

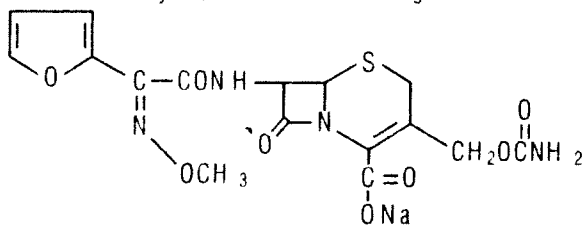
Cefuroxime for Injection, USP

R_x only

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

DESCRIPTION

Cefuroxime is a sterile semisynthetic, broad-spectrum, cephalosporin antibiotic for parenteral administration. It is the sodium salt of (6R, 7R)-3-carbamoyloxymethyl-7-[Z-2-methoxyimino-2-(fur-2-yl)acetamido]ceph-3-em-4-carboxylate, and it has the following structural formula:



The molecular formula is $C_{16}H_{15}N_4NaO_8S$, representing a molecular weight of 446.4.

Cefuroxime for Injection contains approximately 54.2 mg (2.4 mEq) of sodium per gram of cefuroxime activity.

Cefuroxime for Injection in sterile crystalline form is supplied in vials equivalent to 750 mg or 1.5 g of cefuroxime as cefuroxime sodium. Solutions of cefuroxime range in color from light yellow to amber, depending on the concentration and diluent used. The pH of freshly constituted solutions usually ranges from 6 to 8.5.

CLINICAL PHARMACOLOGY

After intramuscular (IM) injection of a 750 mg dose of cefuroxime to normal volunteers, the mean peak serum concentration was 27 mcg/mL. The peak occurred at approximately 45 minutes (range, 15 to 60 minutes). Following IV doses of 750 mg and 1.5 grams, serum concentrations were approximately 50 and 100 mcg/mL, respectively, at 15 minutes. Therapeutic serum concentrations of approximately 2 mcg/mL or more were maintained for 5.3 hours and 8 hours or more, respectively. There was no evidence of accumulation of cefuroxime in the serum following IV administration of 1.5 g doses every 8 hours to normal volunteers. The serum half-life after either IM or IV injections is approximately 80 minutes.

Approximately 89% of a dose of cefuroxime is excreted by the kidneys over an 8-hour period, resulting in high urinary concentrations.

Following the IM administration of a 750 mg single dose, urinary concentrations averaged 1300 mcg/mL during the first 8 hours. Intravenous doses of 750 mg and 1.5 g produced urinary levels averaging 1150 and 2500 mcg/mL, respectively, during the first 8-hour period.

The concomitant oral administration of probenecid with cefuroxime slows tubular secretion, decreases renal clearance by approximately 40%, increases the peak serum level by approximately 30%, and increases the serum half-life by approximately 30%. Cefuroxime is detectable in therapeutic concentrations in pleural fluid, joint fluid, bile, sputum, bone, and aqueous humor.

Cefuroxime is detectable in therapeutic concentrations in cerebrospinal fluid (CSF) of adults and pediatric patients with meningitis. The following table shows the concentrations of cefuroxime achieved in cerebrospinal fluid during multiple dosing of patients with meningitis.

Table 1: Concentrations of Cefuroxime Achieved in Cerebrospinal Fluid During Multiple Dosing of Patients with Meningitis

Patients	Dose	Number of Patients	Mean (Range) CSF Cefuroxime Concentrations (mcg/mL) Achieved Within 8 hours Post-Dose
Pediatric patients (4 weeks to 6.5 years)	200 mg/kg/day, divided q 6 hours	5	6.6 (0.9 - 17.3)
Pediatric patients (7 months to 9 years)	200 to 230 mg/kg/day, divided q 8 hours	6	8.3 (<2 - 22.5)
Adults	1.5 grams q 8 hours	2	5.2 (2.7 - 8.9)
Adults	1.5 grams q 6 hours	10	6 (1.5 - 13.5)

Cefuroxime is approximately 50% bound to serum protein.

Microbiology

Cefuroxime has *in vitro* activity against a wide range of gram-positive and gram-negative organisms, and it is highly stable in the presence of beta-lactamases of certain gram-negative bacteria. The bactericidal action of cefuroxime results from inhibition of cell-wall synthesis.

Cefuroxime is usually active against the following organisms *in vitro*.

