Cefazolin for Injection, USP

PHARMACY BULK PACK – NOT FOR DIRECT INJECTION

Only

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefazolin for the treatment of other antibacterial drugs, Cefazolin for injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Cefazolin for injection, USP is a semi-synthetic parenteral antibiotic. It is the sodium salt of (6R,7R)-(3S)-7-[[(2-methyl-1,3-thiazol-4-yl)-acetamido]-3-methyl-7-oxo-1-oxa-4-azaspiro[4.5]dec-6-ene-2-carboxylic acid. The molecular formula is C_{15}H_{17}NO_5Na_2. The sodium salt is a white powder. Cefazolin for injection, USP, is supplied in 10 grams Pharmacy Bulks Pack. Each Pharmacy Bulks Pack contains 10 grams of Cefazolin for injection, USP.

Cefazolin is indicated for parenteral use only. After reconstitution with either 45 mL or 96 mL of diluent the concentration is 1 gram Cefazolin per 5 mL or 1 gram Cefazolin per 10 mL, respectively. The pH of the reconstituted solution is between 4.0 and 6.0.

A Pharmacy Bulks Pack is sterile dosage form for parenteral use that contains many single doses. The contents are reserved for use in a pharmacy ambulatory service and are intended for the preparation of admixtures for intravenous use. NOT FOR INJECTION. FURTHER DILUTION IS REQUIRED BEFORE USE.

Stability

Studies have shown that following intravenous administration of Cefazolin to normal volunteers, mean serum concentrations peaked at approximately 185 mcg/mL and were approximately 4 mcg/mL at 24 hours after administration.

CROSS-RESISTANCE AND USAGE

Cefazolin for injection, USP is indicated in the treatment of the following infections due to susceptible organisms:

Respiratory Tract Infections: Due to S. pneumoniae, S. aureus (including methicillin-resistant strains) and S. pyogenes.

Biliary Tract Infections: Due to E. coli, various strains of Staphylococcus, P. mirabilis, and E. coli.

Genital Infections: Due to E. coli, P. mirabilis, E. coli.

Endocarditis: Due to S. aureus and S. pyogenes (including beta-lactamase-producing strains) and S. epidermidis.

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Cefazolin.

Pharmacokinetics

The pharmacokinetics of Cefazolin for injection, USP, have been studied following intravenous and intramuscular administration to healthy volunteers and patients. Cefazolin is rapidly and efficiently absorbed following both routes of administration.

Microbiology

In vitro tests demonstrate that the bactericidal action of cephalosporins results from inhibition of cell wall synthesis. Cefazolin has been shown to be active against most of the strains of the following microorganisms both in vitro and in clinical infections as indicated in the INDICATIONS AND USAGE.

Gram-Positive Aerobes

Staphylococcus aureus (including beta-lactamase-producing strains)

Staphylococcus epidermidis

Streptococcus pyogenes

Streptococcus agalactiae, and other strains of Streptococcus

Streptococcus pneumoniae

In vitro tests have demonstrated that Cefazolin is bactericidal against penicillin-susceptible strains of Staphylococcus aureus and penicillin-resistant strains of Staphylococcus epidermidis. Cefazolin is resistant to acid and is stable in the presence of test drug.

Contraindications

Cefazolin is contraindicated in patients with known ALLERGY TO THE CEPHALOSPORIN GROUP OF ANTIBIOTICS.

BACTERIAL INFECTIONS

BEFORE THERAPY WITH CEFAZOLIN FOR INJECTION USP IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD AN ALLERGY TO PENCILLINS OR OTHER PENICILLIN-RELATED SUBSTANCES. IF AN ALLERGIC REACTION TO A PENICILLIN-RELATED SUBSTANCE HAS OCCURRED, TREATMENT WITH PENCILLINS OR CEPHALOSPORINS SHOULD BE AVOIDED. CROSS HYPERSENSITIVITY BETWEEN MEMBERS OF THE PENCILLIN AND CEPHALOSPORIN GROUPS HAS BEEN REPORTED TO OCCUR IN AS MANY AS 25% OF PATIENTS WITH A HISTORY OF PENCILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEFAZOLIN FOR INJECTION USP OCCURS, DISCONTINUE TREATMENT WITH THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY BE FACILITATED BY SIMULTANEOUS EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTISTAMINES, CORONARY INJURIES, PRESSURIZED AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

Cephalosporins are generally well tolerated. The incidence of reactions is less than that associated with penicillins. Rare cases of anaphylaxis have been reported. No reports of urticaria, angioedema, arthralgia, or arthralgias have been reported. Cefazolin is not associated with the development of pseudomembranous colitis after extended use.

