PREScribing INFORMATION

PrCeftriaxone for Injection USP
(IM / IV Use)

250 mg, 1 g, 2 g and 10 g ceftriaxone per vial
(as Ceftriaxone Sodium)
Antibiotic

Hospira Healthcare Corporation
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St. Laurent (Quebec)
H4M 2X6

Made in: Canada

Manufactured by:
Hospira Healthcare India Pvt. Ltd.
Irungattukottai - 602 105
India

Distributed by:
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Date of Preparation: November 12, 2010
Control number: 140672
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**Antibiotic**

**ACTION**

*In vitro* studies indicate that the bactericidal action of ceftriaxone results from the inhibition of cell-wall synthesis. In *E. coli*, ceftriaxone showed a high affinity for penicillin binding proteins (PBP) 1a and 3 and a moderate affinity for 1b and 2. In *H. influenzae*, the highest affinity was shown for PBP 4 and PBP 5. The binding affinity to PBP 4 was 35-fold that of PBP 3, 10-fold that of PBP 2 and approximately 100-fold that of PBP 1. The morphological changes resulting from the PBP binding include filament formation or cell wall and septal thickening, and then cell lysis.

**INDICATIONS AND CLINICAL USES**

The treatment of the following infections when caused by susceptible strains of the designated micro-organisms:

**Lower Respiratory tract infections** caused by *E. coli*, *H. influenzae*, *K. pneumoniae* and species, *Staph. aureus*, *Strep. pneumoniae* and species (excluding enterococci).

**Urinary tract infections** (complicated and uncomplicated) caused by *E. coli*, *Klebsiella* species, *P. mirabilis* and *P. vulgaris*.

**Bacterial Septicemia** caused by *E. coli*, *H. influenzae*, *K. pneumoniae*, *Staph. aureus* and *Strep. pneumoniae*, (excluding enterococci).

**Skin and Skin Structure Infections** caused by *K. pneumoniae* and species, *P. mirabilis*, *Staph. aureus*, *Staph. epidermidis* and *Streptococcus* species (excluding enterococci).

**Bone and Joint Infections** caused by *Staph. aureus*, *Strep. pneumoniae* and *Streptococcus* species (excluding enterococci).

**Intra-Abdominal Infections** caused by *E. coli* and *K. pneumoniae*.

**Meningitis** caused by *H. influenzae*, *N. meningitidis*, and *Strep. pneumoniae*. Ceftriaxone for injection USP should not be used for the treatment of meningitis caused by *L. monocytogenes*. 
Uncomplicated Gonorrhea (cervical/urethral, pharyngeal and rectal) caused by *N. gonorrhoeae* (penicillinase and nonpenicillinase producing strains).

Susceptibility Testing: Specimens for bacteriologic culture should be obtained prior to therapy in order to identify the causative organisms and to determine their susceptibilities to ceftriaxone. Therapy may be instituted before results of susceptibility testing are known. However, modification of the treatment may be required once these results become available.

Prophylaxis: The preoperative administration of a single 1 g dose of ceftriaxone sodium may reduce the incidence of postoperative infections in patients undergoing vaginal or abdominal hysterectomy, coronary artery bypass surgery, or in patients at risk of infection undergoing biliary tract surgery. If signs of post surgical infection should appear, specimens for culture should be obtained for identification of the causative organism(s) so that the appropriate therapy may be instituted.

**CONTRAINDICATIONS**

Ceftriaxone for Injection USP is contraindicated in patients with known hypersensitivity to ceftriaxone sodium or any component of the container, other cephalosporins or penicillins (see **WARNINGS**).

Hyperbilirubinemic neonates and preterm neonates should not be treated with ceftriaxone. *In vitro* studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin, leading to a possible risk of bilirubin encephalopathy in these patients (see **PRECAUTIONS**).

Ceftriaxone for Injection USP is contraindicated in neonates (≤28 days old) if they require (or are 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 **WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, PHARMACEUTICAL INFORMATION, and PHARMACOLOGY**).

