FRESENIUS KABI

451182E/Revised: March 2016

Cefazolin for Injection, USP

Rx only

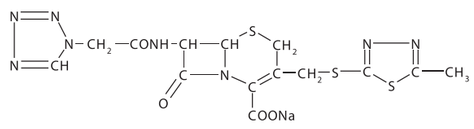
PHARMACY BULK PACKAGE – NOT FOR DIRECT INFUSION

To reduce the development of drug-resistant bacteria and maintain the effectiveness 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 bacteria.

DESCRIPTION:

Cefazolin for Injection, USP is a semi-synthetic cephalosporin for parenteral administration. It is the sodium salt of 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-carboxylic acid.

Cefazolin sodium USP has the following structural formula:



$C_{14}H_{13}N_8NaO_4S_3$ M.W. 476.5

The pH of the reconstituted solution is between 4 and 6.

Cefazolin for Injection, USP is a white to cream sterile powder. The color of Cefazolin for Injection, USP solutions may range from pale yellow to yellow without a change in potency.

Cefazolin for Injection, USP is supplied in 10 or 20 grams Pharmacy Bulk Packages. Each Pharmacy Bulk Package contains cefazolin sodium equivalent to 10 grams or 20 grams of cefazolin. The sodium content is approximately 48 mg (2.1 mEq) per gram of cefazolin sodium.

It is to be administered by intravenous route.

A Pharmacy Bulk Package is a container of a sterile preparation for parenteral use that contains many single doses. The contents of this pharmacy bulk package are intended for use by a pharmacy admixture service for addition to suitable parenteral fluids in the preparation of admixtures for intravenous infusion (See **DOSAGE AND ADMINISTRATION, Directions for Proper Use of Pharmacy Bulk Package**.) FURTHER DILUTION IS REQUIRED. NOT FOR DIRECT INFUSION.

CLINICAL PHARMACOLOGY:

After intramuscular administration of Cefazolin for Injection to normal volunteers, the mean serum concentrations were 37 mcg/mL at 1 hour and 3 mcg/mL at 8 hours following a 500 mg dose, and 64 mcg/mL at 1 hour and 7 mcg/mL at 8 hours following a 1 gram dose.

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

The serum half-life for Cefazolin for Injection is approximately 1.8 hours following I.V. 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 for Injection produced a steady serum level at the third hour of approximately 28 mcg/mL.

Studies in patients hospitalized with infections indicate that Cefazolin for Injection produces mean peak serum levels approximately equivalent to those seen in normal volunteers.

Bile levels in patients without obstructive biliary disease can reach or exceed serum levels by up to 5 times; however, in patients with obstructive biliary disease, bile levels of Cefazolin for Injection are considerably lower than serum levels (less than 1 mcg/mL).

In synovial fluid, the level of Cefazolin for Injection becomes comparable to that reached in serum at about 4 hours after drug administration.

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

Cefazolin for Injection 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 for Injection 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 for Injection produced mean serum levels 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 for Injection is usually well tolerated.

10000000139055

10000000139055

Controlled studies on adult normal volunteers, receiving 1 gram 4 times a day for 10 days, monitoring CBC, SGOT, SGPT, bilirubin, alkaline phosphatase, BUN, creatinine, and urinalysis, indicated no clinically significant changes attributed to Cefazolin for Injection.

Microbiology

Mechanism of Action

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

Resistance

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

Antimicrobial Activity

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 agalactiae*
  - *Streptococcus pneumoniae*
  - *Streptococcus pyogenes*

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 cumulative reports 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 1.

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 1.

Table 1: Susceptibility Test Interpretive Criteria for Cefazolin*

Pathogen	Minimum Inhibitory Concentration (mcg/mL)			Disk Diffusion Zone Diameter (mm)		
	S	I	R	S	I	R
Enterobacteriaceae	≤ 1	2	≥ 4	-	-	-

Abbreviations: S= susceptible, I= intermediate, R= resistant

*Interpretive criteria are based on 1 g every 8 hr

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.

NOTE: Susceptibility of staphylococci to cefazolin may be deduced from testing either cefoxitin or oxacillin.

A report of *Susceptible* indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations at the infection site necessary 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 that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant* indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound 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 2. For the diffusion technique using the 30 mcg disk, the criteria in Table 2 should be achieved.

Table 2: Acceptable Quality Control Ranges for Cefazolin

Quality Control Strain	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

INDICATIONS AND USAGE:

Cefazolin for Injection, USP is indicated for the treatment of the following serious infections due to susceptible organisms.

Respiratory Tract Infections: Due to *S. pneumoniae, Klebsiella* species, *H. influenzae, S. aureus* (penicillin-sensitive and penicillin-resistant), and group A beta-hemolytic streptococci.

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

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

Urinary Tract Infections: Due to *E. coli, P. mirabilis, Klebsiella* species, and some strains of enterobacter and enterococci.

