

CEFTRIAXONE + SULBACTAM

CEFSUL IV

1 g / 500 mg Powder for injection (IM/IV)



ANTIBACTERIALS

Formulation:

Each vial contains:

Ceftriaxone (as sodium), USP

Equivalent to Ceftriaxone..... 1g

Sulbactam (as sodium), USP

Equivalent to Sulbactam.....500 mg

Description: White to off white crystalline powder, filled in clear glass vial, sealed with grey coloured butyl rubber stopper and coloured flip of seal.

Clinical Pharmacology: Ceftriaxone sodium + Sulbactam sodium (Cefsul IV) 1g/500mg Powder for injection (I.M./I.V.) is a anti-infective combination of Ceftriaxone with Sulbactam. Ceftriaxone is a broadspectrum semi-synthetic third generation cephalosporin with a potent bactericidal activity against a wide range of Gram-positive and Gram negative-bacteria. Sulbactam is B-lactamase inhibitor.

Pharmacodynamics:

Pharmacotherapeutic group:

Combinations of Cephalosporin and beta-lactamase inhibitors;

Mode of action:

Ceftriaxone is a beta-lactam antibiotic like the penicillin with bactericidal action. Penicillin-binding proteins (PBPs) are responsible for several steps in the synthesis of the cell wall of bacteria and are found in large quantities (several hundred to several

thousand molecules/bacterial cell). Ceftriaxone inhibits the third and final stage of bacterial cell wall synthesis by preferentially binding to the specific PBPs located inside the bacterial cell wall. Ceftriaxone interferes with PBP-mediated cell wall synthesis leading to cell lysis, which is mediated by bacterial cell wall autolytic enzymes (autolysins), possibly through interference with an autolysin inhibitor. The presence of an aminothiazolylacetyl side chain with an alpha methoxymino group at the 7-position of the beta-lactam ring provides Ceftriaxone with enhanced antibacterial activity, particularly against the Enterobacteriaceae (e.g., *E. coli*, *Klebsiella*, *Proteus*, and *Serratia*) and increased stability against many of the beta lactamases. Many strains of *Pseudomonas aeruginosa* are susceptible to Ceftriaxone. Other susceptible gram-negative organisms include *Enterobacter*, *Citrobacter*, *Morganella*, *Providencia*, *Moraxella* (*Branhamella*) *catarrhalis*, and *N. meningitidis*. Ceftriaxone has exceptional activity against *H. influenzae* and *N. gonorrhoeae* and is the drug of choice for uncomplicated *N. gonorrhoeae* infections. It has no activity against *B. fragilis* but is active against many other anaerobes.

However, recently it has been observed that the bacteria, through formation of betalactamases hydrolyze the beta-lactam ring of cephalosporins to inactivate them, thereby developing resistance to the drug. Recently, such a development of resistance to ceftriaxone has been observed, which can be judged by an increase in the MIC. Sulbactam, by irreversibly binding to the beta-lactamases produced by the common gram-positive or negative bacteria protects the beta-lactam ring of ceftriaxone, and conserves the activity. Thus on combining ceftriaxone with sulbactam, the combination product- Ceftriaxone & Sulbactam for Injection extends its utility in the treatment of broad range of infections caused by organism's resistant to the antibiotic alone, making them susceptible, possibly through lowering of MIC.

Pharmacokinetics

Following intramuscular administration, peak serum concentrations of Ceftriaxone and Sulbactam are seen between 15 minutes to 2 hrs. 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. Ceftriaxone is highly bound to human serum protein by about 83-90%. Ceftriaxone sodium penetrates well into the extravascular spaces, tissue fluid and the synovial fluid

of inflamed joints.

Ceftriaxone crosses the placenta and is distributed in the amniotic fluid. It is also distributed in the milk.

Ceftriaxone is eliminated unchanged via two pathways, urine and bile. Metabolism of sulbactam is less than 25%. 70-80% of Sulbactam is excreted by the kidney & biliary excretion is minimal.

