

ADVOJET-T-1.25 GM. INJ.

FOR I.V./I.M.USE ONLY

Composition :

Each Vial contains
Sterile Ceftriaxone Sodium I.P.
Eq. to Ceftriaxone 1000mg.
Sterile Tazobactam Sodium
Eq. to Tazobactam 125mg.

DESCRIPTION :

The combination of tazobactam and ceftriaxone is active against all the organisms sensitive to ceftriaxone. In addition, it demonstrates synergistic activity like reduction in MICs as compare to those of each component in a variety of organisms.

Ceftriaxone is a parenteral third-generation cephalosporin antimicrobial agent. It exerts its bactericidal effect by inhibiting the bacterial cell wall synthesis.

The unique molecular structure of Ceftriaxone provides the wide coverage against pathogens.

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.

PHARMACOLOGY :

Pharmacodynamics :-

Ceftriaxone is a 2-aminothiazolyl methoxylmino 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.

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 also has some activity against chromosomally-mediated induced enzymes of *Morganella morganii*, *Citrobacter freundii*, *Enterobacter cloacae*, *Serratia marcescens* and *Pseudomonas aeruginosa*.

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, approximately 33-67% removed as unchanged drug through urine.

Tazobactam: Removed mainly via kidneys with 80% of an 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.
- Perioperative prophylaxis of infections associated with surgery.

CONTRAINDICATIONS :

Hypersensitivity to cephalosporins and beta-lactamase inhibitors.

Lactating mother : Caution when used during lactation

Neonates upto 28 days : Hyperbilirubinemic neonates, especially premature, 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 :

History of penicillin allergy; lactation. Consider possibility of pseudomembranous colitis in patients who present with diarrhoea subsequent to the admin of antibacterial agents. Monitor prothrombin time in patients with impaired Vit. K synthesis or low Vit. K stores during treatment. Prolonged treatment may result in overgrowth of non-susceptible organisms. Caution in patients with a history of GI disease, especially colitis. Discontinue treatment in patients who develop signs/symptoms suggestive of gallbladder disease. Not to be used in hyperbilirubinemic neonates, especially premature.

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/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/tazobactam should not exceed 2 gm daily without close monitoring of serum concentrations. No data are available in the case of pediatric patients with impaired hepatic function.

Pregnancy : Ceftriaxone/tazobactam Injection should be used during pregnancy only if clearly needed.

Lactation : Low concentrations of ceftriaxone/tazobactam are excreted in human milk. Hence, caution should be exercised when ceftriaxone/tazobactam is administered to a nursing mother.

Pediatric : Ceftriaxone/Tazobactam should not be administered to hyperbilirubinemic neonates, especially premature.

Geriatric Use : The pharmacokinetics of ceftriaxone/tazobactam were only minimally altered in geriatric patients compared to healthy adult patients and dosage adjustments are not necessary for geriatric patients with ceftriaxone/tazobactam dosages up to 2 grams per day.

UNDESIRABLE EFFECTS :

The following adverse effects may occur with Advojet-T Inj. :

Super infection, anaphylaxis, diarrhea, local reaction, blood dyscrasias, rash fever, pruritus, elevated transaminases and alkaline phosphatase. GI effects, pseudomembranous colitis, hematologic effects, hypersensitivity reactions, CNS disturbances, hypertension, chest pain, edema, moniliasis, rhinitis, dyspnea, hypotension and local Inj. Site reactions.

Potentially Fatal: Pseudomembranous colitis and nephrotoxicity.

OVER DOSAGE :

In the case of over dosage, 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 ceftriaxone 1000mg. and Tazobactam 125mg. 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 gm (in terms of ceftriaxone).

For pre-operative use (surgical prophylaxis), a single I.V. dose of 1 gm administered half an hour to 2 hours before surgery is recommended. Generally, ceftriaxone/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 gm (in terms of ceftriaxone). For the treatment of acute bacterial otitis media, a single intramuscular dose of 50 mg/kg (not to exceed 1 gram) 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 1gm. should be divided and injected at more than one site.

Reconstitute Advojet –T Injection with the appropriate diluents like water for Injection IP, normal Saline Water, or dextrose Solutions.

Use reconstituted solution in the vial immediately.

INCOMPATIBILITY :

Vancomycin, aminoglycosides, and fluconazole are physically incompatible with Advojet-T Injection in admixtures. When any of these drugs are to be administered concomitantly by intermittent intravenous infusion, it

is recommended that they be given sequentially, with thorough flushing of the intravenous lines (with one of the compatible fluids) between the administrations.

STORAGE AND HANDLING INSTRUCTIONS :

Store in a cool, dry place. Protect from light. Keep out of reach of children. Discard if reconstituted solution contains visible particulate matter. Discard unused portion.

PRESENTATION :

1 Vial with water for injection in a carton.