Aerobes, Gram-positive: *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes* (and other streptococci)
NOTE: Most strains of enterococci, e.g., *Enterococcus faecalis* (formerly *Streptococcus faecalis*) are resistant to cefuroxime. Methicillin-resistant staphylococci and *Listeria monocytogenes* are resistant to cefuroxime.

Aerobes, Gram-negative: *Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Haemophilus influenzae* (including ampicillin-resistant strains), *Haemophilus parainfluenzae*, *Klebsiella* spp., (including *Klebsiella pneumoniae*), *Moraxella (Branhamella) catarrhalis* (including ampicillin- and cephalothin-resistant strains), *Morganella morganii* (formerly *Proteus morganii*), *Neisseria gonorrhoeae* (including penicillinase- and non-penicillinase-producing strains), *Neisseria meningitidis*, *Proteus mirabilis*, *Providencia rettgeri* (formerly *Proteus rettgeri*), *Salmonella* spp. and *Shigella* spp.

NOTE: Some strains of *Morganella morganii*, *Enterobacter cloacae* and *Citrobacter* spp. have been shown by *in vitro* tests to be resistant to cefuroxime and other cephalosporins. *Pseudomonas* and *Campylobacter* spp., *Acinetobacter calcoaceticus*, and most strains of *Serratia* spp. and *Proteus vulgaris* are resistant to most first- and second-generation cephalosporins.

Anaerobes: Gram-positive and gram-negative cocci (including *Peptococcus* and *Peptostreptococcus* spp.), gram-positive bacilli (including *Clostridium* spp.), and gram-negative bacilli (including *Bacteroides* and *Fusobacterium* spp.)

NOTE: *Clostridium difficile* and most strains of *Bacteroides fragilis* are resistant to cefuroxime.

Susceptibility Tests: Diffusion Techniques: Quantitative methods that require measurement of zone diameters give an estimate of antibiotic susceptibility. One such standard procedure¹ that has been recommended for use with disks to test susceptibility of organisms to cefuroxime uses the 30 mcg cefuroxime disk. Interpretation involves the correlation of the diameters obtained in the disk test with the minimum inhibitory concentration (MIC) for cefuroxime.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited by generally achievable blood levels. A report of "Moderately Susceptible" suggests that the organism would be susceptible if high dosage is used or if the infection is confined to tissues and fluids in which high antibiotic levels are attained. A report of "Intermediate" suggests an equivocal or indeterminate result. A report of "Resistant" indicates that achievable concentrations of the antibiotic are unlikely to be inhibitory and other therapy should be selected.

Reports from the laboratory giving results of the standard single-disk susceptibility test for organisms other than *Haemophilus* spp. and *Neisseria gonorrhoeae* with a 30-mcg cefuroxime disk should be interpreted according to the following criteria:

Zone Diameter (mm)	Interpretation
≥ 18	(S) Susceptible
15 - 17	(MS) Moderately Susceptible
≤ 14	(R) Resistant

Results for *Haemophilus* spp. should be interpreted according to the following criteria:

Zone Diameter (mm)	Interpretation
≥ 24	(S) Susceptible
21 - 23	(I) Intermediate
≤ 20	(R) Resistant

Results for *Neisseria gonorrhoeae* should be interpreted according to the following criteria:

Zone Diameter (mm)	Interpretation
≥ 31	(S) Susceptible
26 - 30	(MS) Moderately Susceptible
≤ 25	(R) Resistant

Organisms should be tested with the cefuroxime disk since cefuroxime has been shown by *in vitro* tests to be active against certain strains found resistant when other beta-lactam disks are used. The cefuroxime disk should not be used for testing susceptibility to other cephalosporins.

Standardized procedures require the use of laboratory control organisms. The 30 mcg cefuroxime disk should give the following zone diameters.