Adverse Reactions

The following reactions have been reported:

GI side effects: Nausea, vomiting, abdominal pain, flatulence, diarrhea, or constipation

Skin reactions: Rashes, pruritus, urticaria, erythema, angioedema

Other reactions: Fever, chills, myalgia, headache, hives

References:

Reference ID: 3246685
treated with cefazolin, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Allergic reactions, urticaria, serum sickness-like reaction, erythema multiforme, toxic epidermal necrolysis, colitis, renal dysfunction, toxic nephropathy, anaphylaxis, reversible hypoprothrombinemia, hypersensitivity, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemoptysis, and suppurative sinusitis.

Altered Laboratory Tests: Prolonged prothrombin time, positive direct Coombs’ test, false-positive test for urinary glucose, elevated bilirubin, elevated LFT, increased creatinine, pancreatitis, and agranulocytosis.

Several cephalosporines have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see DOSAGE AND ADMINISTRATION). If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

To report SUSPECTED ADVERSE EVENTS, contact FDA at 1-800-FDA-1088 or www.fda.gov.

**DOSAGE AND ADMINISTRATION**

### Usual Adult Dosage

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Dose (mg)</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate to severe infections</td>
<td>500 mg to 1 gram</td>
<td>every 6 to 8 hrs.</td>
</tr>
<tr>
<td>Mild infections caused by susceptible gram-positive cocci</td>
<td>250 mg to 500 mg</td>
<td>every 8 hours</td>
</tr>
<tr>
<td>Acute, uncomplicated urinary tract infections</td>
<td>1 gram</td>
<td>every 12 hours</td>
</tr>
<tr>
<td>Pneumococcal pneumonia</td>
<td>500 mg</td>
<td>every 12 hours</td>
</tr>
</tbody>
</table>

In rare instances, doses of up to 12 grams of Cefazolin for injection per day have been used.

### Perioperative Prophylactic Use

To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are:

a. 1 gram IV administered 1/2 hour to 1 hour prior to the start of surgery.

b. For lengthy operative procedures (e.g., 2 hours or more), 500 mg to 1 gram IV during surgery (administration modified depending on the duration of the operative procedure).

c. 500 mg to 1 gram IV every 6 to 8 hours for 24 hours postoperatively.

It is important that (1) the preoperative dose be given just (1/2 to 1 hour) prior to the start of surgery so that adequate antibiotic levels are present in the serum and tissues at the time of initial surgical incision; and (2) Cefazolin for injection be administered, if necessary, at appropriate intervals during surgery to provide sufficient levels of the antibiotic at the anticipated moments of greatest exposure to infective organisms. In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prothetic arthroplasty), the prophylactic administration of Cefazolin for injection may be continued for 3 to 5 days following the completion of surgery.

### Dosage Adjustment for Patients with Reduced Renal Function

Cefazolin for injection may be used in patients with reduced renal function with the following dosage adjustments. Patients with a creatinine clearance of 55 mL/min. or greater or a serum creatinine of 1.5 mg% or less can be given full doses. Patients with creatinine clearance rates of 30 to 54 mL/min. or serum creatinine of 1.6 to 3 mg% can also be given full doses but dosage should be restricted to at least 8 hour intervals. Patients with creatinine clearance rates of 11 to 34 mL/min. or serum creatinine of 3.1 to 4.5 mg% should be given 1/2 the usual dose every 12 hours. Patients with creatinine clearance rates of 10 mL/min. or less or serum creatinine of 4.6 mg% or greater should be given 1/3 the usual dose every 12 to 18 hours. All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection. Patients undergoing peritoneal dialysis: See CLINICAL PHARMACOLOGY.

