CEFAZOLIN- cefazolin sodium injection, powder, for solution
General Injectables & Vaccines, Inc

Cefazolin for Injection USP 1 gram

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CEFAZOLIN FOR INJECTION, USP safely and effectively. See full prescribing information for CEFAZOLIN FOR INJECTION, USP.
CEFAZOLIN FOR INJECTION, USP, for intravenous use
Initial U.S. Approval: 1973
To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefazolin for injection and 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.

INDICATIONS AND USAGE

Cefazolin for Injection, USP is a cephalosporin antibacterial indicated in the treatment of the following infections caused by susceptible isolates of the designated microorganisms:

- Respiratory tract infections. (1.1)
- Urinary tract infections. (1.2)
- Skin and skin structure infections. (1.3)
- Billiary tract infections. (1.4)
- Bone and joint infections. (1.5)
- Genital infections. (1.6)
- Septicemia. (1.7)
- Endocarditis. (1.8)
- Perioperative prophylaxis. (1.9)

DOSAGE AND ADMINISTRATION

For intravenous or intramuscular use. (2)

----------DOSAGE AND ADMINISTRATION----------

For intravenous or intramuscular use. (2)

Recommended Dosing Schedule in Adult Patients with CrCl Greater Than or Equal to 55 mL/min. (2.1)

Site and Type of Infection	Dose	Frequency
Moderate to severe infections	500 mg to 1 gram	every 6 to 8 hours
Mild infections caused by susceptible gram-positive cocci	250 mg to 500 mg	every 8 hours
Acute, uncomplicated urinary tract infections	1 gram	every 12 hours
Pneumococcal pneumonia	500 mg	every 12 hours
Severe, life-threatening infections (e.g.,endocarditis, septicemia)*	1 gram to 1.5 grams	every 6 hours
Perioperative prophylaxis	1 gram to 2 grams	1/2 to 1 hour prior to start of surgery
	500 mg to 1 gram	during surgery for lengthy procedures
	500 mg to 1 gram	every 6 to 8 hours for 24 hours postoperatively

*In rare instances, doses of up to 12 grams of cefazolin per day have been used.

DOSAGE FORMS AND STRENGTHS

- 1 g per vial (3)

CONTRAINDICATIONS

- Hypersensitivity to cefazolin or other cephalosporin class antibacterial drugs, penicillins, or other beta-lactams. (4.1)

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Cross-hypersensitivity may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction occurs, discontinue the drug. (5.1)
- Use in Patients with Renal Impairment: Dose adjustment required for patients with CrCl less than 55 mL/min. (5.2)
- *Clostridium difficile*-associated Diarrhea: May range from mild diarrhea to fatal colitis. Evaluate if diarrhea occurs. (5.3)

ADVERSE REACTIONS

- Most common Adverse Reactions: Gastrointestinal (nausea, vomiting, diarrhea), and allergic reactions (anaphylaxis, urticaria, skin rash). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Hospira, Inc. at 1-800-441-4100 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

DRUG INTERACTIONS

Probenecid: May decrease renal tubular secreation of cephalosporins when used concurrently, resulting in increased and more prolonged cephalosproin blood concentrations. (7.1)

USE IN SPECIFIC POPULATIONS

- Pediatric Use: Safety and effectiveness for use in premature infants and neonates have not been established. See Dosage and Administration (2.4) for recommended dosage in pediatric patients older than 1 month. (8.4)

- Renal Impairment: Lower daily dosage of cefazolin for injection is required in patients with impaired renal function (creatinine clearance less than 55 mL/min). (8.6)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 3/2015

See 17 for PATIENT COUNSELING INFORMATION. **Revised: 3/2015**

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION
1 INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectivness of Cefazolin for Injection, USP and other antibacterial drugs. Cefazolin for Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Cefazolin for Injection, USP is indicated for the treatment of the following infections when caused by susceptible bacteria.

1.1 Respiratory Tract Infections

Respiratory tract infections due to *Streptococcus pneumoniae, Staphylococcus aureus* and *Streptococcus pyogenes.*

Injectable benzatine penicillin is considered the drug of choice in treatment and prevention of streptococcal infections, including prophylaxis of rheumatic fever.

