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Ceftriaxone & Sulbactam for Injection

WIAXONE®-SB

विएक्सोन–एसबी

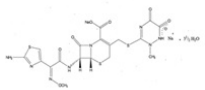
Composition :
Each vial contains:
Ceftriaxone Sodium (Sterile) IP
Eq. to Anhydrous Ceftriaxone 1000 mg
Sulbactam Sodium (Sterile) IP
Eq. to Anhydrous Sulbactam 500 mg

This pack also contains one FFS ampoule of Sterile Water for Injections I.P. 10 ml.

PROPERTIES:

Ceftriaxone Sodium

Ceftriaxone is a 2-aminothiazolyl methyoxylimino third-generation cephalosporin derivative. Ceftriaxone, a bactericidal antimicrobial, inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). Its emperical formula is $C_{18}H_{16}N_8Na_2O_7S_3.3\frac{1}{2}H_2O$ and molecular weight is 661.6. Structural formula is as shown:



Sulbactam Sodium

As Sulbactam also binds with some penicillin-binding proteins, sensitive strains are also often rendered more susceptible to Sulbactam/Ceftriaxone than to Ceftriaxone alone. The combination of Sulbactam and Ceftriaxone is active against all organisms sensitive to ceftriaxone. Its emperical formula is $C_8H_{10}NNaO_5S$ and molecular weight is 255.22. Structural formula is as shown:

CLINICAL PHARMACOLOGY:

Pharmacodynamics

Pharmacotherapeutic group: Third generation cephalosporins;
ATC code: J01DD54.
Ceftriaxone Sulbactam Injection improves the patient's condition by performing the following functions:
Preventing destruction of antibiotics, from chemicals released from bacteria Inhibiting the bacterial cell wall synthesis.

Mechanism of action

Ceftriaxone is a 2-aminothiazolyl methyoxylimino third-generation cephalosporin derivative. Ceftriaxone, a bactericidal antimicrobial, inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). These proteins are associated with the bacterial cell membrane and probably serve in synthesis. The result is the formation of a defective cell wall that is osmotically unstable. Bacterial species have a unique set of PBPs. The affinity pattern of ceftriaxone for the PBPs for different bacterial species affects the drug's antimicrobial spectrum of activity. It is also felt that cephalosporins, as well as penicillins, may increase the breakdown of the cell wall of the bacteria by decreasing the availability of an inhibitor of murein hydrolase, an enzyme involved in cell division. If unimposed, this enzyme can destroy the integrity of the cell wall. Sulbactam does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. As Sulbactam also binds with some penicillin-binding proteins, sensitive strains are also often rendered more susceptible to Sulbactam/Ceftriaxone than to Ceftriaxone alone. The combination of Sulbactam and Ceftriaxone is active against all organisms sensitive to ceftriaxone.

Pharmacokinetics

Absorption:

Ceftriaxone: 98% bound to plasma proteins; crosses the blood brain barrier. After 500 mg IV Sulbactam are 21-40 mcg/ml and 48-88 mcg/ml respetively.

Metabolism and Excretion:

Ceftriaxone: Elimination half-life is about 8.7 hours; 33-67% removed as unchanged drug. About 75-85% of Sulbactam is excreted in the urine during the first eight hours of administration.

INDICATIONS:

Infections caused by pathogens sensitive to Ceftriaxone & Sulbactam for 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 defense mechanisms;
- Renal and urinary tract infections;
- Respiratory tract infections, particularly pneumonia, and ear, nose and throat infections;
- Genital infections, including gonorrhea.
- Perioperative prophylaxis of infections.
-Considerations should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND 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 body weights 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.
Reconstitution or the preparation for use:
Dissolve the contents in 10 ml of sterile water for injection IP provided with this vial & Inject slowly within 3 to 5 minutes. The reconstituted solution should be used immediately after preparation.

Method of administration
Route of Administration: Intramuscular Injection/ slow Intravenous Injection.

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 Sulbactamis contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins.

WARNING AND PRECAUTIONS:

This product should be given cautiously to penicillin-sensitive patients. Serious acute hypersensitivity reactions may require the use of subcutaneous epinephrine and other emergency measures.
Clostridium difficile associated diarrhea has been reported with nearly all antibacterial agents, including ceftriaxone/Sulbactam, and may range in severity from mild to lifethreatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.
An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class anti-bacterial including Ceftriaxone. If a patient develops anemia while on ceftriaxone, the diagnosis of a cephalosporin associated anemia should be considered and ceftriaxone stopped until the etiology is determined.

Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of ceftriaxone/ Sulbactam is similar to that of other cephalosporins.

DRUG INTERACTIONS:

Calcium-containing diluents, such as Ringer's solution or Hartmann's solution, should not be used to reconstitute ceftriaxone vials or to further dilute a reconstituted vial for intravenous administration because a precipitate can form. Precipitation of ceftriaxone- calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same intravenous administration line. Ceftriaxone must not be administered simultaneously with calcium-containing intravenous solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid. In vitro studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium.