**WARNINGS**

Hypersensitivity

Before therapy with ceftriaxone sodium is instituted, careful inquiry should be made concerning previous hypersensitivity reactions to ceftriaxone, other cephalosporins, penicillins or other allergens. Ceftriaxone for Injection USP should only be administered with caution to any patient who has demonstrated any form of allergy particularly to drugs. As with other cephalosporins, anaphylactic reactions with fatal outcome have been reported, even if a patient is not known to be allergic or previously exposed. Ceftriaxone for Injection USP should be administered with caution to patients with type I hypersensitivity reaction to penicillin. Cross-hypersensitivity among p-lactam antibiotics have been clearly documented and may
occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction occurs, the administration of Ceftriaxone for Injection USP should be discontinued and appropriate therapy instituted (see CONTRAINDICATIONS and ADVERSE REACTIONS).

Hemolytic Anemia

CEFTRIAXONE FOR INJECTION USP SHOULD NOT BE USED IN PATIENTS WITH A HISTORY OF CEPHALOSPORIN-ASSOCIATED HEMOLYTIC ANEMIA SINCE THE RECURRENCE OF HEMOLYSIS IS MUCH MORE Severe.

An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class antibacterials, including ceftriaxone. Severe cases of hemolytic anemia, including fatalities, have been reported in both adults and children. If a patient develops anemia anytime during, or within 2-3 weeks subsequent to the administration of ceftriaxone, the diagnosis of a cephalosporin-associated anemia should be considered and the drug discontinued until the etiology is determined.

Patients who receive prolonged or frequent courses of Ceftriaxone for Injection USP may benefit from periodic monitoring for signs and symptoms of hemolytic anemia, including measurement of haematological parameters or drug-induced antibody testing, where appropriate (see ADVERSE REACTIONS).

Clostridium Difficile-Associated Disease

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including ceftriaxone. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of Clostridium difficile. Clostridium difficile produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against Clostridium difficile. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against Clostridium difficile. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases (see ADVERSE REACTIONS).
Interaction with Calcium-Containing Products

Do not use diluents containing calcium, such as Ringer’s solution or Hartmann’s solution, to reconstitute Ceftriaxone for Injection USP vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when Ceftriaxone for Injection USP is mixed with calcium-containing solutions in the same IV administration line. Ceftriaxone for Injection USP must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, Ceftriaxone for Injection USP and calcium-containing solutions may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid. In vitro studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone calcium (see CONTRAINDICATIONS, ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, and PHARMACOLOGY).

Though no reports of intravascular calcium-ceftriaxone precipitates have been reported in other than neonatal patients treated with ceftriaxone and calcium-containing intravenous products, caution is nevertheless warranted during intravenous treatment (see INCOMPATIBILITY).

There have been reports of sonographic abnormalities in the gallbladder of patients treated with ceftriaxone sodium; some of these patients also had symptoms of gallbladder disease. These abnormalities appear on sonography as an echo without acoustical shadowing suggesting sludge or as an echo with acoustical shadowing which may be misinterpreted as gallstones. The chemical nature of the sonographically-detected material has been determined to be predominantly a ceftriaxone-calcium salt. The condition appears to be transient and reversible upon discontinuation of ceftriaxone sodium and institution of conservative management. Therefore, Ceftriaxone for Injection USP should be discontinued in patients who develop signs and symptoms suggestive of gallbladder disease and/or the sonographic findings described above. The effect of pre-existing gallbladder disease is not known.

Cases of pancreatitis, possibly of biliary obstruction etiology, have been rarely reported in patients treated with ceftriaxone sodium. Most patients presented with risk factors for biliary stasis and biliary sludge, e.g. preceding major therapy, severe illness and total parenteral nutrition. A trigger or cofactor role of ceftriaxone sodium-related biliary precipitation can not be ruled out.

Ceftriaxone may cause renal lithiasis through precipitation of calcium ceftriaxonate. When using this product in subjects with hypercalciuria or a history of renal lithiasis, benefit must be weighed against risk. Very rare cases of nephrolithiasis (renal precipitation) have been reported, mostly in children older than 3 years and who have been treated with either high daily doses (e.g. ≥80 mg/kg/day) or total doses exceeding 10 grams and presenting other risk factors (e.g. fluid restrictions, confinement to bed, etc.).
This event may be symptomatic, may lead to renal insufficiency, and appears to be reversible upon discontinuation of ceftriaxone sodium.

Sonography for biliary sludge or renal lithiasis is recommended in cases of right hypochondrial and/or abdominal pain. Ceftriaxone for injection USP treatment should be withdrawn to allow signs and symptoms to resolve.

