

Cefuroxime

for Injection, USP

750 mg/15 mL vial

1.5 g/50 mL vial

7.5 g/100 mL Pharmacy Bulk Package Vial

THERAPEUTIC CLASSIFICATION

Antibiotic

ACTION AND CLINICAL PHARMACOLOGY

In vitro studies demonstrate that the bactericidal action of cefuroxime results from inhibition of bacterial cell wall synthesis by inhibiting the transpeptidase and carboxypeptidase enzymes.

INDICATIONS AND CLINICAL USES

Treatment

Cefuroxime for Injection, USP may be indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

Lower Respiratory Tract Infections

Pneumonia caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* including ampicillin-resistant strains, *Klebsiella* species, *Staphylococcus aureus* including ampicillin-resistant (but not methicillin-resistant) strains, *Streptococcus pyogenes*, and *Escherichia coli*.

Urinary Tract Infections

Caused by *Escherichia coli*, and *Klebsiella* species.

Soft Tissue Infections

Caused by *Staphylococcus aureus*, including ampicillin-resistant (but not methicillin-resistant) strains, *Streptococcus pyogenes*, *Escherichia coli*, and *Klebsiella* species.

Meningitis

Caused by *Staphylococcus aureus* including ampicillin-resistant (but not methicillin-resistant) strains, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*.

Gonorrhea

Caused by *Neisseria gonorrhoeae* including ampicillin-resistant strains.

Bone and Joint Infections

Caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing strains).

Specimens for bacteriologic culture should be obtained prior to therapy in order to identify the causative organisms and to determine their susceptibility to cefuroxime. Therapy may be instituted before results of susceptibility testing are known. However, modification of the treatment may be required once these results become available.

Prevention

The pre-operative prophylactic administration of Cefuroxime for Injection, USP may prevent the growth of susceptible disease-causing bacteria and thereby may decrease the incidence of certain post-operative infections:

- in patients undergoing surgical procedures (e.g., vaginal hysterectomy) that are classified as clean contaminated or potentially contaminated;
- in patients undergoing open heart surgery in whom infections at the operative site would present a serious risk.

If signs of infection occur post-operatively, culture specimens should be obtained for identification of the causative organism and appropriate anti-microbial therapy should be instituted.

CONTRAINDICATIONS

Cefuroxime for Injection, USP is contraindicated for patients who have shown Type I hypersensitivity to cefuroxime or to the cephalosporin group of antibiotics.

WARNINGS

Before therapy with Cefuroxime for Injection, USP is instituted, careful enquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefuroxime, cephalosporins, penicillins, or other drugs. Cefuroxime for Injection, USP should be administered with caution to any patient who has shown some form of allergy, particularly to drugs. There is some clinical and laboratory evidence of partial cross-allergenicity of the cephalosporins and penicillins. If an allergic reaction to Cefuroxime for Injection, USP occurs, treatment should be discontinued and standard agents (e.g., epinephrine, antihistamines, corticosteroids) administered as required.

Pseudomembranous colitis has been reported to be associated with cefuroxime therapy (and other broad-spectrum antibiotics). Therefore, it is important to consider its diagnosis in patients administered Cefuroxime for Injection, USP who develop diarrhea. Treatment with broad-spectrum antibiotics, including cefuroxime, changes 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. Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as needed. When the colitis is not relieved by discontinuance of Cefuroxime for Injection, USP administration or when it is severe, consideration should be given to the administration of vancomycin or other suitable therapy. Other possible causes of colitis should also be considered.

PRECAUTIONS

Cefuroxime for Injection, USP should be administered with caution to individuals with a history of gastrointestinal disease, particularly colitis.

Patients with markedly impaired renal function (i.e., creatinine clearance of 20 mL/min/1.73m² or less) should be placed on the special dosage schedule for Cefuroxime for Injection, USP recommended under **DOSAGE AND ADMINISTRATION**. Normal dosages in these individuals are likely to produce excessive serum concentrations of cefuroxime.

The concomitant administration of aminoglycosides and some cephalosporins has caused nephrotoxicity. Although transient elevations of BUN and serum creatinine have been seen in clinical studies, there is no evidence that Cefuroxime For Injection, USP, when administered alone, is significantly nephrotoxic.

Studies suggest that the concurrent use of potent diuretics, such as furosemide and ethacrynic acid, may increase the risk of renal toxicity with cephalosporins.

Prolonged treatment with Cefuroxime for Injection, USP may result in the overgrowth of nonsusceptible organisms, including species originally sensitive to the drug. Repeated evaluation of the patient's condition is required. If superinfection occurs during therapy, appropriate measures should be taken. Should an organism become resistant during antibiotic therapy, another antibiotic should be substituted.

