



Microorganism	MIC (mcg/mL)
<i>S. aureus</i> ATCC 25923	0.25-1.0
<i>E. coli</i> ATCC 25922	1.0-4.0

## INDICATIONS AND USAGE

Cefazolin for Injection USP and Dextrose 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 beta-lactamase-producing strains) and *S. pyogenes*.

Injectable benzathine penicillin is considered to be the drug of choice in treatment and prevention of streptococcal infections, including the 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.

**Urinary Tract Infections:** Due to *E. coli*, *P. mirabilis*.

**Skin And Skin Structure Infections:** Due to *S. aureus* (including beta-lactamase-producing strains), *S. pyogenes*, and other strains of streptococci.

**Biliary Tract Infections:** Due to *E. coli*, various strains of streptococci, *P. mirabilis*, and *S. aureus*.

**Bone And Joint Infections:** Due to *S. aureus*.

**Genital Infections:** (i.e., prostatitis, epididymitis) due to *E. coli*, *P. mirabilis*.

**Septicemia:** Due to *S. pneumoniae*, *S. aureus* (including beta-lactamase-producing strains), *P. mirabilis*, *E. coli*.

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

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

**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).

The perioperative use of cefazolin may also be effective in surgical patients in whom infection at the operative site would present a serious risk (e.g., during open-heart surgery and prosthetic arthroplasty).

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 cefazolin may be continued for 3 to 5 days following the completion of surgery.

If there are signs of infection, specimens for cultures should be obtained for the identification of the causative organism so that appropriate therapy may be instituted. (See **DOSAGE AND ADMINISTRATION**.)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefazolin for Injection USP and Dextrose Injection USP and other antibacterial drugs, Cefazolin for Injection USP and Dextrose 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.

## CONTRAINDICATIONS

CEFAZOLIN FOR INJECTION USP AND DEXTROSE INJECTION USP IS CONTRAINDICATED IN PATIENTS WITH KNOWN ALLERGY TO THE CEPHALOSPORIN GROUP OF ANTIBIOTICS.

Solutions containing dextrose may be contraindicated in patients with hypersensitivity to corn products.

## WARNINGS

BEFORE THERAPY WITH CEFAZOLIN FOR INJECTION USP AND DEXTROSE INJECTION USP IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFAZOLIN, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS 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 USP AND DEXTROSE INJECTION USP OCCURS, DISCONTINUE TREATMENT WITH THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE

AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTIHISTAMINES, CORTICOSTEROIDS, PRESSOR AMINES AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

*Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefazolin for Injection USP and Dextrose Injection USP, 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 strains 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 diarrhea following antibiotic 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 antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

## PRECAUTIONS

### General

Prolonged use of Cefazolin for Injection USP and Dextrose Injection USP may result in the overgrowth of nonsusceptible organisms. Careful clinical observation of the patient is essential.

When Cefazolin for Injection USP and Dextrose Injection USP is administered to patients with low urinary output because of impaired renal function, lower daily dosage is required (see **DOSAGE AND ADMINISTRATION**).

As with other beta-lactam antibiotics, seizures may occur if inappropriately high doses are administered to patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**).

Cefazolin for Injection USP and Dextrose Injection USP, as with all cephalosporins, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

As with other dextrose-containing solutions, Cefazolin for Injection USP and Dextrose Injection USP should be prescribed with caution in patients with overt or known subclinical diabetes mellitus or carbohydrate intolerance for any reason.

Prescribing Cefazolin for Injection USP and Dextrose Injection USP in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

If administration is controlled by a pumping device, care must be taken to discontinue pumping action before the container runs dry or air embolism may result.

Use only if solution is clear and container and seals are intact.

### Drug Interactions

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

### Drug/Laboratory Test Interactions

A false positive reaction for glucose in the urine may occur with Benedict's solution, Fehling's solution or with Clinistix® tablets, but not with enzyme-based tests such as Clinistix®.

Positive direct and indirect antiglobulin (Coombs) tests have occurred; these may also occur in neonates whose mothers received cephalosporins before delivery.

### Information for Patients

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, 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 antibiotic. If this occurs, patients should contact their physician as soon as possible.

Patients should be counseled that antibacterial drugs including Cefazolin for Injection USP and Dextrose Injection USP should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefazolin for Injection USP and Dextrose Injection USP 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 USP and Dextrose Injection USP or other antibacterial drugs in the future.

