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Cefazolin for Injection, USP

500 mg/15 mL Vial
 1 g/15 mL Vial
 10 g/100 mL Pharmacy Bulk Package Vial
 20 g/100 mL Pharmacy Bulk Package Vial

Antibiotic

THERAPEUTIC CLASSIFICATION

Antibiotic

ACTION AND CLINICAL PHARMACOLOGY

Cefazolin sodium is a cephalosporin antibiotic for parenteral administration. It exerts its bacterial effect by inhibiting bacterial cell wall synthesis.

INDICATIONS AND CLINICAL USES

Cefazolin for Injection, USP may be indicated in the treatment of the following infections when caused by susceptible strains of the listed organisms:

- RESPIRATORY TRACT INFECTIONS caused by *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Hemophilus influenzae*, *Staphylococcus aureus* (penicillin-sensitive and penicillin-resistant) and group A beta-hemolytic streptococci.
- URINARY TRACT INFECTIONS caused by *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae* and some strains of *enterobacter* and enterococci.
- SKIN AND SOFT TISSUE INFECTIONS caused by *Staphylococcus aureus* (penicillin-sensitive and penicillin-resistant), group A beta-hemolytic streptococci and other strains of streptococci.
- BONE AND JOINT INFECTIONS caused by *Staphylococcus aureus*.
- SEPTICEMIA caused by *Streptococcus pneumoniae*, *Staphylococcus aureus* (penicillin-sensitive and penicillin-resistant), *Proteus mirabilis*, *Escherichia coli* and *Klebsiella pneumoniae*.
- ENDOCARDITIS caused by *Staphylococcus aureus* (penicillin-sensitive and penicillin-resistant) and group A beta-hemolytic streptococci.

In order to determine the susceptibility of the causative organism to cefazolin sodium, appropriate culture and susceptibility studies should be performed.

Most strains of Enterococci, indole positive *Proteus (P. vulgaris)*, *Enterobacter cloacae*, *Morganella morganii*, *Providencia rettgeri* and methicillin-resistant staphylococci are resistant. *Serratia*, *Pseudomonas*, and *Acinetobacter calcoaceticus* (formerly *Mima* and *Herellea* species) are almost uniformly resistant to cefazolin.

Perioperative Prophylaxis

In patients undergoing potentially contaminated surgical procedures, and in patients in whom infection would pose a serious risk (e.g., during open-heart surgery and prosthetic arthroplasty), the preoperative, intraoperative, and postoperative administration of cefazolin sodium may reduce the incidence of certain postoperative infections.

Should signs of infection occur, identification of the causative organisms should be made by culture in order that appropriate therapy may be instituted.

CONTRAINDICATIONS

In patients with known allergy or hypersensitivity to the cephalosporin group of antibiotics, Cefazolin for Injection, USP is contraindicated.

WARNINGS

CEPHALOSPORIN DERIVATIVES SHOULD BE USED WITH CAUTION IN PENICILLIN-ALLERGIC PATIENTS. THERE ARE INSTANCES OF PATIENTS WHO HAVE HAD REACTIONS TO BOTH PENICILLINS AND CEPHALOSPORINS (INCLUDING FATAL ANAPHYLAXIS AFTER PARENTERAL USE). CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY FOR THESE TWO DRUG CLASSES EXISTS.

FOR ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS, CEFAZOLIN FOR INJECTION, USP SHOULD BE ADMINISTERED CAUTIOUSLY AND THEN ONLY WHEN ABSOLUTELY NECESSARY. IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE IS REQUIRED FOR SERIOUS ANAPHYLACTOID REACTIONS. OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT INCLUDING INTUBATION, SHOULD ALSO BE EMPLOYED, AS NECESSARY.

There have been reports of pseudomembranous colitis with the use of cephalosporins. It is therefore important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

PRECAUTIONS

The overgrowth of non-susceptible organisms may result from the prolonged use of Cefazolin for Injection, USP. It is essential that careful clinical observation be maintained. Appropriate measures should be taken if superinfection occurs during therapy.

In patients with a history of lower gastrointestinal disease, and in particular, colitis, cefazolin should be prescribed with caution.

Caution should be used in treating patients with pre-existing renal damage even though cefazolin has not shown evidence of nephrotoxicity.

In patients with low urinary output due to impaired renal function, cefazolin is not readily excreted and these patients should be administered reduced daily dosages of cefazolin (see **DOSAGE AND ADMINISTRATION, Adult Dosage, Dosage in Patients with Reduced Renal Function**). Blood levels of cefazolin in dialysis patients remain fairly high and should be monitored.