1. Testing for organisms other than *Haemophilus* spp. and *Neisseria gonorrhoeae*:

<u>Organism</u>	<u>Zone Diameter (mm)</u>
<i>Staphylococcus aureus</i> ATCC 25923	27 - 35
<i>Escherichia coli</i> ATCC 25922	20 - 26

2. Testing for *Haemophilus* spp.:

<u>Organism</u>	<u>Zone Diameter (mm)</u>
<i>Haemophilus influenzae</i> ATCC 49766	28 - 36

3. Testing for *Neisseria gonorrhoeae*:

<u>Organism</u>	<u>Zone Diameter (mm)</u>
<i>Neisseria gonorrhoeae</i> ATCC 49226	33 - 41
<i>Staphylococcus aureus</i> ATCC 25923	29 - 33

Dilution Techniques: Use a standardized dilution method¹ (broth, agar, microdilution) or equivalent with cefuroxime powder. The MIC values obtained for bacterial isolates other than *Haemophilus* spp. and *Neisseria gonorrhoeae* should be interpreted according to the following criteria:

<u>MIC (mcg/mL)</u>	<u>Interpretation</u>
≤ 8	(S) Susceptible
16	(MS) Moderately Susceptible
≥ 32	(R) Resistant

MIC values obtained for *Haemophilus* spp. should be interpreted according to the following criteria:

<u>MIC (mcg/mL)</u>	<u>Interpretation</u>
≤ 4	(S) Susceptible
8	(I) Intermediate
≥ 16	(R) Resistant

MIC values obtained for *Neisseria gonorrhoeae* should be interpreted according to the following criteria:

<u>MIC (mcg/mL)</u>	<u>Interpretation</u>
≤ 1	(S) Susceptible
2	(MS) Moderately Susceptible
≥ 4	(R) Resistant

As with standard diffusion techniques, dilution methods require the use of laboratory control organisms. Standard cefuroxime powder should provide the following MIC values.

1. For organisms other than *Haemophilus* spp. and *Neisseria gonorrhoeae*:

<u>Organism</u>	<u>MIC (mcg/mL)</u>
<i>Staphylococcus aureus</i> ATCC 29213	0.5 - 2
<i>Escherichia coli</i> ATCC 25922	2 - 8

2. For *Haemophilus* spp.:

<u>Organism</u>	<u>MIC (mcg/mL)</u>
<i>Haemophilus influenzae</i> ATCC 49766	0.25 - 1

3. For *Neisseria gonorrhoeae*:

<u>Organism</u>	<u>MIC (mcg/mL)</u>
<i>Neisseria gonorrhoeae</i> ATCC 49226	0.25 - 1
<i>Staphylococcus aureus</i> ATCC 29213	0.25 - 1

INDICATIONS AND USAGE

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

Cefuroxime for Injection is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases

1. **Lower Respiratory Tract Infections**, including pneumonia, caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (including ampicillin-resistant strains), *Klebsiella* spp., *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains), *Streptococcus pyogenes*, and *Escherichia coli*
2. **Urinary Tract Infections** caused by *Escherichia coli* and *Klebsiella* spp.
3. **Skin and Skin-Structure Infections** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains), *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp.
4. **Septicemia** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase producing strains), *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae* (including ampicillin resistant strains), and *Klebsiella* spp.
5. **Meningitis** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (including ampicillin-resistant strains), *Neisseria meningitidis*, and *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains).
6. **Gonorrhoeae**, uncomplicated and disseminated gonococcal infections due to *Neisseria gonorrhoeae* (penicillinase- and non-penicillinase-producing strains in both males and females).
7. **Bone and Joint Infections** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin-structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. Cefuroxime has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to cefuroxime.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, cefuroxime may be used concomitantly with an aminoglycoside (see **PRECAUTIONS**). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

When culture and susceptibility information are available, they should be considered in selecting or modifying antimicrobial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Prevention: The preoperative prophylactic administration of cefuroxime may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (e.g., vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. Cefuroxime should usually be given one-half to 1 hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of cefuroxime has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that cefuroxime therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism, and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS

Cefuroxime is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS

BEFORE THERAPY WITH CEFUROXIME IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO CEFUROXIME OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefuroxime, 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 one primary cause of "antibiotic-associated colitis". After the diagnosis of pseudomembranous colitis has been established, appropriate 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, electrolytes and protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. Other causes of colitis should also be considered.

PRECAUTIONS

General: Prescribing the antibacterial drug product in the absence of a proven or strongly suspected bacterial infection of a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. Although cefuroxime rarely produces alterations in kidney function evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of cefuroxime should be reduced in patients with transient or persistent renal insufficiency (see **DOSAGE AND ADMINISTRATION**), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of cefuroxime may result in overgrowth of non-susceptible organisms. Careful observation of the patient is essential. Superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

As with other therapeutic regimens used in the treatment of meningitis, mild-to-severe hearing loss has been reported in some pediatric patients treated with cefuroxime. Persistence of positive CSF (cerebrospinal fluid) cultures at 18 to 36 hours, particularly in patients with *Haemophilus influenzae* isolates, has also been noted, however, the precise clinical impact of this is unknown.