Cefazolin is effective in the eradication of streptococci from the nasopharynx; however, data establishing the efficacy of cefazolin in the subsequent prevention of rheumatic fever are not available.

1.2 Urinary Tract Infections

Urinary tract infections due to *Escherichia coli,* and *Proteus mirabilis.*

1.3 Skin and Skin Structure Infections

Skin and skin structure infections due to *S. aureus, S. pyogenes, and Streptococcus agalactiae.*

1.4 Biliary Tract Infections

Biliary tract infections due to *E. coli,* various isolates of streptococci, *P. mirabilis,* and *S. aureus.*

1.5 Bone and Joint Infections

Bone and joing infections due to *S. aureus.*

1.6 Genital Infections

Genital infections due to *E. coli,* and *P. mirabilis.*

1.7 Septicemia

Septicemia due to *S. pneumoniae, S. aureus, P. mirabilis,* and *E. coli.*

1.8 Endocarditis

Endocarditis due to *S. aureus* and *S. pyogenes.*

1.9 Perioperative Prophylaxis

The prophylactic administration of cefazolin preoperatively, intraoperatively, and postoperatively may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures which are classified as contaminated or potentially contaminated (e.g., vaginal hysterectomy, and cholecystectomy in high-risk patients such as those older than 70 years, with acute cholecystitis,obstructive jaundice, or common duct bile stones).

DOSAGE AND ADMINISTRATION

2.1 Adult Population

The recommended adult dosages are outlined in Table 1. Cefazolin for injection should be administered intravenously (IV) or intramuscularly (IM).

Table 1: Recommended Dosing Schedule in Adult Patients with CrCl Greater Than or Equal to 55 mL/min.

Site and Type of Infection	Dose	Frequency
Moderate to severe infections	500 mg to 1 gram	every 6 to 8 hours
Mild infections caused by susceptible gram-positive cocci	250 mg to 500 mg	every 8 hours
Acute, uncomplicated urinary tract infections	1 gram	every 12 hours
Pneumococcal pneumonia	500 mg	every 12 hours
Severe, life-threatening infections (e.g., endocarditis, septicemia)*	1 gram to 1.5 grams	every 6 hours

* In rare instances, doses of up to 12 grams of cefazolin per day have been used.

2.2 Perioperative Prophylactic Use

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

- 1 to 2 gram IV administered 1/2 hour to 1 hour prior to the start of surgery.
- 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).
- 500 mg to 1 gram IV every 6 to 8 hours for 24 hours postoperatively.

It is important that (i) the preoperative dose be given to just prior (1/2 hour to 1 hour) to the start of surgery so that adequate antibacterial concentrations are present in the serum and tissues at the time of initial surgical incision; and (ii) cefazolin be administered, if necessary, at appropriate intervals during surgery to provide sufficient concentrations of the antibacterial drug at the anticipated moments of greatest exposure to infective organisms.

The prophylactic administration of cefazolin should usually be discontinued within a 24-hour period after the surgical procedure. In surgery where the occurrence of infection may be particularly devastating (e.g.,open-heart surgery and prosthetic arthroplasty), the prophylactic administration of cefazolinmay be continued for 3 to 5 days following the completion of surgery.

2.3 Patients with Renal Impairment

Cefazolin may be used in patients with renall impairment with the dosage adjustments outlined in Table 2. All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection.

Table 2: Dosage Adjustment for Patients with Renal Impairment

Creatinine Clearance	Dose	Frequency
55 mL/min. or greater	full dose	normal frequency
35 to 54 mL/min.	full dose	every 8 hours or longer
11 to 34 mL/min.	1/2 usual dose	every 12 hours
10 mL/min. or less	1/2 usual dose	every 18 to 24 hours

2.4 Pediatric Population

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.

