CEFTIZONE®

IM / IV injection

Ceftriaxone sodium USP

Description:

Ceftizone® (ceftriaxone) is a sterile, semisynthetic, broad-spectrum, long acting third generation cephalosporin antibiotic for parenteral administration. **Ceftizone®** is a white to yellowish-orange crystalline powder which is readily soluble in water. The pH of 1% aqueous solution is approximately 6.7. The color of **Ceftizone®** solution ranges from light yellow to amber, depending on the length of storage, concentration and diluent used. **Ceftizone®** contains approximately 83mg (3.6meq) of sodium per g of ceftriaxone activity.

Composition:

Each 250mg and 500mg **Ceftizone®** vial contains dry substance equivalent to 250mg & 500mg ceftriaxone (as sterile ceftriaxone sodium USP) respectively accompanied by a solvent ampoule of 2ml lidocaine 1% USP for IM injection or 5ml Water for injection USP for IV injection. Each 1g **Ceftizone®** vial contains dry substance equivalent to 1g ceftriaxone (as sterile ceftriaxone sodium USP) accompanied by a solvent ampoule of 4ml lidocaine 1% USP for IM injection or 10ml Water for injection USP for IV injection. Each 2g **Ceftizone®** Vial contains dry substance eqivalent to 2g ceftriaxone (as sterile ceftriaxone sodium USP) accompanied by 1 ampoule of 20ml water for injection USP.

Microbiology :

The bactericidal activity of ceftriaxone results from inhibition of cell wall synthesis. **Ceftizone®** has a high degree of stability in the presence of beta - lactamases, both penicillinase and cephalosporinases of gram-positive and gram-negative bacteria. Ceftriaxone is usually active against the following micro-organisms in-vitro and clinical infections (see indications).

Gram-negative aerobes: *Enterobacter spp., Escherichia coli, Haemophilus influenzae, Haemophilus ducreyi, Klebsiella spp., Neisseria gonorrhoea, Neisseria meningitidis, Proteus spp., Salmonella spp., Vibrio spp., Shigella spp., Pseudomonas aeruginosa, Citrobacter spp., Yersinia spp.*

Gram-positive aerobes: *Staphylococcus aureus and staphylococcus epidermidis (both penicillinase and non-penicillinase producing strains but methicillin resistant staphylococci are resistant to cephalosporins including ceftriaxone), Streptococcus pyogenes and Streptococcus pneumoniae.*

Anaerobes: *Bacteroides spp., Clostridium spp.* (most strains of C. difficile are resistant), *Fusobacterium spp. (except F. mortiferum & F. varium), Peptococcus spp.*

Indications: Ceftizone® is indicated for the treatment of infections caused by pathogens sensitive to ceftriaxone e.g.:

(1) Lower respiratory tract infections
(2) Acute bacterial otitis media
(3) Uncomplicated gonorrhoea
(4) Urinary tract infections
(5) Bacterial septicemia
(6) Bone and joint infections
(7) Intra-abdominal infections
(8) Bacterial meningitis
(9) ENT infections
(10) In surgical prophylaxis

The preoperative administration of a single 1g dose of ceftriaxone may reduce the incidence of post operative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated and in surgical patients for whom infections at the operative side would present serious risks When administered prior to surgical procedures, for which it is indicated, a single 1g dose of **Ceftizone®** IV provides protection from most infections due to susceptible organisms throughout the course of procedure. Before instituting treatment with **Ceftizone®** appropriate specimen 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.

Contra-indications :

Ceftizone® (ceftriaxone) is contraindicated in patients with known hypersensitivity to the cephalosporin class of antibiotics.

Warning :

Before therapy with **Ceftizone®** is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins and other drugs. This product should be given cautiously to penicillin hypersensitive patients. Serious acute hypersensitivity reactions may require the use of subcutaneous epinephrine and other emergency measures. Pseudomembranous 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 develop diarrhoea 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.

Precautions :

Ceftriaxone is excreted via both biliary and renal route. Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of ceftriaxone is administered but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly. Although transient elevations in BUN and serum creatinine have been observed at recommended dosage nephrotoxic potential of ceftriaxone is similar to that of other cephalosporins. Dosage adjustments should not be necessary in patients with hepatic dysfunction; however, in patients with both hepatic dysfunction and significant renal disease, **Ceftizone®** dosage should not exceed 2mg daily without close monitoring of serum concentrations. Alterations in prothrombin times have occurred rarely in patients treated with ceftriaxone. Patients with impaired vitamin-K synthesis or low vitamin-K stores (e.g. chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during **Ceftizone®** treatment. Vitamin-K administration (10mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy. Prolonged use of ceftriaxone may result in overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy appropriate measures should be taken. Ceflriaxone should be prescribed with caution in individuals with a history of gastrointestinal disease especially colitis.

Pregnancy:

In studies in mice and rats with ceftriaxone up to 20 times human dose there was no evidence of embryotoxicity, fetotoxicity or teratogenicity. 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 **Ceftizone®** is administered to a nursing woman.

