Ceftriaxone for Injection, USP

**Dosage and Administration**

Ceftriaxone for injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

**Table 1.** Mean Plasma Ceftriaxone Levels in Healthy Subjects Following IV and IM Administration of Various Doses

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>IM 0.5 g</th>
<th>IM 1 g</th>
<th>IM 2 g</th>
<th>IV 0.5 g</th>
<th>IV 1 g</th>
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**Half-Life**

In an adult following administration of a 50 mg/kg IM dose, the mean (±SD) half-life was 5.8 ± 1.5 hours.

**Volume of Distribution (mL/kg)**

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<tr>
<th>Dose (mg/kg)</th>
<th>IM 0.5 g</th>
<th>IM 1 g</th>
<th>IM 2 g</th>
<th>IV 0.5 g</th>
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**Creatinine Clearance**

The results of **Table 3** indicate that ceftriaxone is highly bound to plasma proteins. The mean (±SD) plasma clearance and volume of distribution after a 50 mg/kg IV dose are also shown in Table 3.

**Table 2.** Mean Plasma Ceftriaxone Levels in Healthy Subjects Following IV and IM Administration of Various Doses

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**Susceptibility Test Methods**

* Gram-positive bacteria
  - *Staphylococcus aureus*
  - *Streptococcus pyogenes*
  - *Porphyromonas (Bacteroides) melaninogenicus*
  - *Peptostreptococcus species*

* Gram-negative bacteria
  - *Citrobacter freundii*
  - *Haemophilus influenzae*
  - *Haemophilus parainfluenzae*
  - *Klebsiella pneumoniae*
  - *Klebsiella oxytoca*
  - *Providencia*

**Resistance to Ceftriaxone**

Resistance to ceftriaxone is primarily through hydrolysis by beta-lactamase. Resistance can also occur due to target modification or an altered outer membrane composition.

**Pharmacokinetics in Special Populations**

**Hyperbilirubinemic Neonates, Especially Prematures**

Hyperbilirubinemic neonates, especially preterms, should not be expected to require treatment with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition because of the risk of precipitation of ceftriaxone-calcium (see **Table 3**).

**Patients With Renal Impairment**

In some of these cases, the same intravenous infusion line was used for both ceftriaxone and calcium-containing fluids and in some a precipitate was observed, including in patients with hypercalcemia. In an expected to require treatment with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition because of the risk of precipitation of ceftriaxone-calcium (see **Table 3**).

**Hypersensitivity**

Antibiotics should be administered with caution to any patient known to have hypersensitivity to cephalosporins. Inquiries should be made to determine whether the patient has been previously exposed. Appropriate therapy for the anemia should be carried out.

**Ceftriaxone Associated Anemia**

An immune mediated hemolytic anemia has been observed in patients previously exposed.

**Caution for Use**

Ceftriaxone for injection is contraindicated in patients with known or suspected cephalosporin allergy. Anaphylactic and other severe reactions to cephalosporins have been observed in patients with no history of cephalosporin allergy.

**General**

**Cephalosporin Associated Anemia**

Ceftriaxone is generally well tolerated and few side effects have been observed. However, an immune mediated hemolytic anemia has been observed in patients previously exposed. A report of ceftriaxone associated anemia has been observed in a patient with a history of cephalosporin allergy.

**Nephrotoxicity**

Prolonged use of ceftriaxone may result in overgrowth of nonsusceptible flora.

**Prolonged Prothrombin Time**

A report of prolonged prothrombin time is prolonged before or during therapy.

**Hypersensitivity Reaction**

Hypersensitivity reactions have been reported. The diagnosis of a cephalosporin associated anemia should be considered when patients experience anemia and other effects suggestive of a cephalosporin associated anemia. The diagnosis of a cephalosporin associated anemia may be confirmed by the following: a measured or calculated serum creatinine level.

**Acute Renal Failure**

A report of acute renal failure has been observed in patients with known or suspected cephalosporin allergy.

**Pseudomembranous Colitis**

A report of pseudomembranous colitis has been observed in patients with known or suspected cephalosporin allergy.

**Gastrointestinal Effects**

A report of gastrointestinal effects has been observed in patients with known or suspected cephalosporin allergy.

**Neutropenia**

A report of neutropenia has been observed in patients with known or suspected cephalosporin allergy.

**Infections Caused by Antimicrobially Resistant Organisms**

The following organisms have been observed to be resistant to ceftriaxone: *Salmonella typhi*, *Shigella sonnei*, *Neisseria gonorrhoeae*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.
compatibility studies have been conducted with the Flagyl® IV RTU® (metronidazole hydrochloride). The concentration should not exceed 5 to 7.5 mg/mL admixture as precipitation will occur.

Further dilute a reconstituted vial for IV administration. Particulate for suspension may be vortexed or gently shaken for distribution of the contents. (A sterile substance which must be further diluted before parenteral administration.)

The solution that has been transferred into a container varies according to the administration line. Ceftriaxone must not be administered simultaneously with other drugs through the same line.

The duration of therapy is 4 to 14 days; in complicated infections, longer therapy may be required. Following the completion of therapy, a follow-up course of oral therapy may be indicated as appropriate for the infection.

If seizures associated with ceftriaxone administration occur, the patient should be treated as indicated by the clinical situation. Generally, convulsions lasting less than 30 minutes can usually be managed with intravenous administration of diazepam or benzodiazepines. Convulsions greater than 30 minutes or repeated seizures should be treated with phenytoin or phenobarbital. The use of i.v. diazepam should be monitored closely since i.v. diazepam can lower the seizure threshold.

The therapeutic dose be 100 mg/kg (not to exceed 4 grams). Thereafter, a total cumulative dose of 2 grams may be given over several days if indicated.

Pediatric Patients:

Neonates:

Therapeutic doses to 100 mg/kg of body weight can be given initially. The dosage should be continued for at least 10 days.

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 cumulative dose of 2 grams may be given over several days if indicated.

Gastrointestinal:

Diarrhea and vomiting may occur. In some patients, the diarrhea may be antibiotic associated pseudomembranous colitis. Ceftriaxone is not associated with an increased risk of pseudomembranous colitis compared to other cephalosporins. Infections caused by Clostridium difficile should be treated with metronidazole or vancomycin.

The use of i.v. diazepam can lower the seizure threshold.

There may be reports of rash (1.7%). Less frequently reported (<1%) were pruritus, fever or thrombocytopenia. There have been no reports of an interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and oral anticoagulants in patients with histories of significant anticoagulant therapy.

Treatment of overdosage should be symptomatic. In the case of overdosage, drug concentration would not be reduced by hemodialysis or peritoneal dialysis.

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In addition to the adverse reactions reported during clinical trials, the occurrence of these reactions is too infrequent to be reliably estimated when used in combination with other agents. The possibility of superinfection exists. The presence of Gram-negative bacilli has been reported in cases of fever caused by Staphylococcus species and the development of a Gram-negative superinfection is presumably related to the mechanism of action of the antibiotic.

Superinfections may be caused by fungi or other local pathogens or pathogens in the body. It is generally recommended that antibiotic therapy be continued for at least 10 days following recovery from infection to prevent superinfection. In patients treated with ceftriaxone, the possibility of infection with Pseudomonas species or other Gram-negative bacilli should be considered. Infections caused by Pseudomonas species have been reported.

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