Trijject®

Ceftriaxone for Injection

DESCRIPTION

Trijject® is the preparation of Ceftriaxone. It is a sterile semisynthetic, broad spectrum antibiotic for intravenous or intramuscular administration. **Trijject®** is highly stable to beta-lactamases, both penicillinases and cephalosporinases of gram-negative and gram-positive bacteria. The bactericidal activity of **Trijject®** results from inhibition of cell wall synthesis. It is most effective against the following microorganisms; **Gram-negative bacteria:** *Escherichia coli, Haemophilus influenzae, Klebsiella sp., Enterobacter sp., Citrobacter sp., Proteus sp., Serratia sp.* and *Bacteroides sp.;* **Gram-positive bacteria:** *Staphylococcus aureus* (including penicillinase-producing strains), *Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Viridans group streptococci* . The plasma half-life of Ceftriaxone is not dependent on the dose and varies between 6 and 9 hours; it may be prolonged in neonates. The half-life does not change appreciably in patients with moderate renal impairment, but it may be prolonged in severe renal impairment especially when there is also hepatic impairment. Ceftriaxone is widely distributed in body tissues and fluids. It crosses both inflamed and non-inflamed meninges, generally achieves therapeutic concentrations in the CSF. It crosses the placenta and low concentrations have been detected in breast milk.

INDICATIONS

It is indicated in the treatment of the following infections caused by the Gram-positive and Gram-negative bacteria:

- Surgical prophylaxis
- Prevention of post-operative infections
- Renal and urinary tract infections
- Lower respiratory tract infections particularly pneumonia
- Serious bacterial infections e.g. septicemia
- Gonococcal infections
- Primary syphilis and chancroid
- Skin, soft tissue, bone and joint infections
- Pelvic inflammatory diseases
- Intra abdominal infections
- Bacterial meningitis
- Typhoid fever
- Ear, nose and throat infections
- Acute bacterial otitis media
- Bacterial endocarditis (Streptococcal or Heamophilus)
- Infections in cancer patients, neutropenic and immunosuppressed

DOSAGE AND ADMINISTRATION

Standard dosage

Adults and children over 12 years: The usual dosage is 1-2 g of Ceftriaxone administered once daily (every 24 hours). In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4 g, administered once daily.

Elderly patients: The dosages recommended for adults require no modification in the case of geriatric patients.

Surgical prophylaxis: To prevent postoperative infections in contaminated or potentially contaminated surgery, the recommended approach is a single dose of 1-2 g Ceftriaxone (depending on the risk of infection) administered 30-90 minutes prior to surgery. In colorectal surgery, concurrent (but separate) administration of Ceftriaxone with or without a 5-nitroimidazole, e.g. ornidazole, has proven effective.

Gonorrhoea: For the treatment of gonorrhoea (penicillinase-producing and nonpenicillinase-producing strains), a single intramuscular dose of 250 mg ceftriaxone is recommended.

For uncomplicated gonorrhoea: A single intramuscular dose of 250 mg is recommended.

Children up to twelve years:

The following dosage schedules are recommended for once daily administration:

Skin and Soft tissue Infections (SSTI): The recommended total daily dose is 50 to 75 mg/kg body-weight once daily (or in equally divided doses twice daily). The total daily doses should not exceed 2 g.

Acute Otitis Media: In acute bacterial otitis media a single intramuscular dose of 50 mg/kg body-weight (not to exceed 1 g) is recommended.

Meningitis: In bacterial meningitis in infants and children, treatment begins with doses of 100 mg/kg (not to exceed 4g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly. The best results have been found with the following duration of therapy:

- *Neisseria meningitidis:* 4 days
- *Haemophilus influenzae:* 6 days
- *Streptococcus pneumoniae:* 7 days
- *Susceptible Enterobacteriaceae:* 10-14 days

Serious Infections other than Meningitis: The recommended total daily dose is 50-75 mg/kg body-weight , given in divided doses every 12 hours. The total daily dose should not exceed 2 g.

Infants and children (15 days to 12 years): A daily dose of 20-80 mg/kg.

Neonates (up to 14 days): The recommended total daily dose is 20-50 mg/kg body-weight daily by intravenous infusion over 60 minutes, (max. 50 mg/kg daily).

NOTE: For children with bodyweights of 50 kg or more, the usual adult dosage should be used. Intravenous doses of 50 mg or more per kg should be given by infusion over at least 30 minutes.

Impaired renal and hepatic function: In patients with impaired renal function, there is no need to reduce the dosage of Ceftriaxone provided hepatic function is intact. Only in cases of preterminal renal failure (creatinine clearance <10 mL/min), the Ceftriaxone dosage should not exceed 2 g daily. In patients with liver damage, there is no need for the dosage to be reduced provided renal function is intact. In cases of concomitant severe renal and hepatic dysfunction, the plasma concentrations of Ceftriaxone should be determined at regular intervals. In patients undergoing dialysis no additional supplementary dosing is required following the dialysis. Serum concentrations should be monitored, however, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be reduced.

DURATION OF THERAPY

The duration of therapy varies according to the course of the disease. As with antibiotic therapy in general, administration of Ceftriaxone should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

COMBINATION THERAPY

Synergy between Ceftriaxone and aminoglycosides has been demonstrated with many Gram-negative bacilli under experimental conditions. Although enhanced activity of such combinations is not always predictable, it should be considered in severe, life-threatening infections due to microorganisms such as Pseudomonas aeruginosa. Because of physical incompatibility the two medicines must be administered separately at the recommended dosages.

