Ceftriaxone and Sulbactam For Injection 1000mg/500mg, 500mg/250mg and 250mg/125mg Taj Pharma

COMPOSITIONS:

a) Each vial contains Ceftriaxone Sodium IP Eq. to Ceftriaxone – 1000mg. Sulbactam Sodium USP Eq. to Sulbactam – 500mg.

b) Each vial contains Ceftriaxone Sodium IP Eq. to Ceftriaxone – 500mg. Sulbactam Sodium USP Eq. to Sulbactam – 250mg.

c) Each vial contains Ceftriaxone Sodium IP Eq. to Ceftriaxone – 250mg. Sulbactam Sodium USP Eq. to Sulbactam – 125mg.

DESCRIPTION:

The combination of Ceftriaxone Sodium and Sulbactam Sodium consist of a beta – lactam antibiotic and beta – lactamase inhibitor. 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.

Sulbactam is a beta lactamase inhibitor. It acts as a beta-lactamase inhibitor; to increase the antibacterial activity of cefoperazone against beta-lactamase-producing organisms. Sulbactam sodium is a derivative of the basic penicillin nucleus. Chemically it is sodium penincillinate sulfone and is an off-white crystalline powder highly soluble in water.

PHARMACOLOGY:

Pharmacodynamics –

The bactericidal activity of ADVOJET-S 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.

Pharmacokinetics:

Absorption:
ADVOJET-S 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.

MICROBIOLOGY:

The combination of Ceftriaxone sodium and Sulbactam sodium is active against Gram +ve Aerobes, Gram – ve Aerobes and Aerobes that are sensitive to ceftriaxone.

INDICATIONS:

ADVOJET-S is indicated for the treatment of following infections when caused by susceptible bacteria-

1. For treatment of Nosocomial infections.
2. Surgical prophylaxis.
3. Urinary tract infections (complicated by underlying urological abnormalities).
4. Skin and soft tissue infections Like cellulites, erysipelas etc.
5. Cholecystitis and Osteomyelitis.
6. Sexually transmitted diseases (Gonorrhoea, Chancroid, Syphilis).
7. Chronic suppurative bacterial otitis media.
8. Meningitis.

SAFETY AND TOLERABILITY:

Clinical studies revealed that the combination of Ceftriaxone and Sulbactum had no major problem after intravenous use.

Incidence of side-effects due to Ceftriaxone is very negligible.

CONTRAINDICATION:

ADVOJET-S is contraindicated in patients with known allergy to penicillins and cephalosporins.

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.

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:

ADVOJET-S should not be administered to hyperbilirubinemic neonates, especially premature.

TAJ PHARMA®
16 Years of Good Life

DOSAGE AND 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 ADVOJET-S 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 500mg of sulbactam every 12 hours (maximum dose 1 gram of sulbactam).

Paediatric 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.

STORAGE AND STABILITY:

ADVOJET-S is a sterile powder to be stored at or below 25° C and protected from light.

HOW SUPPLIED:

Vial with diluent in a carton.

7. Manufactured By:
Taj Pharmaceuticals Ltd.
at: Plot. No. 220, Mahagujarat
Industrial Estate, At & Post-Moraiya,
Tal-Sanand, Dist- Ahmedabad Gujarat (India)