Pediatric Dosage Guide

Weight		25 mg/kg/Day Divided into 3 Doses		25 mg/kg/Day Divided into 4 Doses	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (mL) needed with dilution of 125 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 125mg/mL
10	4.5	40 mg	0.35 mL	30 mg	0.25 mL
20	9	75 mg	0.6 mL	55 mg	0.45 mL
30	13.6	115 mg	0.9 mL	85 mg	0.7 mL
40	18.1	150 mg	1.2 mL	115 mg	0.9 mL
50	22.7	190 mg	1.5 mL	140 mg	1.1 mL

Weight		50 mg/kg/Day Divided into 3 Doses		50 mg/kg/Day Divided into 4 Doses	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (mL) needed with dilution of 225 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 225 mg/mL
10	4.5	75 mg	0.35 mL	55 mg	0.25 mL
20	9	150 mg	0.7 mL	110 mg	0.5 mL
30	13.6	225 mg	1 mL	170 mg	0.75 mL
40	18.1	300 mg	1.35 mL	225 mg	1 mL
50	22.7	375 mg	1.7 mL	285 mg	1.25 mL

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 sever 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.

2.5 Preparation of Parenteral Solution

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

When reconstituted or diluted according to the instructions below, cefazolin for injection is stable for 24 hours at room temperature or for 10 days if stored under refrigeration (5°C or 41°F). Reconstituted solutions may range in color from pale yellow to yellow without a change in potency.

Single-Dose Vials

For IM injection, IV direct (bolus) injection or IV infustion reconstitute with Sterile Water for Injection according to the following table. SHAKE WELL.

Vial Size	Amount of Diluent	Approximate Concentration	Approximate Available Volume
1 g	2.5 mL	330 mg/mL	3 mL

2.6 Intramuscular Administration

Reconstitute vials with Sterile Water for Injection acording to the dilution table above. Shake well until dissolved. Cefazolin should be injected into a large muscle mass. Pain on injection is frequent with cefazolin.

2.7 Intravenous Administration

Direct (bolus) injection: Following reconstitution according to the above table, further dilute vials with approximately 5 mL Sterile Water for Injection. Inject the solution slowly over 3 to 5 minutes, directly or through tubing for patients receiving parenteral fluids (see list below).

Intermittent or continuous infusion: Dilute reconstituted cefazolin in 50 to 100 mL of one 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 0.9% 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% or 10% in Sterile Water for Injection

Ringer's Injection, USP

5% Sodium Bicarbonate Injection, USP

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

DOSAGE FORMS AND STRENGTHS

Single-dose vials:

- 1 g cefazolin for injection

CONTRAINDICATIONS

4.1 hypersensitivity to Cefazolin or the Cephalosporin Class of Antibacterial Drugs, Penicillins, or Other Beta-lactams

Cefazolin for injection is contraindicated in patients who have a history of immediate hypersensitivity reactions (e.g., anaphylaxis, serious skin reactions) to cefazolin or the cephalosporin class of antibacterial drugs, penicillins, or other beta-lactams [see *Warnings and Precautions (5.1)].*

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions to Cefazolin, Cephalosporins, Penicillins, or Other Beta-lactams

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam antibacterial drugs. Before therapy with cefazolin for injection is instituted, careful inquiry should be made to determine whether the patient has had previous immediate hypersensitivity reactions to cefazolin, cephalosporins, penicillins, or carbapenems. Exercise caution if this product is to be given to penicillin-sensitive patients because cross-hypersensitivity amove beat-lactam antibacterial drugs has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to cefazolin for injection occurs, discontinue the drug.

5.2 Use in Patients with Renal Impairment

As with other beta-lactam antibacterial drugs, seizures may occur if inappropriately high doses are administered to patients with impaired renal function (creatinine clearance less than 55 mL/min.) [see *Dosage and Administration 2.3)].*

5.3 *Clostridium difficile*-associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefazolin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

C. difficile produces toxins A and B, which contribute to the development of CDAD. Hypertoxin-producing isolates of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhead following antibacterial drug use. Careful medical history is necessary since

CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial drugs use not direct against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial drug treatment of *C. difficile,* and surgical evaluation should be instituted as clincially indicated.

5.4 Drug/Laboratory Test Interactions

Urinary Glucose

The administration of cefazolin may result in a false-positive reaction with glucose in the urine when using CLINITEST® tablets. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (e.g., CLINISTIX®) be used.