There have been reports during treatment with cefazolin of positive direct and indirect Coombs' tests. These may also occur in neonates whose mothers received cephalosporins before delivery. The clinical significance of this effect has not been established.

False positive indications of urinary glucose may occur in cefazolin-treated patients where Clinitest* tablets solution are used, but not enzyme-based tests such as Clinistix* and Tes-Tape**.

Drug Interactions

The renal tubular secretions of cefazolin may be decreased when probenecid is used concurrently, resulting in increased and prolonged cefazolin blood levels.

Pregnancy

The safety of cefazolin sodium for use during pregnancy has not been established.

Infants

The safety of cefazolin sodium for use in premature infants and in infants under one month of age has not been established.

Nursing Mothers

Very low concentrations of cefazolin sodium are found in the milk of nursing mothers. Caution should be used when cefazolin sodium is administered to a nursing woman.

ADVERSE REACTIONS

The following reactions have been reported.

Allergic

Anaphylaxis, eosinophilia, itching, drug fever, and skin rash.

Gastrointestinal

Diarrhea, oral candidiasis (oral thrush), cheilitis, vomiting, nausea, stomach cramps, anorexia. During antibiotic treatment, symptoms of pseudomembranous colitis can appear. Nausea and vomiting have been reported rarely.

Hematologic

Neutropenia, anemia, leukopenia, thrombocytopenia, positive direct and indirect antiglobulin (Coombs) tests.

Hepatic and Renal

Transient increases in AST (SGOT), ALT (SGPT), BUN and alkaline phosphatase levels have been observed without clinical evidence of hepatic or renal impairment. Transient hepatitis and cholestatic jaundice have been reported rarely, as with some penicillins and some other cephalosporins.

Local Reactions

Phlebitis at the site of injection has rarely occurred, infrequently there may be pain and induration at the site of injection following intramuscular injection.

Other Reactions

Genital moniliasis, vaginitis, vulvar and anal pruritus.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Supportive therapy should be instituted according to symptoms in cases of suspected overdosage. There is presently a lack of experience with acute cefazolin overdosage.

DOSAGE AND ADMINISTRATION

Cefazolin for Injection, USP may be administered either intramuscularly or intravenously after constitution. In both cases, total daily dosages are the same.

Treatment should be continued in beta-hemolytic streptococcal infections for at least 10 days to minimize possible complications associated with the disease.

Adult Dosage

ADULT DOSAGE GUIDE		
Type of Infection	Dose	Frequency
Pneumococcal pneumonia	500 mg	Every 12 hours
Mild infections caused by susceptible Gram + cocci	250 to 500 mg	Every 8 hours
Acute, uncomplicated urinary tract infections*	1 g	Every 12 hours
Moderate to severe infections	500 mg to 1 g	Every 6 to 8 hours

*This dosage recommendation applies to intramuscular use. The efficacy of cefazolin sodium when administered intravenously at 12-hour intervals has not been established.

Cefazolin sodium has been administered in dosages of 6 grams per day in serious infections such as endocarditis.

Dosage in Patients with Reduced Renal Function:

After an initial loading dose appropriate to the severity of the infections, the following reduced dosage schedule is recommended:

DOSAGE GUIDE FOR RENALLY IMPAIRED PATIENTS		
Creatinine Clearance (mL/s)	Serum Creatinine (µmol/L)	Dosage
≥ 0.91	≤ 140	250 mg to 1 g every 6 - 12 hours
0.58 - 0.90	141 - 273	250 mg to 1 g every 8 - 12 hours
0.18 - 0.57	274 - 406	125 mg to 500 mg every 12 hours
≤ 0.17	≥ 407	125 mg to 500 mg every 18 hours

Perioperative Prophylactic Use:

The following dosage regimens are recommended to prevent postoperative infection in contaminated or potentially contaminated surgery:

- 1 gram i.v. or i.m. administered ½ hour to 1 hour prior to the start of surgery so that at the time of the initial surgical incision, adequate antibiotic levels are present in the serum and tissues.
- 0.5 to 1 gram administered i.v. or i.m. during surgery for lengthy operative procedures (e.g., 2 hours or more). (Administration should be modified according to the duration of the operative procedure and the time of greatest exposure to infective organisms.)
- 0.5 gram to 1 gram i.v. or i.m. every 6 to 8 hours for 24 hours postoperatively. Following the completion of surgery in which the occurrence of infection may be particularly devastating (e.g., open heart surgery and prosthetic arthroplasty), the prophylactic administration of cefazolin sodium may be continued for 3 to 5 days.