### Pediatric Dosage

In pediatric patients, a total daily dosage of 25 to 50 mg per kg (approximately 10 to 20 mg per pound) of body weight, divided into 3 or 4 equal doses, is effective for most mild to moderately severe infections. Total daily dosage may be increased to 100 mg per kg (45 mg per pound) of body weight for severe infections. Since safety for use in premature infants and in neonates has not been established, the use of Cefazolin for injection in these patients is not recommended.

In pediatric patients with mild to moderate renal impairment (creatinine clearance of 70 to 40 mL/min.), 60 percent of the normal daily dose given in equally divided doses every 12 hours should be sufficient. In patients with moderate impairment (creatinine clearance of 40 to 20 mL/min.), 25 percent of the normal daily dose given in equally divided doses every 12 hours should be adequate. Pediatric patients with severe renal impairment (creatinine clearance of 20 to 5 mL/min.) may be given 10 percent of the normal daily dose every 24 hours. All dosage recommendations apply after an initial loading dose.

### RECONSTITUTION

**Preparation of Parenteral Solution**

Parenteral drug products should be SHAKE WELL when reconstituted, and inspected visually for particulate matter prior to administration. If particulate matter is evident in reconstituted fluids, the drug solutions should be discarded.

Reconstituted solutions may range in color from pale yellow to yellow without a change in potency.

**Directions for Proper Use of a Pharmacy Bulk Package**

Not for direct infusion. This Pharmacy Bulk Package is for use in a hospital pharmacy admixture service, only in a suitable work area, such as a laminar flow hood. Using aseptic technique, the container may be penetrated only one time after reconstitution using a suitable sterile dispensing set or transfer device that allows measured dispensing of the contents. Use of a syringe and needle is not recommended as it may cause leakage. The withdrawal of container contents should be accomplished without delay. However, should this not be possible, a maximum time of 4 hours from initial closure entry is permitted to complete fluid transfer operations. This time limit should begin with the introduction of the solvent or diluent into the Pharmacy Bulk Package. DISCARD ANY UNUSED PORTION AFTER 4 HOURS.

**Pharmacy Bulk Package**

Ade Sterile Water for Injection, Bacteriostatic Water for Injection, or Sodium Chloride Injection according to the table below. SHAKE WELL. Use promptly. (Discard vial within 4 hours after initial entry).

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>Amount of Diluent</th>
<th>Approximate Concentration</th>
<th>Approximate Available Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 grams</td>
<td>45 mL</td>
<td>1 gram/5 mL</td>
<td>51 mL</td>
</tr>
<tr>
<td>96 mL</td>
<td></td>
<td>1 gram/10 mL</td>
<td>102 mL</td>
</tr>
</tbody>
</table>

### Intravenous Administration

**Intermittent or continuous infusion:** Dilute reconstituted Cefazolin for injection in 50 to 100 mL of 1 of the following solutions:

- Sodium Chloride Injection, USP
- 5% or 10% Dextrose Injection, USP
- 5% Dextrose In Lactated Ringer’s Injection, USP
- 5% Dextrose and 5.9% Sodium Chloride Injection, USP
- 5% Dextrose and 0.45% Sodium Chloride Injection, USP
- 5% Dextrose and 0.2% Sodium Chloride Injection, USP
- Lactated Ringer’s Injection, USP
- Invert Sugar 5% in 10% Sterile Water for Injection

When diluted according to the instructions above, Cefazolin is stable for 24 hours at room temperature for or 10 days if stored under refrigeration (5°C or 41°F).

Prior to administration parenteral drug products should be inspected visually for particulate matter and discoloration wherever solution and container permit.

### References


CLINITEST is registered trademark of Miles, Inc.

CLINDRIT is a registered trademark of Bayer Corporation.

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Mfg. by: Hospira Healthcare India Pvt. Ltd. (India) 602, 100, Huda, 349025, India

Mfg. for: Cipla Limited (USA) 56505-0769-0 Cefazolin for injection, USP 10 grams carton of 10 Pharmacy Bulk Packages.

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