### Carcinogenesis/Mutagenesis

Mutagenicity studies and long-term studies in animals to determine the carcinogenic potential of Cefazolin for Injection USP and Dextrose Injection USP have not been performed.

### Pregnancy – Teratogenic Effects – Pregnancy Category B.

Reproduction studies have been performed in rats, mice, and rabbits at doses up to 25 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefazolin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

### Labor and Delivery

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

### Nursing Mothers

Cefazolin is present in very low concentrations in the milk of nursing mothers. Caution should be exercised when Cefazolin for Injection USP and Dextrose Injection USP is administered to a nursing woman.

### Pediatric Use

Safety and effectiveness for use in premature infants and neonates have not been established. See **DOSAGE AND ADMINISTRATION** for recommended dosage in pediatric patients older than 1 month.

### 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.

This 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 **PRECAUTIONS, General** and **DOSAGE AND ADMINISTRATION**).

### ADVERSE REACTIONS

The following reactions have been reported:

**Gastrointestinal:** Diarrhea, oral candidiasis (oral thrush), vomiting, nausea, stomach cramps, anorexia and pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see **WARNINGS**). Nausea and vomiting have been reported rarely.

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

**Hematologic:** Neutropenia, leukopenia, thrombocytopenia, thrombocytopenia.

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

**Renal:** As with other cephalosporins, reports of increased BUN and creatinine levels, as well as renal failure, have been received.

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

**Other Reactions:** Genital and anal pruritus (including vulvar pruritus, genital moniliasis, and vaginitis).

### DOSAGE AND ADMINISTRATION

#### Usual Adult Dosage

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.

#### Perioperative Prophylactic Use

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

- 1 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 (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 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 prosthetic arthroplasty), the prophylactic administration of cefazolin may be continued for 3 to 5 days following the completion of surgery.

#### Dosage Adjustment for Patients with Reduced Renal Function

Cefazolin 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 35 to 54 mL/min. or serum creatinine of 1.6 to 3.0 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 1/2 the usual dose every 18 to 24 hours. All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection.

#### 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 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 17.7 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 17.7 mg/mL
10	4.5	40 mg	2.25 mL	30 mg	1.70 mL
20	9.0	75 mg	4.25 mL	55 mg	3.10 mL
30	13.6	115 mg	6.50 mL	85 mg	4.80 mL
40	18.1	150 mg	8.50 mL	115 mg	6.50 mL
50	22.7	190 mg	10.75 mL	140 mg	7.90 mL

Pediatric Dosage Guide					
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 17.7 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 17.7 mg/mL
10	4.5	75 mg	4.25 mL	55 mg	3.10 mL
20	9.0	150 mg	8.50 mL	110 mg	6.20 mL
30	13.6	225 mg	12.70 mL	170 mg	9.60 mL
40	18.1	300 mg	16.95 mL	225 mg	12.70 mL
50	22.7	375 mg	21.20 mL	285 mg	16.10 mL

Pediatric dosage can only be accomplished by delivering a portion of one DUPLEX® unit. This may be accomplished by control of infusion volume such as use with programmable infusion pump or buret with a delivery accuracy of ±0.05 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 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.

## DUPLEX® Drug Delivery System Directions for Use

### Removal from Multi-Pack Tray

- Tear tape strips from one or both sides of the tray. Remove top tray.
- To avoid inadvertent activation, DUPLEX Container should remain in the folded position until activation is intended.

### Patient Labeling and Drug Powder/Diluent Inspection

- Apply patient-specific label on foil side of container. USE CARE to avoid activation. Do not cover any portion of foil strip with patient label.
- Unlatch side tab and unfold DUPLEX Container. (See Diagram 1.)
- Visually inspect diluent chamber for particulate matter.
- Use only if container and seals are intact.
- To inspect the drug powder for foreign matter or discoloration, peel foil strip from drug chamber. (See Diagram 2.)
- Protect from light after removal of foil strip.

**Note: If foil strip is removed, the 500 mg dose size must be used within 30 days and the 1 gram dose size must be used within 7 days, but not beyond the labeled expiration date.**

- The product should be re-folded and the side tab latched until ready to activate.