PREGNANCY AND LACTATION:

Pregnancy
Category B: Either animal-reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of a risk in later trimesters).
Lactation
Caution when used during lactation.
Fertility
Reproductive studies have shown no evidence of adverse effects on male or female fertility.

SIDE EFFECTS:

The most frequently reported adverse reactions for Ceftriaxone are eosinophilia, leucopenia, thrombocytopenia, diarrhoea, rash, and hepatic enzymes increased.
Data to determine the frequency of ceftriaxone ADRs was derived from clinical trials. The following convention has been used for the classification of frequency:
Very common (≥ 1/10) Common (≥ 1/100 - < 1/10) Uncommon (≥ 1/1000 - < 1/100) Rare (≥ 1/10000 - < 1/1000)

Infections and infestations
Uncommon: Genital fungal infection
Rare: Pseudo membranous colitis
Not Known: Superinfection
Blood and lymphatic system disorders
Common: Eosinophilia, Leucopenia, Thrombocytopenia
Uncommon: Granulocytopenia, Anaemia, Coagulopathy
Not known: Haemolyticanaemia, Agranulocytosis
Immune system disorders
Not Known: Anaphylactic shock, Anaphylactic reaction, Anaphylactoid reaction, Hypersensitivity, Jarisch- Herxheimer reaction
Nervous system disorders
Uncommon- Headache, Dizziness
Rare: Encephalopathy
Not Known: Convulsion
Ear and labyrinth disorders
Not Known: Vertigo
Respiratory, thoracic and mediastinal disorders
Rare: Bronchospasm
Gastrointestinal disorders
Common: Diarrhoea, Loose stools
Uncommon: Nausea, Vomiting
Not Known: Pancreatitis, Stomatitis, Glossitis
Hepatobiliary disorders
Common: Hepatic enzyme increased
Not known: Gall bladder precipitation, Kernicterus
Skin and subcutaneous tissue disorders
Common: Rash
Uncommon: Pruritus
Rare: Urticaria
Not known: Stevens Johnson Syndrome Toxic epidermal necrolysis, Erythema multiforme, Acute generalised exanthematous pustulosis, Drug reaction with eosinophilia and systemic symptoms (DRESS)
Renal and urinary disorders
Rare: Haematuria, Glycosuria
Not known: Oliguria, Renal precipitation (reversible)
General disorders and administration site conditions
Uncommon- Phlebitis, Injection site pain, Pyrexia
Rare: Oedema, Chills
Investigations
Uncommon: Blood creatinine increased
Not known: Coombs test false positive, Galactosaemia test false positive, Non enzymatic methods for glucose determination false positive

Description of selected adverse reactions

Infections and infestations
Reports of diarrhoea following the use of ceftriaxone may be associated with *Clostridium difficile*. Appropriate fluid and electrolyte management should be instituted.
Ceftriaxone-calcium salt precipitation
Rarely, severe, and in some cases, fatal, adverse reactions have been reported in pre-term and full-term neonates (aged < 28 days) who had been treated with intravenous ceftriaxone and calcium. Precipitations of ceftriaxone-calcium salt have been observed in lung and kidneys post-mortem. The high risk of precipitation in neonates is a result of their low blood volume and the longer half-life of ceftriaxone compared with adults.
Cases of ceftriaxone precipitation in the urinary tract have been reported, mostly in children treated with high doses (e.g. ≥ 80 mg/kg/day or total doses exceeding 10 grams) and who have other risk factors (e.g. dehydration, confinement to bed). This event may be asymptomatic or symptomatic, and may lead to ureteric obstruction and postrenal acute renal failure, but is usually reversible upon discontinuation of ceftriaxone.
Precipitation of ceftriaxone calcium salt in the gallbladder has been observed, primarily in patients treated with doses higher than the recommended standard dose. In children, prospective studies have shown a variable incidence of precipitation with intravenous application - above 30 % in some studies. The incidence appears to be lower with slow infusion (20 - 30 minutes). This effect is usually asymptomatic, but the precipitations have been accompanied by clinical symptoms such as pain, nausea and vomiting in rare cases. Symptomatic treatment is recommended in these cases. Precipitation is usually reversible upon discontinuation of ceftriaxone.

OVERDOSE:

Symptoms: In the case of Ceftriaxone overdose nausea, vomiting, diarrhoea, can occur. Ceftriaxone concentration cannot be reduced by haemodialysis or peritoneal dialysis.
Treatment: There is no specific antidote. Treatment is symptomatic.

Storage Condition: Store in a cool & dry place, protected from light.

Shelf Life: 2 Years

Following reconstitution: 24 hours
From a microbiological point of view, 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 not be longer than the times stated above for the chemical and physical in- use stability.

DOSAGE FORM AND PACKAGING AVAILABLE:

Ceftriaxone & Sulbactam for Injection 1.5gm is packed in a 20ml clear & colourless glass vial with grey bromobutyl rubber stopper and aluminium flip off seal. Such 1 vial is packed in a mono carton along with one 10ml FFS ampoule of sterile water for Injection IP with package insert .

Manufactured in India by:
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windlas

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