As with other therapeutic regimens used in the treatment of meningitis, hearing loss has been reported in a few pediatric patients treated with Cefuroxime for Injection, USP. Persistence of positive CSF cultures of *Haemophilus influenzae* at 18-36 hours has been noted with Cefuroxime for Injection, USP.

Pregnancy

The safety of Cefuroxime for Injection, USP in pregnancy has not been established. The use of Cefuroxime for Injection, USP in pregnant women requires that the potential benefit from the drug be weighed against the possible risk to the mother and fetus. Animal studies have shown cefuroxime to affect bone calcification in the fetus and to show maternal toxicity in the rabbit.

Nursing Mothers

Cefuroxime is excreted in human milk in low concentrations (0.5 mg/L). The clinical significance of this is unknown, therefore, caution should be exercised when Cefuroxime for Injection, USP is administered to a nursing mother.

Elderly Patients

The elimination of cefuroxime may be decreased due to impairment of renal function.

Drug-Laboratory Test Interactions

Cefuroxime may interfere with Benedict's and Fehling's tests for glycosuria. It may cause false-negative reactions in the ferricyanide test, and therefore it is recommended that either the glucose oxidase or hexokinase methods be used to determine blood/plasma glucose levels in patients receiving Cefuroxime for Injection, USP. Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

ADVERSE REACTIONS

The following reactions have been observed during treatment with Cefuroxime for Injection, USP.

Hypersensitivity

Rash, and eosinophilia. Anaphylaxis, urticaria, pruritus and drug fever have also been observed with cephalosporin treatment. Like other cephalosporins, there have been rare reports of erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (exanthematic necrolysis).

Local reactions

Thrombophlebitis, stiffness at the site of injection, and inflammatory reactions at the site of injection; some degree of pain, after intramuscular injections when using water as diluent, has been observed.

Blood

Increased erythrocyte sedimentation rate and decreased hemoglobin; eosinophilia, leukopenia and neutropenia; some patients developed a positive direct Coombs' test.

Renal

Increases in BUN and serum creatinine.

Hepatic

Transient increases in serum bilirubin, transaminases and alkaline phosphatase.

Others

Drowsiness, loose stools, faint feeling, sweating, palpitations and *Candida* intertrigo.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Other than general supportive treatment, no specific antidote is known. Excessive serum levels of cefuroxime can be reduced by dialysis. For treatment of hypersensitivity reactions, see **WARNINGS**.

DOSAGE AND ADMINISTRATION

DOSAGE

Cefuroxime for Injection, USP (sterile cefuroxime sodium) may be administered intravenously after constitution.

Treatment

Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organism(s), and condition of the patient. The intravenous route is preferable for patients with severe or life-threatening infections.

The usual duration of treatment is 5 to 14 days. For β -hemolytic streptococcal infections, therapy should be continued for at least 10 days.

Adults

For most infections, the usual recommended dosage is 750 mg every 8 hours (2.25 g/day), administered intravenously. For severe or life-threatening infections, and for Gram-negative infections of the lower respiratory tract, a dosage of 1.5 g i.v. every 8 hours (4.5 g/day) is recommended.

For treatment of bacterial meningitis a dosage of 3 g i.v. every 8 hours (9 g/day) should be used.

For bone and joint infections, a dosage of 1.5 g i.v. every 8 hours (4.5 g/day) is recommended. Surgical intervention should be performed when indicated as an adjunct to cefuroxime therapy. A course of oral antibiotics should be administered when appropriate following the completion of parenteral administration of Cefuroxime for Injection, USP.

Infants and Children (1 month to 12 years)

The usual dosage range is 30 to 100 mg/kg/day in 3 or 4 equally divided doses. A dose of 60 mg/kg/day is appropriate for most infections.

In cases of bacterial meningitis*, a dosage of 200 to 240 mg/kg/day i.v. in 3 or 4 equally divided doses should be used.

For bone and joint infections, a dosage between 70 to 150 mg/kg/day administered intravenously every 8 hours is recommended. In clinical trials, a course of oral antibiotics was administered to children following the completion of parenteral administration of Cefuroxime for Injection, USP.

Doses in excess of the maximum adult dose should not be used in infants and children.

Neonates (up to 1 month)

In the first few weeks of life, the serum half-life of cefuroxime can be 3 to 5 times that in adults. Infections in neonates should be treated with dosages in the range of 30 to 100 mg/kg/day in 2 or 3 equally divided doses.