Coombs' Test

Positive direct Coombs' tests have been reported during treatment with cefazolin. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whos mothers have received cephalosporin antibacterial drugs before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

ADVERSE REACTIONS

The following serious adverse reactions to cefazolin are described below and elsewhere in the labeling:

- Hypersensitivity reactions [*see Warnings and Precautions (5.1)]*
- *Clostridium difficile*-associated diarrhea [*see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

The following adverse reactions were reported from clinical trials:

Gastrointestinal: Diarrhea, oral candidiasis (oral thrush), mouth ulcers, vomiting, nausea, stomach cramps, epigastric pain, heartburn, flatus, anorexia and pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment [*see Warnings and Precautions (5.3)].*

Allergic: Anaphylaxis, eosinophilia, urticaria, itching, drug fever, skin rash, Stevens-Johnson syndrome.

Hematologic: Neuropenia, leukopenia, thrombocytopenia, thrombocythemia.

Hepatic: Transient rise in SGOT, SGPT, and alkaline phosphatase levels have been observed. As with other cephalosporins, reports of hepatitis have been received.

Local Reactions: Instances of phlebitis have been reported at site of injection. Some induration has occurred.

Other Reactions: Pruritus (including genital, vulvar andanal pruritus, genital moniliasis, and vaginitis). Dizziness, fainting, lightheadedness, confusion, weakness, tiredness, hypotension, somnolence and headache.

6.2 Cephalosporin-class Adverse Reactions

In addition to the adverse reactions listed above that have been observed in patients treated with cefazolin, the follwoing adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibacterials: Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal impairment, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic impairment including cholestasis, and pancytopenia.

DRUG INTERACTIONS

Probenecid may decrease renal tubular secretion of cephalosporins when used concurrently, resulting in increased and more prolonged cephalosporin blood levels.

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

Reproduction studies have been performed in rats, mice and rabbits at doses of 2000, 4000 and 240 kg/kg/day or 1 to 3 times the maximum recommended human dose on a body surface area basis. There was no evidence of impaired fertility or harm to the fetus due to cefazolin.

8.2 Labor and Delivery

When cefazolin has been administered prior to caesarean section, drug concentrations in cord blood habe been approximately one quarter to one third of maternal drug levels. The drug appears to have no adverse effect on the fetus.

8.3 Nursing Mothers

Cefazolin is present in very low concentrations in the milk of nursing mothers. Caution should be exercised when cefazolin for injection is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness for use in premature infants and neonates have not been established. *See Dosage and Administration (2.4)* for recommended dosage in pediatric patients older than 1 month.

8.5 Geriatric Use

Of the 920 subjects who received cefazolin in clinical studies, 313 (34%) were 65 years and over, while 138 (15%) were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

The drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function [*see Dosage and Administration (2.3) and Warnings and Precautions (5.2)].*

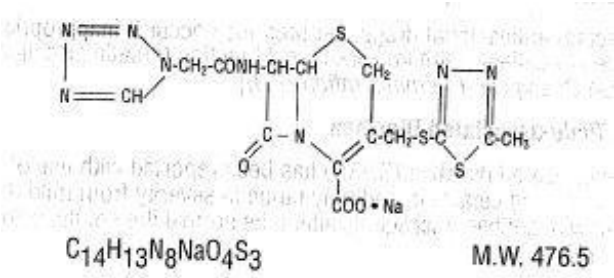
8.6 Patients with Renal Impairment

When cefazolin for injection is administered to patients with low urinary output because of impaired renal function (creatinine clearance less than 55 mL/min.), lower daily dosage is required [*see Dosage and Administration (2.3) and Warnings and Precautions (5.2)].*

DESCRIPTION

Cefazolin for Injection, USP is a semi-synthetic cephalosporin for parenteral administration. It is the sodium salt of (6R, 7R)-3[[(5-methyl-1,3,4-thiadiazol-2-yl)thio]methyl]-8-oxo-7-[2(1*H*-tetrazol-1-yl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

Structural Formula:



Cefazolin for Injection, USP is a sterile white to off-white crystalline powder.

Each vial contains 48 mg (2 mEq) of sodium/1 gram of cefazolin sodium.

CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cefazolin is an antibacterial drug [*see Microbiology (12.4)]*.

12.2 Pharmacodynamics

The pharmacokinetic/pharmacodynamic relationship for cefazolin has not been evaluated in patients.

12.3 Pharmocokinetics

After intramuscular administration of cefazolin to normal volunteers, the mean serum concentrations were 37 mcg/mL at 1 hour and 3 mcg/mL at 8 hours following a 1 gram dose.