PRECAUTIONS

General
Alterations in prothrombin time (see ADVERSE REACTIONS) and hypoprothrombinemia have occurred rarely in patients treated with ceftriaxone sodium. Patients with impaired vitamin K synthesis or low vitamin K stores (e.g., chronic hepatic disease and malnutrition) may require monitoring of hematology and coagulation parameters during Ceftriaxone for Injection USP treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during treatment.

Prolonged treatment with ceftriaxone sodium may result in overgrowth of non-susceptible organisms and organisms initially sensitive to the drug. Development of resistant organisms during the administration of Ceftriaxone for Injection USP in clinical trials has been observed in 6% of the 94 patients infected with P. aeruginosa, in 33% of 3 patients infected with Citrobacter species and in 10% of the 10 patients infected with Enterobacter species. If superinfection occurs, appropriate measures should be taken.

Ceftriaxone for Injection USP should be administered with caution to individuals with a history of gastrointestinal disease, particularly colitis.

Renal and Hepatic Impairment
Although transient elevations of BUN and serum creatinine have been observed in clinical studies, there is no other evidence that ceftriaxone sodium, when administered alone, is nephrotoxic.

In severe renal impairment (creatinine clearance of less than 10 mL/min), periodic monitoring of serum ceftriaxone concentrations is recommended. The maximum daily dose should not exceed 2 g. In severe renal impairment associated with clinically significant hepatic impairment, close monitoring of serum ceftriaxone concentrations, at regular intervals, is recommended. If there is evidence of accumulation, dosage should be decreased accordingly.

Interactions
Interactions between ceftriaxone sodium and other drugs have not been fully evaluated.
Pregnancy

The safety of ceftriaxone sodium in the treatment of infections during pregnancy has not been established. Ceftriaxone sodium should only be used during pregnancy if the likely benefit outweighs the potential risk to the fetus and/or the mother. Ceftriaxone has been detected in the umbilical cord blood, amniotic fluid and placenta. At parturition, 1 hour after a 2 g I.V. dose of Ceftriaxone for Injection USP, average ceftriaxone concentrations in maternal serum, umbilical cord serum, amniotic fluid, and placenta were 106 ± 40 μg/mL, 19.5 ± 11.5 μg/mL, 3.8 ± 3.2 μg/mL and 20.9 ± 4.4 μg/g.

Nursing Mothers

Ceftriaxone is excreted in human milk at low concentrations, (e.g., the peak concentration of total drug in milk ranged between 0.45 to 0.65 μg/mL, approximately five hours after the administration of 1 g I.V. or I.M.). The clinical significance of this is unknown, therefore, caution should be exercised when Ceftriaxone for Injection USP is administered to a nursing mother.

Neonates

The safety of ceftriaxone sodium in neonates (birth to 28 days of age) has not been established (see HUMAN PHARMACOLOGY). In vitro studies have shown that ceftriaxone can displace bilirubin from serum albumin. Ceftriaxone for Injection USP should not be used in neonates (especially prematures), at risk of developing bilirubin encephalopathy (see CONTRAINDICATIONS).

Elderly Patients

The elimination of ceftriaxone may be reduced in elderly patients possibly due to impairment of both renal and hepatic function (see HUMAN PHARMACOLOGY).

Drug-Laboratory Test Interactions

Ceftriaxone may interfere with urine glucose determinations utilizing the copper-reduction test (Clinitest), but not utilizing the glucose-oxidase test (Diastix or Tes Tape). In patients treated with Ceftriaxone for Injection USP the Coombs’ test may rarely become false-positive; and ceftriaxone, like other antibiotics, may result in false-positive tests for galactosemia.

ADVERSE REACTIONS

During clinical trials and post-marketing experience with ceftriaxone sodium the following adverse reactions have been observed:
Clinical Adverse Experiences

**Dermatological:** Rash (1.3%); exanthema, allergic dermatitis and pruritis (0.1 - 1.0%); urticaria (post-marketing reports). Isolated cases of severe cutaneous adverse reactions (erythema multiforme, Stevens Johnson Syndrome, or Lyell’s Syndrome/toxic epidermal necrolysis) have also been reported.

**Hematological:** Anemia (0.1 - 1.0%); auto-immune hemolytic anemia and serum sickness (< 0.1%); immune hemolytic anemia (post-marketing reports - see WARNINGS for more information on hemolytic anemia); granulocytopenia (post-marketing reports). Isolated cases of agranulocytosis (<500/mm³) have been reported, most of them after 10 days of treatment and following total doses of 20g or more.