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.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest™ tablets) but not with enzyme-based tests for glycosuria. As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving cefuroxime.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although lifetime studies in animals have not been performed to evaluate carcinogenic potential, no mutagenic activity was found for cefuroxime the mouse lymphoma assay and a battery of bacterial mutation tests. Positive results were obtained in an *in vitro* chromosome aberration assay, however, negative results were found in an *in vivo* micronucleus test at doses up to 10 g/kg. Reproduction studies in mice at doses up to 3200 mg/kg per day (3.1 times the recommended maximum human dose based on mg/m²) have revealed no impairment of fertility.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproduction studies have been performed in mice at doses up to 6400 mg/kg per day (6.3 times the recommended maximum human dose based on mg/m²) and rabbits at doses up to 400 mg/kg per day (2.1 times the recommended maximum human dose based on mg/m²) and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. 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.

Nursing Mothers: Since cefuroxime is excreted in human milk, caution should be exercised when cefuroxime is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

Geriatric Use: Of the 1914 subjects who received cefuroxime in 24 clinical studies of Cefuroxime, 901 (47%) were 65 and over while 421 (22%) were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater susceptibility of some older individuals to drug effects cannot be ruled out. This drug is known 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**).

Information for Patients: Patients should be counseled that antibacterial drugs, including the antibacterial drug product prescribed, should only be used to treat bacterial infections and that they do not treat viral infections (e.g., the common cold).

When an antibacterial drug product 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.

Physicians are advised to counsel patients that 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 the antibacterial drug product or other antibacterial drugs in the future.

ADVERSE REACTIONS

Cefuroxime is generally well-tolerated. The most common adverse effects have been local reactions following IV administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with IV administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). The onset of pseudomembranous colitis may occur during or after antibacterial treatment (see **WARNINGS**).

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in fewer than 1% of the patients treated with Cefuroxime for Injection and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in fewer than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylactic drug fever, erythema multiforme, interstitial nephritis, toxic epidermal necrolysis, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (fewer than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence were seen with other cephalosporins used in controlled studies. As with other cephalosporins, there have been rare reports of thrombocytopenia.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

Postmarketing Experience with Cefuroxime for Injection, USP Products: In addition to the adverse events reported during clinical trials, the following events have been observed during clinical practice in patients treated with Cefuroxime for Injection, USP and were reported spontaneously. Data are generally insufficient to allow an estimate of incidence or to establish causation.

Neurologic: Seizure.

Non-site specific: Angioedema.

Cephalosporin-class Adverse Reactions: In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

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

Altered Laboratory Tests: Prolonged prothrombin time, pancytopenia, agranulocytosis.

OVERDOSAGE

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal dialysis.

DOSAGE AND ADMINISTRATION

Dosage: Adults: The usual adult dosage range for cefuroxime is 750 mg to 1.5 grams every 8 hours, usually for 5 to 10 days. In uncomplicated urinary tract infections, skin and skin-structure infections, disseminated gonococcal infections, and uncomplicated pneumonia, a 750 mg dose every 8 hours is recommended. In severe or complicated infections, a 1.5 gram dose every 8 hours is recommended.

In bone and joint infections, a 1.5-gram dose every 8 hours is recommended. In clinical trials, surgical intervention was performed when indicated as an adjunct to cefuroxime therapy. A course of oral antibiotics was administered when appropriate following the completion of parenteral administration of cefuroxime.

In life-threatening infections or infections due to less susceptible organisms, 1.5 grams every 6 hours may be required. In bacterial meningitis, the dosage should not exceed 3 grams every 8 hours. The recommended dosage for uncomplicated gonococcal infection is 1.5 gram given intramuscular as a single dose at two different sites together with 1 gram of oral probenecid. For preventive use for clean-contaminated or potentially contaminated surgical procedures, a 1.5-gram dose administered intravenously just before surgery (approximately one-half to 1 hour before the initial incision) is recommended. Thereafter, give 750 mg intravenously or intramuscularly every 8 hours when the procedure is prolonged.

For preventive use during open heart surgery, a 1.5 gram dose administered intravenously at the induction of anesthesia and every 12 hours thereafter for a total of 6 grams is recommended.