Skin and Skin Structure Infections: Due to *S. aureus* (penicillin-sensitive and penicillin-resistant), group A beta-hemolytic streptococci, and other strains of streptococci.

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

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

Genital Infections: (i.e., prostatitis, epididymitis) due to *E. coli*, *P. mirabilis*, *Klebsiella* species, and some strains of enterococci.

Septicemia: Due to *S. pneumoniae*, *S. aureus* (penicillin-sensitive and penicillin-resistant), *P. mirabilis*, *E. coli*, and *Klebsiella* species.

Endocarditis: Due to *S. aureus* (penicillin-sensitive and penicillin-resistant) and group A beta-hemolytic streptococci.

Perioperative Prophylaxis: The prophylactic administration of Cefazolin for Injection 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 for Injection 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 for Injection 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 for Injection 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 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 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 IS CONTRAINDICATED IN PATIENTS WITH KNOWN ALLERGY TO THE CEPHALOSPORIN GROUP OF ANTIBIOTICS.

WARNINGS:

BEFORE THERAPY WITH CEFAZOLIN FOR INJECTION 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 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.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefazolin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an oral antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS:

General

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

When Cefazolin for Injection 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 β-lactam antibiotics, seizures may occur if inappropriately high doses are administered to patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**).

Cefazolin for Injection, 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.

Prescribing Cefazolin for Injection 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.

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 CLINITEST® 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

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.

Carcinogenesis/Mutagenesis

Mutagenicity studies and long-term studies in animals to determine the carcinogenic potential of Cefazolin for Injection 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 for Injection. 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 for Injection 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.

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 for Injection 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 antibacterial 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, thrombocythemia.

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. Pain at the site of injection after intramuscular administration has occurred infrequently. Some induration has occurred.

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

To report SUSPECTED ADVERSE EVENTS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov.

DOSAGE AND ADMINISTRATION:

THE INTENT OF THE PHARMACY BULK PACKAGE FOR THIS PRODUCT IS FOR PREPARATION OF SOLUTIONS FOR I.V. INFUSION ONLY.

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:

a) 1 gram I.V. administered ½ 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 I.V. during surgery (administration modified depending on the duration of the operative procedure).
c) 500 mg to 1 gram I.V. every 6 to 8 hours for 24 hours postoperatively.

It is important that (1) the preoperative dose be given just prior (1/2 hour to 1 hour) 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 prosthetic 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 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. 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.

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/q 8 h	Vol. (mL) needed with dilution of 125 mg/mL	Approximate Single Dose mg/q 6 h	Vol. (mL) needed with dilution of 125 mg/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/q 8 h	Vol. (mL) needed with dilution of 225 mg/mL	Approximate Single Dose mg/q 6 h	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 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 SHAKEN 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.

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.

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

CAUTION: NOT TO BE DISPENSED AS A UNIT.

Directions for Proper Use of a Pharmacy Bulk Package

a. The container closure may be penetrated only one time after reconstitution, utilizing a suitable sterile dispensing set which allows measured distribution of the contents.
b. Use of this product is restricted to a suitable work area, such as a laminar flow hood.
c. Once this container closure has been punctures, withdrawal of the contents should be completed without delay. If prompt fluid transfer cannot be accomplished, discard the contents no later than 4 HOURS after initial closure puncture. This time limit should begin with the introduction of solvent for diluent into the Pharmacy Bulk Package.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not add supplementary medication to Cefazolin for Injection, USP.

Pharmacy Bulk Vials

Add 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.)

Vial Size	Amount of Diluent	Approximate Concentration	Approximate Available Volume
10 grams	45 mL	1 gram/5 mL	51 mL
	96 mL	1 gram/10 mL	102 mL
20 grams	87 mL	1 gram/5 mL	99 mL

ADMINISTRATION:

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 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

HOW SUPPLIED:

Cefazolin for Injection, USP

Product No.	NDC No.	Cefazolin for Injection, USP
238B1	63323-238-61	10 grams per vial
449B1	63323-449-61	20 grams per vial

Cefazolin for Injection, USP, is supplied in 10 and 20 grams Pharmacy Bulk Package. Each Pharmacy Bulk Package contains cefazolin sodium equivalent to 10 or 20 grams of cefazolin and is packaged 10 per carton.

Preservative Free.

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].

The container closure is not made with natural rubber latex.

REFERENCES:

1. Clinical and Laboratory Standards Institute (CLSI). *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*; *Approved Standard-Tenth Edition*. CLSI document M07-A10, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.

2. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-fifth Informational Supplement, CLSI document M100-S25, Clinical and Laboratory Standards Institute, 950 West Valley road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.

3. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard – Twelfth Edition. CLSI document M02-A12, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2015.

CLINITEST is a registered trademark of Miles, Inc.
CLINISTIX is a registered trademark of Bayer Corporation.

Manufactured for:

FRESENIUS KABI
Lake Zurich, IL 60047

Made in Italy

www.fresenius-kabi.us

451182E

Revised: March 2016

10000000139055