Indications

Ceftriaxone sodium + Sulbactam sodium (Cefsul IV) 1g/500mg Powder for Injection (I.M./I.V.) is indicated for the treatment of meningitis, nosocomial infections surgical prophylaxis, urinary tract infections (complicated by underlying urological abnormalities), skin and soft tissue infections like cellulitis, erysipelas etc., cholecystitis, osteomyelitis, sexually transmitted diseases (gonorrhea, chancroid, syphilis), chronic suppurative bacterial otitis media, infections in dialysis unit.

Dosage and Administration

The recommended adult dosage is 1.5 g to 3 g every six hours. It may be administered intravenously.

This 1.5 to 3 g range represent the total of ceftriaxone/ 500 mg sulbactam to 2 g ceftriaxone / 1g sulbactam to 1 g sulbactam. For children with body weights of 50 kg or more, the usual adult dosage should be used.

Contraindication

Ceftriaxone & Sulbactam for Injection is contraindicated in patients with known allergy to Cephalosporin group of antibiotics. Hypersensitivity to penicillin may pre-dispose the patient to the possibility of allergic cross-reactions.

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.

Direction for reconstitution

Dissolve the content in sterile water for injection. After reconstruction discard any unused portion.

Precautions

General: Transient elevations of BUN (blood urea nitrogen) and serum creatinine have been observed, at recommended doses, the nephrotoxic potential of ceftriaxone is the same as other cephalosporins.

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 2g daily with close monitoring of serum concentrations.

Carcinogenesis, Mutagenesis and impairment of Fertility: Carcinogenic studies with ceftriaxone in animals have not been performed. Ceftriaxone showed no potential mutagenic activity. Ceftriaxone produced no impairment of fertility in animal studies.

Pregnancy: Teratogenic effects: Pregnancy category B.

No evidence of embryotoxicity, fetotoxicity or teratogenicity in animal studies. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Low concentrations of Ceftriaxone are excreted in human milk. Caution should be exercised when ceftriaxone + sulbactam is administered nursing women.

Pediatric use: Ceftriaxone sodium + Sulbactam sodium (Cefsul IV) 1g/500 mg powder for injection (I.M./I.V.) should not be administered to hyperbilirubinemic neonates, especially premature.

Interactions

No impairment of renal function has been observed after concurrent administration of large doses of Ceftriaxone and potent diuretics.

There is no evidence to suggest that Ceftriaxone increases renal toxicity of aminoglycosides. The elimination of Ceftriaxone is not altered by probenecid.

Ceftriaxone and chloramphenicol have been shown to be antagonistic in in vitro studies. In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals.

Coombs test may show false-positive results during Ceftriaxone & Sulbactam therapy. Non-enzymatic urinary glucose estimation methods may give false-positive results.

Adverse Drug Reaction

Gastro-intestinal complaints: Loose stools/ diarrhea, nausea, vomiting, stomatitis, glossitis.

Haematological changes: Eosinophilia, haematoma or bleeding, thrombocytopenia, neutropenia, leukopenia, granulocytopenia and haemolytic anaemia. Isolated cases of agranulocytosis (<500/mm) have been reported, most of them following total doses of 20 g or more.

Exanthema, allergic dermatitis, pruritus, urticaria, oedema, erythema multiforme may occur.

Other adverse effects include headaches and dizziness, increase in liver enzymes, oliguria, and increase in serum creatinine, mycosis of the genital tract fever, shivering and anaphylactic or anaphylactoid reactions.

Local: Inflammatory reactions in the vein wall may occur after IV administration. These may be minimized

By slow (2-4 minutes) injection. Intramuscular injection without lidocaine solution is painful.

Overdose and Treatment

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

Storage: Store at temperatures not exceeding 30°C

ADR REPORTING

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph and pv@biocarelifesciences.com. Seek medical attention immediately at the first sign of any adverse drug reaction.

CAUTION:

Foods, Drugs, Devices, and Cosmetics Acts prohibits dispensing without prescription

Dosage Form and Packaging Available: One vial of Ceftriaxone+Sulbactam 1 g/ 500 mg Powder to Injection in a carton along with an insert, box of 1's

DR-XY 46353

Date of First Authorization: 30 May 2018

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ZP/PI/0474-01