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Ceftriaxone & Tazobactam For Injection 1.125g

SUPRAVA TZ® सुप्रवा टि ज़ेड

Composition:
Each Vial Contains:
Ceftriaxone Sodium I.P. (Sterile)
Eq. to Anhydrous Ceftriaxone 1000 mg
Tazobactam Sodium I.P. (Sterile)
Eq. to Anhydrous Tazobactam 125 mg

ATC Code: Ceftriaxone (J01DD04) and Tazobactam (J01CG02)

Pharmaceutical Form: POWDER FOR INJECTION

PHARMACOLOGY
Pharmacodynamics
Ceftriaxone is a 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 of peptidoglycan which is the major component of bacterial cell wall. 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.

Tazobactam is a penicillinate sulfone, structurally related to sulbactam. Being a beta-lactamase inhibitor, it is synergistic with many beta-lactamase labile drugs such as penicillins and cephalosporins. Tazobactam inhibits all beta-lactamases inhibited by clavulanic acid, but, in addition, it also has some activity against chromosomally-mediated induced (or derepressed) enzymes of *Morganella morganii, Citrobacter freundii, Enterobacter cloacae, Serratia marcescens* and *Pseudomonas aeruginosa*. Tazobactam also appears to be a weaker enzyme inducer than other beta-lactamase inhibitors.

Combination of Tazobactam and Ceftriaxone
The combination of tazobactam and ceftriaxone is active against all the organisms sensitive to ceftriaxone. In addition, it demonstrates synergistic activity (reduction in minimal inhibitory concentration [MIC] for the combination versus those of each component) in a variety of organisms.

Pharmacokinetics
Distribution
Ceftriaxone: 98% bound to plasma proteins; crosses the blood brain barrier.
Tazobactam: About 30% bound to plasma proteins; widely distributed to tissues and body fluids.

Excretion
Ceftriaxone: Elimination half-life is about 8.7 hours; 33-67% removed as unchanged drug.
Tazobactam: Removed mainly via kidneys with 80% of the administered dose as unchanged drug.

INDICATIONS
It is mainly indicated in the following conditions:
- Lower respiratory tract infections and community-acquired pneumonia
- Acute bacterial otitis media
- Skin and skin structure infections
- Urinary tract infections
- Uncomplicated gonorrhea
- Pelvic inflammatory disease
- Bacterial septicemia
- Bone and joint infections
- Intra-abdominal infections
- Bacterial meningitis
- Peri-operative prophylaxis of infections associated with surgery

CONTRAINDICATIONS
Hypersensitivity to cephalosporins and beta-lactamase inhibitors.

Neonates (≤ 28 days)
Hyperbilirubinemic neonates, especially prematures, should not be treated with ceftriaxone. *In vitro* studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in these patients. In neonates, ceftriaxone must not be co-administered with calcium-containing I.V. solutions, including continuous calcium-containing infusions such as parenteral nutrition, because of the risk of precipitation of the ceftriaxone-calcium salt.

WARNINGS 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 and Tazobactam, and may range in severity from mild to life-threatening. 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 antibacterials 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 and Tazobactam is similar to that of other cephalosporins.

Alterations in prothrombin times have occurred infrequently in patients treated with Ceftriaxone and Tazobactam. Patients with impaired vitamin K synthesis or low vitamin K stores (eg, chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Ceftriaxone and Tazobactam treatment.

It should also be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis. There have been reports of sonographic abnormalities in the gall bladder of patients treated with Ceftriaxone and Tazobactam; some of these patients also had symptoms of gall bladder disease. The condition appears to be transient and reversible upon the discontinuation of Ceftriaxone and Tazobactam and the institution of conservative management. Cases of pancreatitis, possibly secondary to biliary obstruction, have been reported rarely in patients treated with Ceftriaxone and Tazobactam.

Renal Impairment
Ceftriaxone is excreted via both biliary and renal excretion. Therefore, patients with renal failure normally require no dosage adjustment when the usual doses of Ceftriaxone and Tazobactam are administered, but concentrations of the drug in the serum should be monitored periodically. If evidence of accumulation exists, the dosage should be decreased accordingly.

No data are available in the case of pediatric patients with impaired renal function.

Hepatic Impairment
Dosage adjustments should not be necessary in patients with hepatic dysfunction; however, in patients with both hepatic dysfunction and significant renal disease, the dosage of Ceftriaxone and Tazobactam should not exceed 2 g daily without close monitoring of serum concentrations. No data are available in the case of pediatric patients with impaired hepatic function.

Pregnancy
Ceftriaxone and Tazobactam Injection should be used during pregnancy only if clearly needed.

Lactation
Low concentrations of Ceftriaxone and Tazobactam are excreted in human milk. Hence, caution should be exercised when Ceftriaxone and Tazobactam is administered to a nursing mother.

Pediatric Use
Ceftriaxone and Tazobactam should not be administered to hyperbilirubinemic neonates, especially prematures.

Geriatric Use
The pharmacokinetics of Ceftriaxone and Tazobactam were only minimally altered in geriatric patients compared to healthy adult subjects and dosage adjustments are not necessary for geriatric patients with Ceftriaxone and Tazobactam dosages up to 2 g per day.

