Zoxidel

Ceftriaxone sodium **Powder for IV. injection**
0.25gm, 0.5gm, 1.0gm, 2.0gm Vial.

Composition:
Each 0.25g vial contains:
Ceftriaxone sodium 3.5 H_2O 0.298 gm (Equ. to 0.25 gm ceftriaxone)
Each 0.5g vial contains:
Ceftriaxone sodium 3.5 H_2O 0.596 gm (Equ. to 0.5 gm ceftriaxone)
Each 1g vial contains:
Ceftriaxone sodium 3.5 H_2O 1.193 gm (Equ. to 1.0 gm ceftriaxone)
Each 2g vial contains:
Ceftriaxone sodium 3.5 H_2O 2.386 gm (Equ. to 2.0 gm ceftriaxone)
Pharmaceutical form: powder for IV injection.
Pharmaceutical action: 3rd Generation Semi-synthetic broad-spectrum cephalosporin. The in vivo bactericidal activity of Ceftriaxone is due to binding to essential target proteins and the resultant inhibition of cell-wall synthesis.
Mechanism of Action:
The principal mode of action of Zoxidel is through its inhibitory effect on the bacterial cell wall synthesis leading to loss of the cellular structures and death of the bacterial cell.
Pharmacokinetics:
Absorption:
Zoxidel was completely absorbed following IM administration with mean maximum plasma concentrations occurring between 2 and 3 hours post-dose. Multiple IV doses ranging from 0.5 to 2 gm at 12- to 24-hour intervals resulted in 15% to 36% accumulation of Zoxidel above single dose values.
Distribution: Ceftriaxone penetrated the inflamed mininges of infants and pediatric patients; CSF concentrations after a 50 mg/kg IV dose and after a 75 mg/kg IV dose are 5.6ug/mL and 6.4 ug/mL respectatively.
Excretion:
33% to 67% of a ceftriaxone dose was excreted in the urine as unchanged drug and the remainder was secreted in the bile and ultimately found in the feces as microbiologically inactive compounds.
The average values of maximum plasma concentration, elimination half-life, plasma clearance and volume of distribution after a 50 mg/kg IV dose(216 ug/mL, 4.6 hr,49 mL/hr/ug,338 mL/kg)and after a 75 mg/kg IVdose(275 ug/mL, 4.3 hr, 60 mL/hr/kg, 373 mL/kg) respectively in pediatric patients suffering from bacterial meningitis .
Microbiology:
The bactericidal activity of Zoxidel results from inhibition of cell wall synthesis. Zoxidel has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria.
Zoxidel has been shown to be active against most strains of the following microorganisms, both in vitro and in vivo:
Aerobic gram-negative microorganisms:
-Acinetobacter calcoaceticus
-Enterobacter aerogenes
-Enterobacter cloacae
-Escherichia coli
-Haemophilus influenzae (including ampicillin-resistant and beta-lactamase producing strains)
-Haemophilus parainfluenzae
-Klebsiella oxytoca
-Klebsiella pneumoniae
-Moraxella catarrhalis (including beta-lactamase producing strains)
-Morganella morganii
-Neisseria gonorrhoeae (including penicillinase- and nonpenicillinase)
-Neisseria meningitidis
-Proteus mirabilis
-Proteus vulgaris
-Serratia marcescens
-Citrobacter diversus
-Citrobacter freundii
-Providencia species (including Providencia rettgeri)
-Salmonella species (including Salmonella typhi)
-Shigella species .
Aerobic gram-positive microorganisms:
-Staphylococcus aureus (including penicillinase-producing strains)
-Staphylococcus epidermidis
-Streptococcus pneumoniae
-Streptococcus pyogenes
-Viridans group streptococci
-Streptococcus agalactiae
-Anaerobic microorganisms:
-Bacteroides fragilis
-Clostridium species
-Peptostreptococcus species.
Indications:
Before instituting treatment with Zoxidel, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.
Zoxidel 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, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Pseudomonas aeruginosa, Serratia marcescens, 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
-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.
CONTRAINDICATIONS :
Hypersensitivity to the active substance, to other cephalosporins or to any of the excipients.
Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other beta-lactam medicinal products.
DOSAGE AND ADMINISTRATION:
Zoxidel is administered intravenously.
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.
For preoperative use (surgical prophylaxis), a single dose of 1 gram administered intravenously 1/2 to 2 hours before surgery is recommended.
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 .
In the treatment of meningitis, it is recommended that the initial therapeutic dose be 100 mg/kg (not to exceed 4 grams). Thereafter, a total daily dose of 100 mg/kg/day (not to exceed 4 grams daily) is recommended. The daily dose may be administered once a day (or in equally divided doses every 12 hours). The usual duration of therapy is 7 to 14 days.
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.
Generally, Ceftriaxone therapy should be continued for at least 2 days after the signs and symptoms of infection have disappeared.
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.
ADVERSE REACTIONS:
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. Phlebitis was reported after IV administration.
-Hypersensitivity: rash.
Less frequently reported was pruritus, fever or chills.
-Hematologic: eosinophilia, thrombocytosis and leukopenia.
Less frequently reported were anemia, hemolytic anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.
-Gastrointestinal: diarrhea. Less frequently reported were nausea or vomiting, and dysgeusia. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment.
-Hepatic: elevations of SGOT or SGPT. Less frequently reported were elevations of alkaline phosphatase and bilirubin.
-renal: elevations of the BUN. Less frequently reported were elevations of creatinine and the presence of casts in the urine.
-Central nervous system: headache or dizziness were reported.
-Genitourinary: moniliasis or vaginitis were reported occasionally.
-Miscellaneous: diaphoresis and flushing were reported occasionally.
Other rarely observed adverse reactions (<0.1%) include:
1-abdominal pain, bronchospasm, colitis, dyspepsia, flatulence, palpitations.
Drug interactions:
zoxidel can interact with a number of medicines. Drugs that can interact with ceftriaxone include the following:
Warfarin
Probenecid
Sulfinpyrazone
Calcium or calcium-containing products.
Warfarin: If ceftriaxone and warfarin are coadministrated , the human body may metabolize the drugs differently than intended. INR and prothrombin time must be frequently checked and adjusted, and dose adjustment may be required.
Probenecid: If ceftriaxone and probenecid are coadministrated , the human body may metabolize the drugs differently than intended and significantly increase the amount of ceftriaxone in the body system , dose adjustment may be required.
Sulfinpyrazone : If you are taking both ceftriaxone and sulfinpyrazone, your body may metabolize the drugs differently than intended and significantly increase the amount of ceftriaxone in the body system. Your healthcare provider may choose to monitor your progress more closely and adjustment of the dose accordingly.
Calcium or Calcium-Containing Products:
Calcium and calcium-containing products can bind to ceftriaxone and cause dangerous deposits in the lungs and kidneys. These products should not be taken with ceftriaxone or within 48 hours of stopping ceftriaxone. It is important to be aware that many different IV medications contain calcium.
WARNINGS:
-Before therapy with Zoxidel is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs, 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.
-Pseudo membranous colitis has been reported with nearly all antibacterial agents, including ceftriaxone, 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.
-Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia, studies indicate that a toxin produced by Clostridium difficile is one primary cause of "antibiotic-associated colitis".
Special warnings and precautions for use:
Special caution is required to determine any other type of previous hypersensitivity reactions to penicillin or to other beta-lactam medicinal products because patients hypersensitive to these medicines may be hypersensitive to (zoxidel) as well (Cross allergy)

