and rats at doses upto 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity, teratotoxocity or teratogenicity was demonstrated at a dose approximately 3 times the human dose.

In rats in the segment I (fertility and general reproduction) and segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and

lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Use in Lactation:

Low concentrations of ceftriaxone are excreted in human milk. No risk to nursing infants has been reported but caution should be exercised when ceftriaxone is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

During treatment with ceftriaxone, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

None Known

4.9 Overdose

Unabsorbed drugs may be removed by gastric lavage or induced emesis. Treatment should be symptomatic.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ceftriaxone is a broad-spectrum semi-synthetic third-generation cephalosporin with a potent bactericidal activity against a wide range of gram-positive and gram-negative bacteria. Sulbactam is ß– lactamase inhibitor.

ATC code: J01DD54

5.2 Pharmacokinetic properties

A 1.5 g dose of Ceftriaxone & Sulbactam for Injection, 1 g dose of ceftriaxone and 0.5 g sulbactam were given intravenously in a balanced two-ways cross-over study. Serially collected plasma sample was analyzed for ceftriaxone and sulbactam by high performance liquid chromatography (HPLC). The mean peaks of ceftriaxone and sulbactam concentrations in plasma were 152.06+/-6.65 microg/ml and 21.32+/-1.80 microg/ml, respectively and plasma half-lives for ceftriaxone and sulbactam were

5.2+/-0.35 hr and 0.94+/-0.038 hr, respectively. The AUC0-24 for ceftriaxone and sulbactam was 760.16+/-27.68 microg.hr/ml and 20.74+/-2.34 microg.hr/ml, respectively, with elimination rate constant of 0.133+/-0.009 hr(-1) and 0.732+/-0.029 hr(-1), respectively. The kinetics of ceftriaxone and sulbactum did not change in combination as compared to the alone treatment. Also, concentration of the ceftriaxone after 24 hr is higher than the minimum inhibitory concentration (MIC) of the most of the gram positive and gram negative bacteria indicating that one dose in a day is sufficient to treat the disease caused by these organisms.

5.3 Preclinical Studies

There is evidence from animal studies that high doses of ceftriaxone calcium salt led to formation of concrements and precipitates in the gallbladder of dogs and monkeys, which proved to be reversible. Animal studies produced no evidence of toxicity to reproduction and genotoxicity. Carcinogenicity studies on ceftriaxone were not conducted.

6.0 PHARMACEUTICAL EXCIPIENTS

6.1 List of excipients

None

6.2 Incompatibilities

None Known

6.3 Shelf life

36 Months

6.4 Special precaution for storage

Prior to reconstitution: Store below 30°C. Protect from light.

After reconstitution: Reconstitute solution should be stored under refrigeration (2-8°C) & should be used within 48 hours.

6.5 Nature contents of container

Ceftriaxone for Injection USP 1 gm is supplied in 15 ml USP Type III flint glass vial with grey butyl rubber stopper and flip-off aluminium seal. This is the pack that is proposed for marketing the product.

6.6 Instruction for use handling and disposal

Keep out of reach of children.

7. Manufacturer name

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8. Marketing Authority

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