### Reconstitution (Activation)

- Do not use directly after storage by refrigeration, allow the product to equilibrate to room temperature before patient use.
- Unfold the DUPLEX Container and point the set port in a downward direction. Starting at the hanger tab end, fold the DUPLEX Container just below the diluent meniscus trapping all air above the fold. To activate, squeeze the folded diluent chamber until the seal between the diluent and powder opens, releasing diluent into the drug powder chamber. (See Diagram 3.)
- Agitate the liquid-powder mixture until the drug powder is completely dissolved.

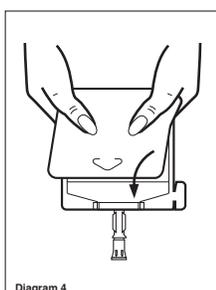
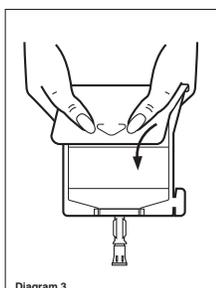
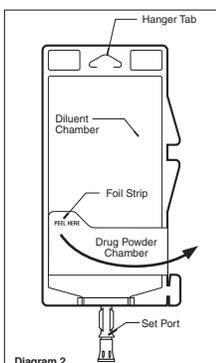
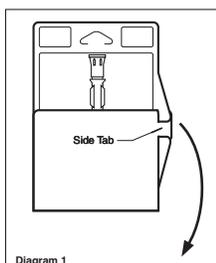
**Note: Following reconstitution (activation), product must be used within 24 hours if stored at room temperature or within 7 days if stored under refrigeration.**

### Administration

- Visually inspect the reconstituted solution for particulate matter.
- Point the set port in a downwards direction. Starting at the hanger tab end, fold the DUPLEX Container just below the solution meniscus trapping all air above the fold. Squeeze the folded DUPLEX Container until the seal between reconstituted drug solution and set port opens, releasing liquid to set port. (See Diagram 4.)
- Prior to attaching the IV set, check for minute leaks by squeezing container firmly. If leaks are found, discard container and solution as sterility may be impaired.
- Using aseptic technique, remove the set port cover from the set port and attach sterile administration set.
- Refer to Directions for Use accompanying the administration set.

### Precautions

- As with other cephalosporins, reconstituted Cefazolin for Injection USP and Dextrose Injection USP tends to darken depending on storage conditions, within the stated recommendations. However, product potency is not adversely affected.
- Use only if prepared solution is clear and free from particulate matter.
- Do not use in series connection.
- Do not introduce additives into the DUPLEX Container.
- Do not freeze.



## HOW SUPPLIED

Cefazolin for Injection USP and Dextrose Injection USP in the DUPLEX Drug Delivery System is a flexible dual chamber container supplied in two concentrations. After reconstitution, the concentrations are equivalent to 500 mg and 1 g cefazolin. The diluent chamber contains approximately 50 mL of Dextrose Injection USP. Dextrose Injection USP has been adjusted to 4.8% and 4.0% for the 500 mg and 1 g doses, respectively, such that the reconstituted solution is iso-osmotic.

Cefazolin for Injection USP and Dextrose Injection USP is supplied sterile and nonpyrogenic in the DUPLEX® Drug Delivery System containers packaged 12 units per tray, 2 trays per case.

NDC	Cat. No.	Dose	Volume
Cefazolin for Injection USP and Dextrose Injection USP			
0264-3103-11	3103-11	1 g	50 mL
Cefazolin for Injection USP and Dextrose Injection USP			
0264-3102-11	3102-11	500 mg	50 mL

Store the unactivated unit at 20-25°C (68-77°F). Excursions permitted to 15-30°C (59-86°F).

## REFERENCES

1. National Committee for Clinical Laboratory Standards (NCCLS). January 2003. *Performance Standards for Antimicrobial Disk Susceptibility Tests*; Approved Standard-Eighth Edition. NCCLS Document M2-A8 and Disk Diffusion Supplemental Tables M100-S13. NCCLS, Wayne, PA, USA.
2. National Committee for Clinical Laboratory Standards (NCCLS). January 2003. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*; Approved Standard-Sixth Edition. NCCLS Document M7-A6 and MIC Testing Supplemental Tables, M100-S13. NCCLS, Wayne, PA, USA.

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