**Hepatic:** Jaundice, reports (in asymptomatic and symptomatic patients) of ultrasonographic shadows suggesting precipitations in the gallbladder and reports of gallbladder sludge (< 0.1%).

**Urogenital:** Moniliasis and vaginitis (0.1 - 1.0%); oliguria and nephrolithiasis (post-marketing reports).

**Gastrointestinal:** Diarrhea (3.3%); nausea, vomiting, dysgeusia and gastric pain (0.1 - 1.0%); abdominal pain, colitis, flatulence, dyspepsia, pseudomembranous colitis and stomatitis (< 0.1%); glossitis (post-marketing reports).

**Neurological:** Dizziness and headache (0.1 - 1.0%); ataxia and paresthesia (< 0.1%).

**Miscellaneous:** Fever, chills, diaphoresis, malaise, burning tongue, flushing, edema and anaphylactic shock (0.1 - 1.0%); bronchospasm, palpitations and epistaxis (< 0.1%); glottic/laryngeal edema (post-marketing reports).

**Local Reactions at Injection Site:** Pain (9.4%)a, induration and tenderness (1 - 2%); phlebitic reactions (0.1 - 1.0%); thrombophlebitis (< 0.1%).

a Pain on intramuscular injection is usually mild and less frequent when the drug is administered in sterile 1% Lidocaine solution.

**Laboratory Abnormalities**

**Hematologic:** Eosinophilia (4.6%), thrombocytosis (5.1%), leukopenia (2.0%); neutropenia, lymphopenia, thrombocytopenia, increase or decrease in hematocrit, prolongation of prothrombin time and decrease in hemoglobin (0.1 - 1.0%); leucocytosis, lymphocytosis, monocytosis, basophilia and decrease in prothrombin time (< 0.1%). (See PRECAUTIONS for information on alterations in prothrombin time.)

**Hepatic:** Increase in AST (SGOT) (4.0%)b, ALT (SGPT) (4.8%)b, increase in alkaline phosphatase (1.0%); increase in bilirubin (0.1 - 1.0%).
Urinary: Increase in BUN (1.1%)\textsuperscript{c}; increase in creatinine, erythrocyturia, proteinuria and presence of casts in urine (0.1 - 1.0%); glycosuria (< 0.1%).

\textsuperscript{b} Incidence is more frequent in patients less than one year old.
\textsuperscript{c} Incidence is more frequent in patients less than one year old and over 50 years old.

**Post-Market Adverse Drug Reactions**

A small number of cases of fatal outcomes in which a crystalline material was observed in the lungs and kidneys at autopsy have been reported in neonates receiving Ceftriaxone for Injection and calcium-containing fluids. In some of these cases, the same intravenous infusion line was used for both Ceftriaxone for Injection and calcium-containing fluids and in some a precipitate was observed in the intravenous infusion line. At least one fatality has been reported in a neonate in whom Ceftriaxone for Injection and calcium-containing fluids were administered at different time points via different intravenous lines; no crystalline material was observed at autopsy in this neonate. There have been no similar reports in patients other than neonates.

**SYMPTOMS AND TREATMENT OF OVERDOSE**

Ultrasonographic shadows suggesting precipitations in the kidneys accompanied by calcium ceftriaxone precipitate in the urine was observed in one patient dosed with ceftriaxone sodium at 10 g/day (2.5 times the maximum recommended dose). No other case of overdosage has been reported to date with Ceftriaxone for Injection USP. No specific information on symptoms or treatment is available. Excessive serum concentration of ceftriaxone cannot be reduced by hemodialysis or peritoneal dialysis. Treatment should be symptomatic.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

**DOSAGE AND ADMINISTRATION**

Ceftriaxone for Injection USP may be administered intravenously or intramuscularly after reconstitution.

Dosage and route of administration should be determined by the severity of infection, susceptibility of the causative organisms, and condition of the patient. The intravenous route is preferable for patients with septicemia or other severe or life-threatening infections.
DOSAGE

Adults

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Route</th>
<th>Dose</th>
<th>Frequency</th>
<th>Total Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate and Severe Infections</td>
<td>I.V. or I.M.</td>
<td>1 or 2 g</td>
<td>q24h</td>
<td>1 or 2 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 or 1 g</td>
<td>q12h</td>
<td>1 or 2 g</td>
</tr>
</tbody>
</table>

There is limited experience with daily doses of 3-4 g administered as a single dose or two equally divided doses. The total daily dose should not exceed 4 g.

