1.3.1 Summary of Product Charecteristics (SmPC)

Attached

1.3.1 Summary of Product Charecteristics (SmPC)

1. Name of the medicinal product

CEFTRAN FORTE-Ceftriaxone 1000mg & Sulbactam 500mg for Injection

2. Qualitative and quantitative composition

Each vial contains:

Ceftriaxone Sodium USP (Sterile)

Equivalent to Ceftriaxone 1000mg

Sulbactam Sodium USP (Sterile)

Equivalent to Sulbactam 500mg

3. Pharmaceutical form

Dry powder for injection

White or almost white powder filled in 20ml type III moulded glass vials with grey butyl rubber stopper. Such vials are sealed with a plain flip off aluminium seal. Such sealed vials are labeled and 1 vial is packed in a carton.

4. Clinical particulars

4.1 Therapeutic indications

Ceftriaxone Sulbactam Injection is a medicine that is used for the treatment of Bacterial infections, Intra-abdominal infections, Gynecological infections, Skin or soft tissue infections, Surgical infections, Surgical site infections and other conditions.

Ceftriaxone Sulbactam Injection contains Ceftriaxone, and Sulbactam as active ingredients.

Ceftriaxone Sulbactam Injection works by preventing destruction antibiotics, from chemicals released from bacteria; inhibiting the bacteria formation;

Ceftriaxone Sulbactam Injection is used for the treatment, control, prevention, & improvement of the following diseases, conditions and symptoms:

- Bacterial infections
- Intraabdominal infections

- Gynecological infections
- Skin or soft tissue infections
- Surgical infections
- Surgical site infections
- Lyme disease
- Typhoid
- Paratyphoid
- Gonorrhea

4.2 Posology and method of administration

Adults:

The usual adult daily dose (in terms of Ceftriaxone) is 1-2 grams given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

Dosage regimen for Ceftriaxone & Sulbactam for Injection should be adjusted in patients with marked decrease in renal function (creatinine clearance of < 30ml/min) and to compensate for reduced clearance less than 15ml/min patient should receive a maximum of 500 mg of sulbactam every 12 hours (maximum dose 1 gram of sulbactam).

Pediatric patients:

For treatment of Skin and Soft tissue infections the recommended total daily dose (in terms of Ceftriaxone) is 50-75mg/kg given once a day or (in equally divided doses twice a day). The total daily dose should not exceed 1 gram.

For treatment of acute bacterial otitis media: A single intramuscular dose of 50 mg/kg (not to exceed 1gram) is recommended.

In treatment of Meningitis: The initial therapeutic dose in terms of Ceftriaxone should be 100 mg/kg (not to exceed 4 grams).

Daily dose may be administered once a day or in equally divided doses 12 hourly. The usual duration of therapy is 7-14 days.

For treatment of serious infections other than meningitis: Recommended total daily dose in terms of Ceftriaxone is 50-75 mg/kg given in divided doses every 12 hours. The total daily dose (in terms of Ceftriaxone) should not exceed more than 2 grams.

4.3 Contraindications

Hypersensitivity to Ceftriaxone Sulbactam Injection is a contraindication. In addition, Ceftriaxone Sulbactam Injection should not be used if you have the following conditions:

- Asthma
- Clostridium difficile bacterial infection
- Diabetes
- Hyperbilirubinemic infants
- Hypersensitivity
- Hypersensitivity to cephalosporins
- Kidney or gastrointestinal disease
- Neonates requiring IV solutions that contain calcium
- Pseudomembranous colitis
- Runny nose due to allergy
- Seizures associated with this drug

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.

Precautions:

General:

Transient elevations of 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

If you use other drugs or over the counter products at the same time, the effects of Ceftriaxone Sulbactam Injection may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that you doctor can help you prevent or manage drug interactions. Ceftriaxone Sulbactam Injection may interact with the following drugs and products:

- Allopurinol
- Calcium
- Chloramphenicol
- Probenecid
- Tetracyclines

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are no well controlled studies in pregnant women.

So, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers:

Low concentrations of Ceftriaxone are excreted in human milk. No risks to nursing infants have been reported but caution should be exercised when Ceftriaxone and Sulbactam is administered to nursing women.

Paediatric use:

Ceftriaxone & Sulbactam for Injection should not be administered to hyper-bilirubinemic neonates, especially premature.

4.7 Effects on ability to drive and use machines

If you experience drowsiness, dizziness, hypotension or a headache as side-effects when using Ceftriaxone & Sulbactam for Injection medicine then it may not be safe to drive a vehicle or operate heavy machinery. One should not drive a vehicle if using the medicine makes you drowsy, dizzy or lowers your blood-pressure extensively.

4.8 Undesirable effects

The following is a list of possible side-effects that may occur from all constituting ingredients of Ceftriaxone & Sulbactam for Injection. This is not a comprehensive list. These side-effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Diarrhea
- Pain at site of injection
- Rash
- Inflammation of a vein caused by a blood clots
- Injection site reactions
- Itchiness
- Fever
- Leukopenia
- Nausea
- Headache

4.9 Overdose

Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of Ceftriaxone & Sulbactam for Injection, please go to the emergency department of the closest hospital or nursing home. Bring a medicine box, container, or label with you to help doctors with necessary information.

Do not give your medicines to other people even if you know that they have the same condition or it seems that they may have similar conditions. This may lead to overdosage. Please consult your physician or pharmacist or product package for more information.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The bactericidal activity of Ceftriaxone & Sulbactam for Injection 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 the 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.

5.2 Pharmacokinetic properties

Absorption:

Ceftriaxone & Sulbactam for Injection can be administered IM or IV. Following intramuscular administration, peak serum concentrations of Ceftriaxone and Sulbactam are seen between 15 minutes to 2 hrs. The maximum plasma concentration of Ceftriaxone

after a single IM dose 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:

Ceftriaxone is highly bound to human serum protein by about 83-90% and that of Sulbactam is 38%. 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, Pneumococcus 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 metabolized 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%. Sulbactam is excreted by the kidney app 70-80%. Biliary excretion is minimal.
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

There are no preclinical safety data of relevance to the prescriber that are additional to those included in other sections.

6. Pharmaceutical particulars

6.1 List of excipients

None

6.2 Incompatibilities

Not available.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not Store above 30°C. Protect from light.

6.5 Nature and contents of container

White or almost white powder filled in 20ml type III moulded glass vial with grey butyl rubber stopper. Such vials are sealed with a plain flip off aluminium seal. Such sealed vials are labeled and 1 vial is packed in a carton.

6.6 Special precautions for disposal and other handling

For single use only. Discard any unused contents.

7. Applicant/Manufacturer

Manufactured in India by:

Innova Captab Ltd.

1281/1, Hilltop Industrial Estate, Near EPIP, Phase -1,

Jharmajri, Baddi, Distt. Soaln (H.P.) India

Marketed by:

Standard Generics Limited

No 7 Agbor Close,Off Osolo Way,

Ajao Estate, Isolo, Lagos, Nigeria