Studies have shown that following intravenous adminstration of cefazolin to normal volunteers, mean serum concentrations peaked at approximately 185 mcg/mL and were approximately 4 mcg/mL at 8 hours of a 1 gram dose.

The serum half-life for cefazolin is approximately 1.8 hours following IV administration and approximately 2 hours following IM administration.

In a study (using normal volunteers) of constant intravenous infusion with dosages of 3.5 mg/kg for 1 hour (approximately 250 mg) and 1.5 mg/kg the next 2 hours (approximately 100 mg), cefazolin produced a steady serum concentration at the third hour of approximately 28 mcg/mL.

Studies in patients hospitalized with infections indicate that cefazolin for injection produces mean peak serum concentrations approximately equivalent to those seen in normal volunteers.

Bile concentrations in patients without obstructive biliary disease can reach or exceed serum concentrations by up to five times; however, in patietns with obstructive biliary disease, bile concentrations of cefazolin are considerably lower than serum concentrations (<1 mcg/mL).

In synovial fluid, the cefazolin concentration becomes comparable to that reached in serum at about 4 hours after drug administration.

Studies of cord blood show prompt transfer of cefazolin across the placenta. Cefazolin is present in very low concentrations in the milk of nursing mothers.

Cefazolin is excreted unchanged in the urine. In the first 6 hours approximately 60% of the drug is excreted in the urine and this increases to 70% to 80% within 24 hours. Cefazolin achieves peak urine concentrations of approximately 2,400 mcg/mL and 4,000 mcg/mL respectively following 500 mg and 1 gram intramuscular doses.

In patients undergoing peritoneal dialysis (2 L/hr.), cefazolin produced mean serum concentrations of approximately 10 and 30 mcg/mL after 24 hours instillation of a dialyzing solution containing 50 mg/L and 150 mg/L, respectively. Mean peak levels were 29 mcg/mL (range 13 to 44 mcg/mL) with 50 mg/L (3 patients), and 72 mcg/mL (range 26 to 142 mcg/mL) with 150 mg/L (6 patients). Intraperitoneal administration of cefazolin is usually well tolerated.

12.4 Microbiology

Mechanism of Action

Cefazolin is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis.

Mechanism of Resistance

Predominant mechanisms of bacterial resistance to cephalosporins include the presence of extended-spectrum beta-lactamases and enzymatic hydrolysis.

Lists of Microorganisms

Cefazolin has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections as described in the *Indications and Usage (1)* section.

- Gram-Positive Bacteria

Staphylococcus aureus

Staphylococcus epidermidis

Streptococcus pyogenes, Streptococcus agalactiae

Streptococcus pneumoniae

Methicillin-resistant staphylococci are uniformly resistant to cefazolin.

- Gram-Negative Bacteria

Escherichia coli

Proteus mirabilis

Most isolates of indole positive Proteus *(Proteus vulgaris), Enterobacter* spp., *Morganella morganii, Providencia rettgeri, Serratia spp.,* and *Pseudomonas* spp. are resistant to cefazolin.

Susceptibility Test Methods

When available, the clinical microbiology laboratory should provide the results of *in vitro* susceptibility test results for antimicrobial drug products used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Dilution Techniques

Quantitative methods are used to determine minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standard test[1,2] (broth and/or agar). The MIC values obtained should be interpreted according to criteria as provided in Table 4.

Diffusion Techniques

Quantitative methods that require measurement of zone diameters provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be interpreted using a standard test method [2,3]. This procedure uses paper disks impregnated with 30 mcg cefazolin to test the susceptibility of microorganisms to cefazolin. The disk diffusion interpretive criteria are provided in Table 4.