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Route</th>
<th>Dose</th>
<th>Frequency</th>
<th>Total Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated Gonorrhea</td>
<td>I.M.</td>
<td>250 mg</td>
<td>Single Dose</td>
<td></td>
</tr>
</tbody>
</table>

Infants and children (One Month to 12 years of Age)

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Route</th>
<th>Dose</th>
<th>Frequency</th>
<th>Total Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Miscellaneous Infections</td>
<td>I.V. or I.M.</td>
<td>25 or 37.5 mg/kg</td>
<td>q12h</td>
<td>50 or 75 mg/kg</td>
</tr>
</tbody>
</table>

The total daily dose should not exceed 2 g. If body weight is 50 kg or more the adult dose should be used.

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Route</th>
<th>Dose</th>
<th>Frequency</th>
<th>Total Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>I.V. or I.M.</td>
<td>50 mg/kg*</td>
<td>q12h</td>
<td>100 mg/kg</td>
</tr>
</tbody>
</table>

*With or without a loading dose of 75 mg/kg. The total daily dose should not exceed 4 g.

With the exception of gonorrhea, which is treated with a single dose, the administration of Ceftriaxone for Injection USP should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained, usually 4 to 14 days. In bone and joint infections the average duration of treatment during clinical trials was 6 weeks, with a range of 1 to 13 weeks, depending on the severity of the infection.

When treating infections caused by beta hemolytic streptococcus, it is recommended that therapy be continued for at least 10 days. The average duration of therapy for infections associated with beta hemolytic streptococcus during clinical trials was 2 weeks, with a range of 1 to 5 weeks, depending on the site and severity of the infection.

Prophylaxis (Vaginal or Abdominal Hysterectomy, Coronary Artery Bypass Surgery, Biliary Tract Surgery): For preoperative use as prophylaxis before vaginal or abdominal hysterectomy, coronary artery bypass surgery, or biliary tract surgery in patients at risk of infection, a single dose of 1 g administered 1/2 to 2 hours before surgery is recommended.

Impairment of Renal and/or Hepatic Function: In patients with mild to moderate renal impairment, changes in the dosage regimen are not required, provided liver function is
not impaired. In cases of preterminal renal failure (creatinine clearance less than 10 mL/min), periodic monitoring of serum ceftriaxone concentrations is recommended. The daily dosage should be limited to 2 g or less. In patients with liver damage, there is no need for the dosage to be reduced provided renal function is not impaired. In cases of coexistent renal and clinically significant hepatic insufficiency, close monitoring of serum ceftriaxone concentrations, at regular intervals, is recommended. If there is evidence of accumulation, dosage should be decreased accordingly.

ADMINISTRATION

Intramuscular: The reconstituted solution of Ceftriaxone for Injection USP should be administered by deep intragluteal injection. It is recommended that not more than 1 g be injected at a single site.

Intravenous (bolus) Injection: The reconstituted solution should be administered over approximately 5 minutes. If the distal port of an intravenous administration set is used, stop the primary flow, inject the reconstituted Ceftriaxone for Injection USP solution and then restart the primary flow. This will prevent mixing with the primary fluid and possible incompatibilities.

Short Intravenous Infusion: The further diluted intravenous solution should be given over a period of 10 to 15 minutes in infants and children and 20 to 30 minutes in adults.

NOTE: Ceftriaxone for Injection USP solution should not be physically mixed with aminoglycoside antibiotics nor administered at the same site because of possible chemical incompatibility. There have also been literature reports of physical incompatibilities between ceftriaxone and vancomycin, amsacrine, or fluconazole.

Do not use diluents containing calcium, such as Ringer’s solution or Hartmann’s solution, to reconstitute Ceftriaxone for Injection USP vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when Ceftriaxone for Injection USP is mixed with calcium-containing solutions in the same IV administration line. Ceftriaxone for Injection USP must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid (see CONTRAINDICATIONS and WARNINGS).

There have been no reports of an interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products (IV or oral).