Pediatric Dosage

A total daily dosage of 25 to 50 mg per kg of body weight, divided into three or four equal doses, is effective for most mild to moderately severe infections in children. Duration of therapy in most cases should be 5 to 10 days.

Treatment should be continued in beta-hemolytic streptococcal infections for at least 10 days to minimize possible complications associated with the disease.

For severe infections, the total daily dosage may be increased to 100 mg per kg of body weight. Cefazolin administration to premature infants and in infants under one month is not recommended since the safety of cefazolin use in these patients has not been established.

Administration of 60 percent of the normal daily dose in divided doses every 12 hours may be used for children with mild to moderate renal impairment (C_{cr} 0.67 - 1.17 mL/s). Children with moderate renal impairment (C_{cr} 0.33 - 0.87 mL/s) should be given 25 percent of the normal daily dose in equally divided doses every 12 hours, and children with severe renal impairment (C_{cr} 0.08 - 0.33 mL/s) should receive 10 percent of the normal daily dose every 24 hours. An initial loading dose precedes all recommended doses.

PEDIATRIC DOSAGE GUIDE – 25 mg/kg/day				
Weight (kg)	25 mg/kg/day – Divided into 3 doses		25 mg/kg/day – Divided into 4 doses	
	Approx. Single Dose mg/q8h	Volume Needed of 125 mg/mL* Solution	Approx. Single Dose mg/q6h	Volume Needed of 125 mg/mL* Solution
4.5	40 mg	0.35 mL	30 mg	0.25 mL
9.0	75 mg	0.60 mL	55 mg	0.45 mL
13.6	115 mg	0.90 mL	85 mg	0.70 mL
18.1	150 mg	1.20 mL	115 mg	0.90 mL
22.7	190 mg	1.50 mL	140 mg	1.10 mL

* 125 mg/mL concentration may be obtained by constituting the 500 mg vial with 3.8 mL of diluent.

PEDIATRIC DOSAGE GUIDE – 50 mg/kg/day				
Weight (kg)	50 mg/kg/day – Divided into 3 doses		50 mg/kg/day – Divided into 4 doses	
	Approx. Single Dose mg/q8h	Volume Needed of 225 mg/mL* Solution	Approx. Single Dose mg/q6h	Volume Needed of 225 mg/mL* Solution
4.5	75 mg	0.35 mL	55 mg	0.25 mL
9.0	150 mg	0.70 mL	110 mg	0.50 mL
13.6	225 mg	1.00 mL	170 mg	0.75 mL
18.1	300 mg	1.35 mL	225 mg	1.00 mL
22.7	375 mg	1.70 mL	285 mg	1.25 mL

* 225 mg/mL concentration may be obtained by constituting the 500 mg vial with 2.0 mL of diluent.

Administration

NOTE: See section under **PHARMACEUTICAL INFORMATION** for constitution and dilution directions.

For Intramuscular Use:

Inject the constituted solution into a large muscle mass. Pain on injection with cefazolin is infrequent.

For Intravenous Use:

The intravenous route is preferred for patients with septicemia, peritonitis, or other severe life threatening infections.

Direct Intravenous (bolus) Injection:

Inject the appropriately diluted constituted solution slowly over 3 to 5 minutes directly into vein or through tubing for patients receiving parenteral fluids. (See list of solutions for intravenous infusion in **PHARMACEUTICAL INFORMATION**.)

Intermittent or Continuous Intravenous Infusion:

The constituted solution can be administered along with primary intravenous fluid management programs in a volume control set or in a separate secondary i.v. bottle. (See list of solutions for intravenous infusion in **PHARMACEUTICAL INFORMATION**.) It is desirable to discontinue the administration of other solutions during the infusion of cefazolin.

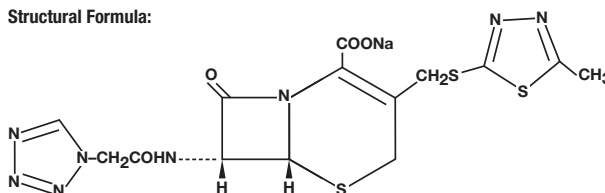
PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Cefazolin Sodium

Chemical Name: Sodium (6R,7R)-3-[[[(5-methyl-1,3,4-thiadiazol-2-yl)thio]methyl]-8-oxo-7-[2-(1H-tetrazol-1-yl)acetamido]-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylate

Structural Formula:



Molecular Formula: C₁₄H₁₃N₅NaO₄S₃

Molecular Weight: 476.5

Description:

Cefazolin sodium is a white, odorless crystalline powder. It is easily soluble in water, slightly soluble in methanol and ethanol, and practically insoluble in benzene, acetone and chloroform. The pH of the constituted solution ranges from 4.5 to 6.0.