Table 4: Susceptibility Test Interpretive Criteria for Cefazolin[a]

Pathogen	Minimum Inhibitory Concentration (mcg/mL)			Disk Diffusion Zone Diameter (mm)[b]		
	S	I	R	S	I	R
Escherichia coli *Proteus mirabilis*	≤1	2	≥4	-	-	-
Staphylococcus aureus	≤8	16	≥32	≥18	15 to 17	≤14

Abbreviations: S= susceptible, I= intermediate, R= resistant
[a] Interpretive criteria are based on 1 g every 8 hr
[b] The cefazolin disk should not be used for determining susceptibility to other cephalosporins

NOTE:

S. pyogenes and S. agalactiae that have a penicillin MIC of ≤0.12 mcg/mL, or disk diffusion zone diameters of ≥24 mm with a 10 mcg penicillin disk, may be interpreted as susceptible to cefazolin. **Non-meningitis isolates** of *S. pneumoniae* that have a penicillin MIC of ≤0.06 mcg/mL, may be interpreted as susceptible to cefazolin.

A report of *Susceptible* indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compund reaches the concentrations at the infection site necessare to inhibit growth of the pathogen. A report of *Intermediate* indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug product is physiologically concentrated or in situations where a high dosage of the drug product can be used. This category also provides a buffer zone also prevents small uncontrolled technical factors from causing major descrepancies in interpretation. A report of *Resistand* indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compund reaches the concentrations usually achievable at the infection site; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individual performing the test [1,2,3]. Standard cefazolin powder should provide the following MIC values noted in Table 5. For the diffusion technique using the 30 mcg disk, the criteria in Table 5 should be achieved.

Table 5: Acceptable Quality Control Ranges for Cefazolin

QC Isolate	Minimum Inhibitory Concentration mcg/mL	Disk Diffusion Zone Diameters (mm)
E. coli ATCC® 25922	1 to 4	21 to 27
S. aureus ATCC® 29213	0.25 to 1	-------
S. aureus ATCC® 25923	-------	29 to 35

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Mutagenicity studies and long-term studies in animals to determine the carcinogenic potential of cefazolin for injection have not been performed.

REFERENCES

1. Clinical Laboratory Standards Institute (CLSI). *Methods for Dilution Antimi crobial Susceptibility Tests for Bacteria the Grow Aerobically;* Approved Standard-Ninth Edition. CLSI Document M07-A9. CLSI, 940 West Valley Road, Suite 2500, Wayne, PA, 2012.

2. Clinical Laboratory Standards Institute (CLSI) *Performance Standards for Antimicrobial Susceptibility Testing*; Twentieth Informational Supplement. CLSI document M100-S20. CLSI, Wayne, PA, 2010.
3. Clinical Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Susceptibility Tests;* Approved Standard-Eleventh Edition. CLSI Document M02-A11. CLSI, Wayne, PA, 2012.

HOW SUPPLIED/STORAGE AND HANDLING

Cefazolin for Injection, USP is supplied as a sterile, white to off-white crystalline powder. Each vial contains cefazolin sodium equivalent to 1 gram of cefazolin.

Unit of Sale	Strength	Each
NDC 0409-0805-01 Carton containing 25	1 Gram	NDC 0409-0805-11 Vial

As with other cephalosporins, cefazolin tends to darken depending on storage conditions; within the stated recommendations, however, product potency is not adversely affected.

Before reconstitution protect from light and store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

PATIENT COUNSELING INFORMATION

Patient should be advised that allergic reactions, including serious allergic reactions could occur and that serious reactions require immediate treatment and discontinuation of cefazolin. Patients should resport to their health care provider any previous allergic reactions to cefazolin, cephalosporins, penicillins, or other similar antibacterials.

Patients should be advised that diarrhea is a common problem caused by antibiotics, which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with anitbacterials, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterials. If this occurs, patients should contact a physician as soon as possible.

Patients should be counseled that antibacterial drugs, including cefazolin for injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When cefazolin for injection is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by cefazolin for injection or other antibacterial drugs in the future.

Manufactured for:
Hospira, Inc.

Lake Forest, IL 60045 USA

Made in India

EN-3547

948026315

SAMPLE PACKAGE LABEL

CEFAZOLIN

cefazolin sodium injection, powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:52584-023(NDC:0409-0805)
Route of Administration	INTRAVENOUS, INTRAMUSCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Cefazolin Sodium (UNII: P380M0454Z) (Cefazolin - UNII:IHS69L0Y4T)	Cefazolin	1 g in 3 mL

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date

1	NDC:52584-023-10	1 in 1 BAG	11/07/2018	
1		3 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065226	09/07/2011	

Labeler - General Injectables & Vaccines, Inc (108250663)

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