Impaired Renal Function: A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 2).

Table 2: Dosage of Cefuroxime in Adults with Reduced Renal Function

Creatinine Clearance (mL/min)	Dose	Frequency
> 20	750 mg to 1.5 grams	q8h
10 - 20	750 mg	q12h
< 10	750 mg	q24h*

*Since cefuroxime is dialyzable, patients on hemodialysis should be given a further dose at the end of the dialysis.

When only serum creatinine is available, the following formula² (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

$$\text{Males: Creatinine clearance (mL/min)} = \frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/dL)}} \qquad \text{Females: } 0.85 \times \text{male value}$$

NOTE: As with antibiotic therapy in general, administration of cefuroxime should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended in infections caused by *Streptococcus pyogenes* in order to guard against the risk of rheumatic fever or glomerulonephritis, frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infection and may be required for several months after therapy has been completed; persistent infections may require treatment for several weeks, and doses smaller than those indicated above should not be used. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

Pediatric Patients Above 3 Months of Age: Administration of 50 to 100 mg/kg per day in equally divided doses every 6 to 8 hours has been successful for most infections susceptible to cefuroxime. The higher dosage of 100 mg/kg per day (not to exceed the maximum adult dosage) should be used for the more severe or serious infections.

In bone and joint infections, 150 mg/kg per day (not to exceed the maximum adult dosage) is recommended in equally divided doses every 8 hours. In clinical trials, a course of oral antibiotics was administered to pediatric patients following the completion of parenteral administration of cefuroxime.

In cases of bacterial meningitis, a larger dosage of cefuroxime is recommended, 200 to 240 mg/kg per day intravenously in divided doses every 6 to 8 hours.

In pediatric patients with renal insufficiency, the frequency of dosing should be modified consistent with the recommendations for adults.

Preparation of Solution and Suspension: The directions for preparing Cefuroxime for Injection for both IV and IM use are summarized in Table 3.

For Intramuscular Use: Each 750 mg vial of Cefuroxime should be constituted with 3 mL of Sterile Water for Injection. Shake gently to disperse and withdraw completely the resulting suspension for injection.

For Intravenous Use: Each 750 mg vial should be constituted with 8 mL of Sterile Water for Injection. Withdraw completely the resulting solution for injection. Each 1.5 gram vial should be constituted with 16 mL of Sterile Water for Injection, and the solution should be completely withdrawn for injection.

Each 750 mg or 1.5 grams infusion pack should be constituted with 100 mL of Sterile Water for Injection, 5% Dextrose Injection, 0.9% Sodium Chloride Injection, or any of the solutions listed under the Intravenous portion of the **Compatibility and Stability** section.

Table 3: Preparation of Solution and Suspension

Strength	Amount of Diluent to be Added (mL)	Volume to be Withdrawn	Approximate Cefuroxime Concentration (mg/mL)
750 mg Vial	3 (IM)	Total*	220
750 mg Vial	8 (IV)	Total	90
1.5 gram Vial	16 (IV)	Total	90
750 mg Infusion Pack	100 (IV)	---	7.5
1.5 gram Infusion Pack	100 (IV)	---	15

*Cefuroxime is a suspension at IM concentrations.

Administration: After constitution, Cefuroxime for Injection may be given intravenously or by deep IM injection into a large muscle mass (such as the gluteus or lateral part of the thigh). Before injecting intramuscularly, aspiration is necessary to avoid inadvertent injection into a blood vessel.

Intravenous Administration: The IV route may be preferable for patients with bacterial septicemia or other severe or life-threatening infections or for patients who may be poor risks because of lowered resistance, particularly if shock is present or impending.

For direct intermittent IV administration, slowly inject the solution into a vein over a period of 3 to 5 minutes or give it through the tubing system by which the patient is also receiving other IV solutions.

For direct intermittent IV infusion with a Y type administration set, dosing can be accomplished through the tubing system by which the patient may be receiving other IV solutions. However, during infusion of the solution containing cefuroxime, it is advisable to temporarily discontinue administration of any other solutions at the same site.

For continuous IV infusion, a solution of cefuroxime may be added to an IV infusion pack containing one of the following fluids: 0.9% Sodium Chloride Injection; 5% Dextrose Injection; 10% Dextrose Injection; 5% Dextrose and 0.9% Sodium Chloride Injection; 5% Dextrose and 0.45% Sodium Chloride Injection; or 1/6 M Sodium Lactate Injection.