Pediatric use :

Safety and effectiveness of ceftriaxone in neonates, infants and children have been established for the dosages described in the dosage and administration section. Ceftriaxone should not be used in hyperbilirubinemic neonates specially permatures.

Adverse effects:

Ceftriaxone is generally well tolerated. Common side effects reported are: **local reactions-pain,** induration or tenderness at the site of injection; **Hypersensitivity**-rash, less frequently reported are pruritus, fever or chills; **hematologic**-eosinophilia,leukopenia, anaemia, neutropenia & thrombocytopenia; **gastrointestinal**- diarrhoea, nausea, vomiting. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment.

Hepatic-elevations of SGOT or **SGPT; renal**-elevations of **BUN; CNS**-headache or dizziness; **genitourinary**-moniliasis or vaginitis was reported.

Dosage and administration :

Ceftizone® can be administered either intravenously or intramuscularly.

Adults & children over 12 years :

The usual adult daily dose is 1 to 2 g once daily (or in equally divided doses twice daily) depending on the type and severity of infection. The total daily dose may be increased but should not exceed 4 g. For surgical prophylaxis, a single dose of 1g administered intravenously 30 minutes to 2 hrs before surgery is recommended.

Children under 12 years:

For the treatment of skin and skin structure infections, the recommended total daily dose to 50-70mg/kg body weight once daily (or twice daily in equally divided doses). In severe infections, up to 75mg/kg body weight daily may be given. divided doses every 12 hrs. The total daily dose should not exceed 2 g. In the treatment of meningitis, the initial dose of 100mg/kg body weight (not exceeding 4 g) There after, a total daily dose of 100 mg/kg/day (not to exceed 4g daily) is recommended once daily or in equally divided doses every 12 hrs) As soon as the causative organism has been identified and its sensitivity determined, the dosage may be reduced accordingly. The usual duration of therapy in meningitis is 7 to 14 days.

Duration of therapy :

Generally **Ceftizone®** therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days; in complicated infections, longer therapy may be required. 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 renal impairment (e.g. dialysis patients) and in patients with both renal and hepatic dysfunction.

Directions for use:

Intramuscular injections:

For IM injection, **Ceftizone®** 250mg or 500mg is dissolved in 2ml of 1% lidocaine solution USP or 1g **Ceftizone®** in 4ml of lidocaine 1% solution USP and administered by deep intragluteal injection. It is recommended that not more than 1g be injected on either side.

The lidocaine solution must never be administered intravenously.

Intravenous injection:

For IV injection. **Ceftizone®** 250mg or 500mg is dissolved in 5ml and **Ceftizone®** 1g in 10 ml of sterile water for injection. The injection should be administered over 2-4 minutes, directly into the vein or via the tubing of an intravenous infusion.

Intervenous infusion:

2g IV: Reconstitute with 19.2ml of IV diluent (e.g. water for injection), for IV infusion, further dilute the reconstituted solution to 50ml or 100 ml volumes with the appropriate IV diluent, the IV infusion should be given over at least 30 minutes.

Compatibility and stability:

Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature and for 24 hours at 5^0C. As a general rule, however, the solutions should be used immediately after preparation. At concentration of 10, 20 & 40mg/ml, reconstituted solutions remain stable (loss of potency less than 10%) for the following time periods when stored in glass or PVC containers:

Diluent	Storage temp: 25^0C	Refrigerated : 4^0C
Sterile water for injection	3 days	10 days
0.9% sodium chloride solution	3 days	10 days
5% dextrose solution	3 days	10 days
10% dextrose solution	3 days	10 days
5% dextrose + 0.9% sodium chloride solution	3 days	10 days

Storage:

Store in a cool (below 30^0C), dry place and away from light and children.

Supply:

Ceftizone® injection is supplied as sterile powder in glass vials.

Ceftizone® 250mg IM/IV injection: Pack of 1 vial containing 250mg ceftriaxone (as ceftriaxone sodium USP) accompanied by 1 ampoule of 2ml lidocaine 1% injection USP for IM injection and 5ml Water for injection USP for IV injection.

Ceftizone® 500 mg IM/IV injection: Pack of 1 vial containing 500 mg ceftriaxone (as ceftriaxone sodium USP) accompanied by 1 ampoule of 2ml lidocaine 1% injection USP for IM injection and 5ml Water for injection USP for IV injection.

Ceftizone® 1g IM/IV injection: Pack of 1 vial containing 1g ceftriaxone (as ceftriaxone sodium USP) accompanied by 1 ampoule of 4ml lidocaine 1% injection USP for IM injection and 10ml water for injection USP for IV injection.

Ceftizone® 2g IV injection: Pack of 1 vial containing 2g ceftriaxone (as sterile ceftriaxone sodium USP) accompanied by 1 ampoule of 20ml water for injection USP for IV injection.

® Trade Mark

Manufactured By

Renata Limited

Rajendrapur, Gazipur, Bangladesh.