Ceftriaxone

Introduction: An antibiotic belonging to the class of drugs called cephalosporins. It is used for fighting bacteria in the body. It treats different types of bacterial infections including Bronchitis, pneumonia, bone infections, abdominal and skin infections, urinary tract infections etc.

Mechanism of action: Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydrolases) while cell wall assembly is arrested.

Pharmacology:
Absorption: I.M.: Well absorbed
Distribution: V_d: 6-14 L; widely throughout the body including gallbladder, lungs, bone, bile, CSF (higher concentrations achieved when meninges are inflamed)
Protein binding: 85% to 95%
Half-life elimination: Normal renal and hepatic function: 5-9 hours; Renal impairment (mild-to-severe): 12-16 hours
Time to peak, serum: I.M.: 2-3 hours
Excretion: Urine (33% to 67% as unchanged drug); feces (as inactive drug)

Indications: Ceftriaxone is indicated for the treatment of the following infections when caused by susceptible organisms:
Lower respiratory tract infections caused by *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis* or *Serratia marcescens.*
Acute bacterial otitis media caused by *Streptococcus pneumoniae, Haemophilus influenzae* (including beta-lactamase producing strains) or *Moraxella catarrhalis* (including beta-lactamase producing strains).
skin and skin structure infections caused by *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes*, Viridans group streptococci, *Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter calcoaceticus, Bacteroides fragilis* or *Peptostreptococcus* species.
Urinary tract infections *(complicated and uncomplicated)* caused by *Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii* or *Klebsiella pneumoniae.*
Uncomplicated gonorrhea *(cervical/urethral and rectal)* caused by*Neisseria gonorrhoeae,* including both penicillinase- and nonpenicillinase-producing strains, and pharyngeal gonorrhea caused by nonpenicillinase-producing strains of *Neisseria gonorrhoeae.*

Pelvic inflammatory disease caused by *Neisseria gonorrhoeae.* Ceftriaxone, like other cephalosporins, has no activity against *Chlamydia trachomatis*. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and *Chlamydia trachomatis* is one of the suspected pathogens, appropriate antichlamydial coverage should be added.

Bacterial septicemia caused by *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae* or*Klebsiella pneumoniae.*

Bone and joint infections caused by *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae* or *Enterobacter* species.

Intra-abdominal infections caused by *Escherichia coli, Klebsiella pneumoniae, Bacteroides fragilis, Clostridium*species (Note: most strains of *Clostridium difficile* are resistant) or *Peptostreptococcus* species.

Meningitis caused by *Haemophilus influenzae, Neisseria meningitidis* or *Streptococcus pneumoniae.* Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infection caused by *Staphylococcus epidermidis* and *Escherichia coli.*

Surgical prophylaxis*:* The preoperative administration of a single 1 gm dose of Ceftriaxone may reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated and in surgical patients for whom infection at the operative site would present serious risk.

Dosage: Ceftriaxone may be administered intravenously or intramuscularly.

Neonates: Hyperbilirubinemic neonates, especially prematures, should not be treated with Ceftriaxone.

Pediatric patients: For the treatment of skin and skin structure infections, the recommended total daily dose is 50 to 75 mg/kg given once a day (or in equally divided doses twice a day). The total daily dose should not exceed 2 grams. For the treatment of acute bacterial otitis media, a single intramuscular dose of 50 mg/kg (not to exceed 1 gram) is recommended. For the treatment of serious miscellaneous infections other than meningitis, the recommended total daily dose is 50 to 75 mg/kg, given in divided doses every 12 hours. The total daily dose should not exceed 2 grams.

Adults: The usual adult daily dose is 1 to 2 grams given once a day (or in equally divided doses twice a day) depending on the type and severity of infection. The total daily dose should not exceed 4 grams. If *Chlamydia trachomatis* is a suspected pathogen, appropriate antichlamydial coverage should be added, because ceftriaxone sodium has no activity against this organism. For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended. For preoperative use (surgical prophylaxis), a single dose of 1 gram administered intravenously 1/2 to 2 hours before surgery is recommended. When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least 10 days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (eg, dialysis patients) and in patients with both renal and hepatic dysfunctions.

Side effects: Ceftriaxone is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Ceftriaxone therapy or of uncertain etiology, were observed:

Local reactions-pain, induration and tenderness wa s 1% overall. Phlebitis was reported in <1% after IV administration. The incidence of warmth, tightness or induration was 17% (3/17) after IM administration of 350 mg/mL and 5% (1/20) after IM administration of 250 mg/mL.

Hypersensitivity-rash (1.7%). Less fr equently reported (<1%) were pruritus, fever or chills.

Hematologic-eosinophilia (6%), thrombocytos is (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. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment.

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 we re 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. Cases of fatal reactions with ceftriaxone-calcium precipitates in lung and kidneys in neonates have been described. In some cases the infusion lines and the times of administration of ceftriaxone and calcium-containing solutions differed.

Post marketing experience: In addition to the adverse reactions reported during clinical trials, the following adverse experiences have been reported during clinical practice in patients treated with Ceftriaxone. Data are generally insufficient to allow an estimate of incidence or to establish causation.

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 e/toxic epidermal necrolysis) have been reported.

Precautions:

General: Prescribing Ceftriaxone in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential

of Ceftriaxone is similar to that of other cephalosporins. Ceftriaxone is excreted via both biliary and renal excretion Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Ceftriaxone are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly. Dosage adjustments should not be necessary in patients with hepatic dysfunction; however, in patients with both hepatic dysfunction and significant renal disease, Ceftriaxone dosage should not exceed 2 gm daily without close monitoring of serum concentrations. Ceftriaxone should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis. Cases of pancreatitis, possibly secondary to biliary obstruction, have been reported rarely in patients treated with Ceftriaxone. Most patients presented with risk factors for biliary stasis and biliary sludge (preceding major therapy, severe illness, total parenteral nutrition). A cofactor role of Ceftriaxone-related biliary precipitation cannot be ruled out.

Pregnancy: ***Teratogenic Effects****:* There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, 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 is administered to a nursing woman.
Pediatric Use: Safety and effectiveness of Ceftriaxone in neonates, infants and pediatric patients have been established. Ceftriaxone should not be administered to hyperbilirubinemic neonates, especially prematures.
Geriatric Use:. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Contraindications: Ceftriaxone is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

How supplied: Customized as per request.