Solutions of cefuroxime, like those of most beta-lactam antibiotics, should not be added to solutions of aminoglycoside antibiotics because of potential interaction. However, if concurrent therapy with cefuroxime and an aminoglycoside is indicated, each of these antibiotics can be administered separately to the same patient.

Compatibility and Stability

Intramuscular: When constituted as directed with Sterile Water for Injection, suspensions of cefuroxime for IM injection maintain satisfactory potency for 24 hours at room temperature and for 48 hours under refrigeration (5°C).

After the periods mentioned above any unused suspensions should be discarded.

Intravenous: When the 750 mg and 1.5 g vials are constituted as directed with Sterile Water for Injection, the solutions of Cefuroxime for Injection for IV administration maintain satisfactory potency for 24 hours at room temperature and for 48 hours under refrigeration (5°C). More dilute solutions, such as 750 mg or 1.5 g plus 100 mL of Sterile Water for Injection, 5% Dextrose Injection, or 0.9% Sodium Chloride Injection, also maintain satisfactory potency for 24 hours at room temperature and for 7 days under refrigeration.

These solutions may be further diluted to concentrations of between 1 and 30 mg/mL in the following solutions and will lose not more than 10% activity for 24 hours at room temperature or for at least 7 days under refrigeration: 0.9% Sodium Chloride Injection; 1/6 M Sodium Lactate Injection, Ringer's Injection, USP; Lactated Ringer's Injection, USP, 5% Dextrose and 0.9% Sodium Chloride Injection, 5% Dextrose Injection; 5% Dextrose and 0.45% Sodium Chloride Injection; 5% Dextrose and 0.225% Sodium Chloride Injection; 10% Dextrose Injection; and 10% Invert Sugar in Water for Injection.

Unused solutions should be discarded after the time periods mentioned above.

Cefuroxime for Injection has also been found compatible for 24 hours at room temperature when admixed in IV infusion with Heparin (10 and 50 U/mL) in 0.9% Sodium Chloride Injection and Potassium Chloride (10 and 40 mEq/L) in 0.9% Sodium Chloride Injection. Sodium Bicarbonate Injection, USP is not recommended for the dilution of Cefuroxime for Injection.

Frozen Stability: Constitute the 750 mg or 1.5 g vial as directed for intravenous administration in Table 3. Immediately withdraw the total contents of the 750 mg or 1.5 g vial and add to 50 or 100 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection and freeze. Frozen solutions are stable for 6 months when stored at -20°C. Frozen solutions should be thawed at room temperature and not refrozen. Do not force thaw by immersion in water baths or by microwave irradiation. Thawed solutions may be stored for up to 24 hours at room temperature or for 7 days in a refrigerator (5°C).

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration before administration whenever solution and container permit.

As with other cephalosporins, Cefuroxime for Injection powder as well as solutions tend to darken, depending on storage conditions, without adversely affecting product potency.

HOW SUPPLIED

Cefuroxime for Injection, USP in the dry state should be stored at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

Cefuroxime for Injection, USP, is a dry, white to off-white powder supplied as follows:

NDC 10019-620-01 *Sterile Cefuroxime Sodium, USP, 750 mg*, Equivalent to Cefuroxime, IM/IV Injection (Carton of 25)

NDC 10019-620-02 *Sterile Cefuroxime Sodium, USP, 750 mg*, Equivalent to Cefuroxime, IV Infusion Pack (Carton of 10)

NDC 10019-621-03 *Sterile Cefuroxime Sodium, USP, 1.5 grams*, Equivalent to Cefuroxime, IV Injection (Carton of 25)

NDC 10019-621-04 *Sterile Cefuroxime Sodium, USP, 1.5 grams*, Equivalent to Cefuroxime, IV Infusion Pack (Carton of 10)

Also available as:

NDC 10019-622-05 *Sterile Cefuroxime Sodium, USP, 7.5 grams, Equivalent to Cefuroxime, Pharmacy Bulk Package (Carton of 10)*

REFERENCES

1. National Committee for Clinical Laboratory Standards. *Performance Standards for Antimicrobial Susceptibility Testing*. Third Informational Supplement. NCCLS Document M100-S3, Vol. 11, No. 17. Villanova, Pa: NCCLS: 1991.
2. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31-41.

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