COMPOSITION

Cefazolin for Injection, USP contains 500 mg, 1 g, 10 g, or 20 g cefazolin in each vial, present as cefazolin sodium. Each gram of cefazolin sodium contains 48 mg of sodium. Contains no preservative.

STABILITY AND STORAGE RECOMMENDATION

Cefazolin for Injection, USP (unconstituted product) should be stored between 15 and 30°C and protected from light.

CONSTITUTION

When constituted, the vial should be SHAKEN WELL and inspected visually for particulate matter prior to administration. The drug solution should be discarded if particulate matter is evident in constituted fluids.

Constituted Cefazolin for Injection, USP is stable for 24 hours at controlled room temperature not exceeding 25°C, or for 72 hours under refrigeration (2 - 8°C) protected from light, from the time of initial puncture of the stopper.

For Intramuscular Injection

Single-dose Vials: Constitute according to the Single-dose Vial Constitution Table below. SHAKE WELL.

For Intravenous Direct (Bolus) Injection

Single-dose Vials: Constitute according to the Single-dose Vial Constitution Table below. SHAKE WELL. For further dilution of the constituted solution, a minimum of 10 mL of Sterile Water for Injection should be used.

Pharmacy Bulk Vial: Add, according to the Pharmacy Bulk Vial Dilution Table below, 45 mL or 96 mL Sterile Water for Injection, or Sodium Chloride Injection 0.9%. One of the solutions listed below under **For Intermittent or Continuous Intravenous Infusion** may be used to further dilute aliquots. SHAKE WELL. The Pharmacy Bulk Vial is intended for multiple dispensing and i.v. use only employing a single puncture. Any unused stock solution remaining after a period of 8 hours should be discarded.

For Intermittent or Continuous Intravenous Infusion

Single-dose Vials: Constitute according to the Single-dose Vial Constitution Table below. SHAKE WELL. Further dilute the constituted cefazolin sodium in 50 to 100 mL of Sterile Water for Injection or one of the following solutions:

- Sodium Chloride Injection 0.9%
- Dextrose Injection 5% or 10%

SINGLE-DOSE VIAL CONSTITUTION TABLE				
Vial Size (mg)	Diluent	Volume to be Added to Vial (mL)	Approx. Available Volume (mL)	Nominal Concentration (mg/mL)
500	0.9% Sodium Chloride Injection	2.0	2.2	225
500	Sterile Water for Injection	3.8	4.0	125
1000	Sterile Water for Injection	2.5	3.0	334

PHARMACY BULK VIAL DILUTION TABLE			
Vial Size (g)	Volume to be Added to Vial (mL)	Approx. Available Volume (mL)	Nominal Concentration (mg/mL)
10	45	50	200
	96	100	100
20	87	100	200

Extended use of IV Admixtures

Although i.v. admixtures may often be physically and chemically stable for longer periods, due to microbiological considerations, they are usually recommended for use within 24 hours at room temperature or 72 hours when refrigerated (2 to 8°C), from the time of initial puncture of the stopper.

SPECIAL INSTRUCTIONS

THE USE OF PHARMACY BULK VIALS IS RESTRICTED TO HOSPITALS WITH A RECOGNIZED INTRAVENOUS ADMIXTURE PROGRAM.

Warning

As with all parenteral products, i.v. admixtures should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used. Discard unused portion.

AVAILABILITY OF DOSAGE FORMS

Cefazolin for Injection, USP is supplied in:

- PF320020 15 mL vials containing cefazolin sodium equivalent to 500 mg of cefazolin, packaged 25 vials per carton.
- PF320021 15 mL vials containing cefazolin sodium equivalent to 1 g of cefazolin, packaged 25 vials per carton.
- PF320022 100 mL "Pharmacy Bulk Package" vials containing cefazolin sodium equivalent to 10 grams of cefazolin, packaged 10 vials per carton.
- C446B1 100 mL "Pharmacy Bulk Package" vials containing cefazolin sodium equivalent to 20 grams of cefazolin, packaged 10 vials per carton.

CEFAZOLIN FOR INJECTION, USP DOES NOT CONTAIN ANY PRESERVATIVE.

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