Zoxidel must not be co-administered with calcium-containing IV solutions, including continuous calcium-containing infusions such as parentral nutrition, in neonates
because of the risk of precipitation of ceftriaxone-calcium salt.

PRECAUTIONS:
- 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. vvvvpatients 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.
-Alterations in prothrombin times have occurred rarely in patients treated with Zoxidel. 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 treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.
-Prolonged use of Ceftriaxone may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.
-Ceftriaxone should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.
There have been reports of sonographic abnormalities in the gallbladder of patients treated with ceftriaxone; some of these patients also had symptoms of gallbladder disease.
The condition appears to be transient and reversible upon discontinuation of ceftriaxone and institution of conservative management.
Pregnancy & Lactation:
Teratogenic Effects:
Pregnancy Category B.
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.
Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when ceftriaxone is administered to a nursing woman.
Information for Patients:
Patients should be counseled that antibacterial drugs including Ceftriaxone should only be used to treat bacterial infections. They do not treat viral infections (eg, common cold).
When Ceftriaxone is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed.
Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Ceftriaxone or other antibacterial drugs in the future.
Package & Storage:
Carton box containing:
-One vial.
-two ampoules of sterile water for injection, contain 5ml.
-Insert pamphlet.
Storage:
Store at temperature not exceeding 30° C and after reconstitution in refrigerator at temperature (2° C - 8° C) for 24 hours.

Manufactured by: RAMEDA
For Delta for pharmaceutical industries
(Delta Pharma)

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