SPECIAL HANDLING INSTRUCTIONS
Disposal of syringes/sharps

The following points should be strictly adhered to regarding the use and disposal of syringes and other medicinal sharps:

- Needles and syringes should never be reused.
- Place all used needles and syringes into a sharps container (puncture-proof disposable container).
- Keep this container out of the reach of children.
- Placing used sharps containers in the household waste should be avoided.
- Dispose of the full container according to local requirements or as instructed by your healthcare provider.

Disposal of unused/expired medicines

The release of pharmaceuticals in the environment should be minimized. Medicines should not be disposed of via wastewater, and disposal through household waste should be avoided. Use established 'collection systems' if available at your location.
PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

Proper Name: ceftriaxone sodium

Chemical Name: (6R,7R)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-[[1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-as-triazin-3-yl)-thio]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7\(^2\)-(Z)-(O-methyloxime, disodium salt, sesquaterhydrate.

Structural Formula:

![Structural Formula]

Molecular Formula: C\(_{18}\)H\(_{16}\)N\(_{8}\)Na\(_{2}\)O\(_{7}\)S\(_{3}\) 3.5H\(_{2}\)O

Molecular Weight: 661.61

Description: Ceftriaxone sodium is a white to pale yellow crystalline powder, soluble in water and methanol, insoluble in other common solvents.

DRUG PRODUCT

Composition: Ceftriaxone for Injection USP vials contain ceftriaxone sodium (expressed in terms of anhydrous free acid). The sodium content of each gram of Ceftriaxone for Injection USP is approximately 83 mg (3.6 mEq sodium ion). The pH of freshly reconstituted solutions usually ranges from 6 to 8. Solutions are yellowish in colour.
RECONSTITUTION

For Intramuscular Use

Reconstitute Ceftriaxone for Injection USP powder with the appropriate diluent:

- Sterile Water for Injection
- 0.9% Sodium Chloride Injection
- 5% Dextrose Injection
- Bacteriostatic Water for Injection
- 1% Lidocaine Solution

Reconstitute as follows:

**Regular Volume Reconstitution Table (I.M.)**

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Volume to be Added to Vial mL</th>
<th>Approximate Available Volume mL</th>
<th>Approximate Average Concentration g/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 g</td>
<td>0.9</td>
<td>1.0</td>
<td>0.25</td>
</tr>
<tr>
<td>1.0 g</td>
<td>3.3</td>
<td>4.0</td>
<td>0.25</td>
</tr>
<tr>
<td>2.0 g</td>
<td>6.6</td>
<td>8.0</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Shake well until dissolved

**Low Volume Reconstitution Table (I.M.)**

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Volume to be Added to Vial mL</th>
<th>Approximate Available Volume mL</th>
<th>Approximate Average Concentration g/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 g</td>
<td>Not recommended for this vial size.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0 g</td>
<td>2.2</td>
<td>2.8</td>
<td>0.35</td>
</tr>
<tr>
<td>2.0 g</td>
<td>4.4</td>
<td>5.6</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Shake well until dissolved.

**NOTE:** SOLUTIONS PREPARED FOR INTRAMUSCULAR USE OR ANY
SOLUTION CONTAINING LIDOCAINE OR BACTERIOSTATIC WATER FOR INJECTION SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

For Intravenous Use

- Reconstitute only with Sterile Water for Injection.
- Reconstitute as follows:

Reconstitution Table (I.V.)

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Volume to be Added to Vial mL</th>
<th>Approximate Available Volume mL</th>
<th>Approximate Average Concentration g/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 g</td>
<td>2.4</td>
<td>2.5</td>
<td>0.1</td>
</tr>
<tr>
<td>1.0 g</td>
<td>9.6</td>
<td>10.1</td>
<td>0.1</td>
</tr>
<tr>
<td>2.0 g</td>
<td>19.2</td>
<td>20.5</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Shake well until dissolved. The prepared solution may be further diluted to the desired volume with any of the “Solutions for I.V. Infusion” listed below.

Solutions for I.V. Infusion

- 0.9% Sodium Chloride Injection
- 5% Dextrose Injection
- Dextrose and Sodium Chloride Injection

Pharmacy Bulk Vial Reconstitution for Preparation of Intravenous Infusion Solutions

The closure of the pharmacy bulk vial shall be penetrated only one time after reconstitution, using a suitable sterile transfer device or dispensing set which allows measured dispensing for the contents.