DIRECTIONS FOR USE

Reconstituted solutions retain their phycical and chemical stability for six hours at controlled room temperature (20-25 °C) and for 24 hours in a refrigerator at 2 -8 °C temperature. As a genral rule, however the solution should be used immediately after preparation. They range in colour from pale yellow to amber, depending on the concentration and the length of storage. This characteristic of active ingredient is of no significance for the efficacy or tolerance of the drug.

Intramuscular Injection

Trijject® 250 Intramuscular Injection: Add 2 mL of 1% Lidocaine HCl Solution for Injections USP to 250 mg vial and shake. Then it should be slowly injected well within the body of a relatively large muscle over a three to five minutes period.

Trijject® 500 Intramuscular Injection: Add 2 mL of 1% Lidocaine HCl Solution for Injections USP to 500 mg vial and shake. Then it should be slowly injected well within the body of a relatively large muscle over a three to five minutes period.

Trijject® 1 g Intramuscular Injection: Add 4 mL of 1% Lidocaine HCl Solution for Injections USP to 1 g vial and shake. Then it should be slowly injected well within the body of a relatively large muscle over a three to five minutes period.

Note: It is recommended that not more than 1 g to be injected at one site. The Lidocaine HCl Solution must never be administered intravenously.

Intravenous Injection

Trijject® 250 Intravenous Injection: Add 5 mL of sterile Water for Injections USP to 250 mg vial and shake. Then it should be slowly injected directly into a vein over a two to four minutes period.

Trijject® 500 Intravenous Injection: Add 5 mL of sterile Water for Injections USP to 500 mg vial and shake. Then it should be slowly injected directly into a vein over a two to four minutes period.

Trijject® 1 g Intravenous Injection: Add 10 mL of sterile Water for Injections USP to 1 g vial and shake. Then it should be slowly injected directly into a vein over a two to four minutes period.

Trijject® 2 g Intravenous Injection: Add 20 mL of sterile Water for Injections USP to 2 g vial and shake. Then it should be slowly injected directly into a vein over a two to four minutes period.

Intravenous infusion

The infusion should last at least 30 minutes. For IV infusion, 2 g Ceftriaxone is dissolved in 40 mL of one of the following calcium-free infusion solutions: sodium chloride 0.9%, sodium chloride 0.45% + dextrose 2.5%, dextrose 5%, dextrose 10%, dextran 6% in dextrose 5%, hydroxyethyl starch 6-10% infusions, sterile water for injections. Ceftriaxone solutions should not be mixed with or piggybacked into solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, owing to possible incompatibility.

CONTRAINDICATION

Ceftriaxone is contraindicated in patients with known hypersensitivity to Ceftriaxone or the excipients or to the cephalosporin class of antibiotics. Trijject is also contraindicated in porphyria, neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding.

PRECAUTIONS

Penicillin sensitivity, severe renal impairment, pregnancy and breast-feeding, false positive urinary glucose (if tested for reducing substances) and false positive Coombs' test, hepatic impairment if accompanied by renal impairment, premature neonates, may displace bilirubin from serum albumin, administer over 60 minutes in neonates, treatment longer than 14 days, renal failure, dehydration, or concomitant total parenteral nutrition-risk of Ceftriaxone precipitation in gall bladder.

USE IN PREGNANCY AND LACTATION

Pregnancy: The safety of Ceftriaxone in pregnancy has not been established, so the drug should not be used in pregnancy (particularly in the first trimester) unless absolutely indicated.

Nursing mothers: Ceftriaxone is secreted in breast milk at low concentration and caution is advised in nursing mothers.

SIDE-EFFECTS

Ceftriaxone is generally well tolerated. A few side-effects such as gastrointestinal effects including diarrhoea, nausea, vomiting, stomatitis & glossitis; hypersensitivity reactions including rash, pruritis, fever or chills; hematologic reactions including eosinophilia, thrombocytosis, leukopenia, anemia, hemolytic anemia and neutropenia; hepatic reactions including elevations of SGOT or SGPT, pancreatitis; CNS including headache and dizziness were reported.

ADVERSE EFFECT

Risk of convulsions and Involuntary movements. Before administering the total dose into patient, apply a test dose to check convulsion. If no symptom of convulsion is observed then administer the total dose slowly.

DRUG INTERACTION

No drug interactions have been observed with diuretics or with aminoglycosides.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Keep out of reach of children. Reconstituted solution is stable for 6 hours at controlled room temperature (20-25 °C) and for 24 hours in a refrigerator at 2-8 °C temperature.

PACKAGING

Trijject® 250 IM Inj : Box containing one vial of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 250 mg and one ampoule of 2 mL1% Lidocaine HCl USP as solvent for Injection.

Trijject® 250 IV Inj : Box containing one vial of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 250 mg and one ampoule of 5 mL Sterile Water for Injection USP.

Trijject® 500 IM Inj : Box containing one vial of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 500 mg and one ampoule of 2 mL 1% Lidocaine HCl USP as solvent for Injection.

Trijject® 500 IV Inj : Box containing one vial of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 500 mg and one ampoule of 5 mL Sterile Water for Injection USP.

Trijject® 1g IM Inj : Box containing one vial or five vials of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 1g and one ampoule or five ampoules of 4 mL 1% Lidocaine HCl USP as solvent for Injection.

Trijject® 1g IV Inj : Box containing one vial or five vials of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 1g and one ampoule or five ampoules of 10 mL Sterile Water for Injection USP.

Trijject® 2 g IV Inj : Box containing one vial or three vials of sterile Ceftriaxone Sodium USP equivalent to Ceftriaxone 2 g and two ampoules or six ampoules of 10 mL Sterile Water for Injection USP.

Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
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