UNDESIRABLE EFFECTS
Local reactions-pain, induration and tenderness was 1% overall. Phlebitis was reported in <1% after IV

For the use only of a Registered Medical Practitioner or Hospital or Laboratory

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administration.
Hypersensitivity-rash (1.7%). Less frequently reported (<1%) were pruritus, fever or chills.
Hematologic-eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (<1%) were anemia, hemolytic anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

Gastrointestinal-diarrhea (2.7%). Less frequently reported (<1%) were nausea or vomiting,and dysgeusia.
Hepatic-elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (<1%) were elevations of alkaline phosphatase and bilirubin.

Renal-elevations of the BUN (1.2%). Less frequently reported (<1%) were elevations of creatinine and the presence of casts in the urine.
Central nervous system-headache or dizziness were reported occasionally (<1%).
Genitourinary-moniliasis or vaginitis were reported occasionally (<1%).

Miscellaneous-diaphoresis and flushing were reported occasionally (<1%). Other rarely observed adverse reactions (<0.1%) include abdominal pain, agranulocytosis, allergic pneumonitis, anaphylaxis, basophilia, biliary lithiasis, bronchospasm, colitis, dyspepsia, epistaxis, flatulence, gallbladder sludge, glycosuria, hematuria, jaundice, leukocytosis, lymphocytosis, monocytosis, nephrolithiasis, palpitations, a decrease in the prothrombin time, renal precipitations, seizures, and serum sickness.

Gastrointestinal-stomatitis and glossitis.
Genitourinary-oliguria.
Dermatologic-exanthema, allergic dermatitis, urticaria, edema. As with many medications, isolated cases of severe cutaneous adverse reactions (erythema multiforme, Stevens-Johnson syndrome or Lyell's syndrome/toxic epidermal necrolysis) have been reported.

OVERDOSAGE
In the case of overdosage, drug concentration would not be reduced by hemodialysis or peritoneal dialysis. There is no specific antidote. Treatment of overdosage should be symptomatic.

DOSAGE AND ADMINISTRATION
Adults: The usual adult dose is 1000/125 mg of Ceftriaxone and Tazobactam given once a day (or in equally divided doses twice a day) depending upon the severity of the infection. The total daily dose should not exceed 4 g (in terms of ceftriaxone).

For pre-operative use (surgical prophylaxis), a single I.V. dose of 1 g administered half an hour to 2 hours before surgery is recommended. Generally, Ceftriaxone and Tazobactam should be continued for at least 2 days after the signs and symptoms of infection have disappeared. The usual duration of therapy is 4-14 days; in complicated infections, longer therapy may be required. When treating *Streptococci pyogenes*, the therapy should be continued for at least 10 days.

Ceftriaxone may be administered by deep intramuscular injection, or as a slow intravenous injection/ infusion, after reconstitution of the solution according to the directions given below.
Pediatric Patients: For the treatment of serious infections, the recommended dose is 50–75 mg/kg (in terms of ceftriaxone) given in divided doses every 12 hours. The total daily dose should not exceed 2 g (in terms of ceftriaxone). For the treatment of acute bacterial otitis media, a single intramuscular dose of 50 mg/kg (not to exceed 1 g) is recommended.

Directions for Use
I.V. injection should be administered over at least 2–4 minutes.
I.V. infusion should be over a period of 30 minutes.
After reconstitution the solution should be administered by deep I.M. injection. Doses greater than 1g should be divided and injected at more than one site.

Reconstitute Ceftriaxone and Tazobactam for Injection with the appropriate diluent as per the below table. e.g., Water for Injections, Normal Saline or Dextrose Solutions.

Strength	Volume of diluent for IM (mL)	Volume of diluent for IV (mL)
1.125g	3.6	9.6

For IV infusion: Withdraw entire contents after reconstitution as per the above table and dilute to the desired concentration with the appropriate IV diluent. Diluents which can be used for IV Infusion are Water for Injections, Normal Saline or Dextrose Solutions.

Use reconstituted solution in the vial immediately.

INCOMPATIBILITY
Vancomycin, aminoglycosides, and fluconazole are physically incompatible with Ceftriaxone and Tazobactam in admixtures. When any of these drugs are to be administered concomitantly by intermittent intravenous infusion, it is recommended that they should be given sequentially, with thorough flushing of the intravenous lines (with one of the compatible fluids) between the administrations.

Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute SUPRAVA TZ® vials or to further dilute a reconstituted vial for IV administration. Particulate formation can result.

NOTE: Parenteral drug products should be inspected visually for particulate matter before administration.

Shelf Life: Please refer carton/label.

STORAGE AND HANDLING INSTRUCTIONS
Store at a temperature not exceeding 30°C. Protect from light. Do not Freeze.
Keep out of reach of children.
Discard if reconstituted solution contains visible particulate matter.
DISCARD UNUSED PORTION.

Special Precautions for Disposal and Other Handling
Any unused medicinal product should be disposed off in accordance with the local requirements.

How supplied
Powder filled in glass vial, labelled vial packed in carton with leaflet.

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

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