Reconstitution Table for Bulk Pharmacy Vial

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Volume to be Added to Vial mL</th>
<th>Approximate Available Volume mL</th>
<th>Approximate Average Concentration g/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 g</td>
<td>95</td>
<td>101</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Shake well until dissolved. Withdraw the required amount and dilute with one of the “Solutions for I.V. Infusion”. Any unused solution remaining within a period of 8 hours should be discarded.

Stability and Storage Recommendations

Ceftriaxone for Injection USP sterile powder should be stored at a controlled room temperature (between 15 and 30°C) and protected from light.
Reconstituted Solutions – Stability and Storage Recommendations

1. For Intramuscular Use:
   Solutions should be reconstituted immediately before use. If storage is required, these solutions may be stored under refrigeration and should be used within 48 hours.

2. For I.V. Bolus Injection (without further dilution):
   Reconstituted solutions should be administered within 24 hours when stored at room temperature and within 72 hours when refrigerated (2-8°C).

3. For I.V. Infusion:
   Further diluted reconstituted solutions should be administered within 24 hours when stored at room temperature.
   a) Solutions further diluted with 0.9% Sodium Chloride Injection, or with 5% Dextrose Injection should be administered within 72 hours when stored under refrigeration (2-8°C).
   b) Solutions further diluted with Dextrose and Sodium Chloride Injection as diluent should not be refrigerated. These solutions are not physically compatible when refrigerated.

4. Extended Use of Intravenous Admixtures:
   Although intravenous admixtures may often be physically and chemically stable for longer periods, DUE TO MICROBIOLOGICAL CONSIDERATIONS, THEY ARE USUALLY RECOMMENDED FOR USE WITHIN A MAXIMUM OF 24 HOURS AT ROOM TEMPERATURE OR 72 HOURS WHEN REFRIGERATED (2-8°C).
   Hospitals and institutions that have recognized admixture programs and use validated aseptic techniques for preparation of intravenous solutions may extend the storage times for Ceftriaxone for Injection USP admixtures with 0.9% Sodium Chloride Injection or 5% Dextrose Injection in glass or polyvinyl chloride infusion containers, in concentrations of 3-40 mg/mL, to seven days when stored under refrigeration (2-8°C).

   WARNING: As with all parenteral drug products, intravenous admixtures should be visually inspected prior to administration, whenever solution and container permit. Solutions showing any evidence of haziness or cloudiness, particulate matter, precipitation, discoloration or leakage should not be used.

5. Frozen I.V. Infusion Solutions:
   Hospitals and institutions that have recognized admixture programs and use validated aseptic techniques for preparation of intravenous solutions may freeze and store Ceftriaxone for Injection USP I.V. infusion solutions when prepared in accordance with the following instructions.
I.V. infusion solutions prepared from reconstituted Ceftriaxone for Injection USP (ceftriaxone sodium) further diluted with 5% Dextrose Injection or 0.9% Sodium Chloride Injection, in flexible polyvinylchloride infusion containers, in concentrations up to 40 mg ceftriaxone per mL, may be stored at –10 to –20°C for periods up to three months.

The frozen solutions should be thawed in a refrigerator (2-8°C) overnight and should subsequently be used within 24 hours when stored at room temperature or seven days when stored under refrigeration (2-8°C).

After thawing, check for leaks by squeezing the bag firmly. If leaks are found, discard the container as sterility may be impaired. Do not use unless the solution is clear and seals/outlet ports are intact. Ceftriaxone solutions range from light yellow to amber in colour. Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever the solution and container permit.

DO NOT REFREEZE the previously frozen ceftriaxone I.V. infusion solutions.

Incompatibility:

Ceftriaxone for Injection USP should not be added to solutions containing calcium such as Hartmann’s solution and Ringer’s solution (see CONTRAINDICATIONS and WARNINGS).

Ceftriaxone for Injection USP should not be physically mixed with other antimicrobial agents, vancomycin, amsacrine, or fluconazole.

Ceftriaxone for Injection USP should not be added to blood products, protein hydrolysates or amino acids.

Availability of Dosage Forms:

1. Ceftriaxone for Injection USP vials containing sterile powder equivalent to 0.25 g, 1 g and 2 g of ceftriaxone.

2. Ceftriaxone for Injection USP Pharmacy Bulk vials containing sterile powder equivalent to 10 g ceftriaxone (not for direct administration). The availability of the pharmacy bulk vial is restricted to hospitals with a recognized intravenous admixture programme.