For bacterial meningitis*, a dosage of 100 mg/kg/day i.v. in 2 or 3 equally divided doses should be used.

Prevention

Clean contaminated or potentially contaminated surgical procedures

The recommended dose is 1.5 g of Cefuroxime for Injection, USP administered intravenously just prior to surgery.

This may be supplemented with 750 mg at 8 and 16 hours when surgery is prolonged.

In general, prophylactic administration is normally not required after the end of surgical procedures, however, intra-operative administrations should be considered if the surgical procedure is lengthy.

In many surgical procedures, continuing prophylactic administration of any antibiotic does not appear to be related with a decreased incidence of subsequent infection, but will increase the possibility of adverse reactions and the development of bacterial resistance.

Open Heart Surgery

The recommended dosage is 1.5 g of Cefuroxime for Injection, USP administered intravenously at the induction of anesthesia and every 12 hours thereafter for 48 hours.

Dosage in Patients with Impaired Renal Function

For patients with markedly impaired renal function, a reduced dosage of Cefuroxime for Injection, USP must be used. For adult patients with moderate infections, dosage adjustment may be made according to the guidelines listed in Table 1.

Creatinine Clearance		Unit Dose	Dosing Frequency
mL/min/ 1.73 m ²	mL/s/ 1.73 m ²		
>20	>0.33	750 mg - 1.5 g	q8h
10-20	0.17 - 0.33	750 mg	q12h
<10	<0.17	750 mg	q24h

For adults with severe infections who require doses higher than those recommended in Table 1, serum levels of cefuroxime should be monitored and dosage adjusted accordingly.

Studies in children with renal impairment are not sufficient to recommend specific dosages. If it is necessary to administer Cefuroxime for Injection, USP to a child with such impairment, consideration should be given to modifying the frequency of drug administration consistent with the recommendations for adults with renal impairment as indicated in Table 1.

When only serum creatinine levels are known, the following formula may be used to estimate creatinine clearance. The serum creatinine must represent a steady state of renal function.

Males:

$$\text{creatinine clearance (mL/min)} = \frac{\text{weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/dL)}} \quad \text{OR}$$

$$\text{creatinine clearance (mL/s)} = \frac{\text{weight (kg)} \times (140 - \text{age})}{49 \times \text{serum creatinine } (\mu\text{mol/L})}$$

Females:

$$0.85 \times \text{male value}$$

For patients on hemodialysis, a further 750 mg dose of Cefuroxime for Injection, USP should be administered at the end of each dialysis treatment.

ADMINISTRATION

Intravenous

Cefuroxime for Injection, USP may be administered intravenously either by a bolus injection or by a short intravenous infusion over a period of approximately 30 minutes.

For continuous intravenous infusions, a solution of Cefuroxime for Injection, USP (1.5 g dissolved in 16 mL of Water for Injection) may be added to a suitable bottle containing an appropriate intravenous infusion fluid in the amount calculated to give the desired antibiotic dose.

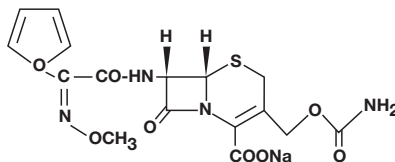
PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

Proper Name: Sterile cefuroxime sodium

Chemical Name: 5-Thia-1-azabicyclo [4.2.0] oct-2-ene-2 carboxylic acid, 3-[[[(aminocarbonyloxy)methyl]-7-[[2-furanyl(methoxy-imino) acetyl]amino-8-oxo-, monosodium salt {6R-[6α, 7β (Z)]}

Structural Formula



Molecular Formula: C₁₆H₁₅N₄NaO₆S

Molecular Weight: 446.4

Description: Cefuroxime sodium is a white to faintly yellow crystalline powder, soluble in water (15% w/v at 25°C), sparingly soluble in ethanol and insoluble in chloroform, toluene, ether, ethyl acetate and acetone.

Composition: Cefuroxime for Injection, USP vials contain cefuroxime sodium (expressed in terms of free acid). Freshly prepared solutions of cefuroxime are yellowish in colour, with some variations in intensity. The pH of freshly constituted solutions range from 6.0 to 8.5.

CONSTITUTION

For Intravenous Use: Constitute with Sterile Water for Injection.

Vial Size	Diluent to be added to Vial	Volume to be With-drawn	Approximate Cefuroxime Concentration
750 mg/ 15 mL vial	8.0 mL	Total	90 mg/mL
1.5 g/ 50 mL vial	16.0 mL	Total	90 mg/mL
Shake well until dissolved.			

The constituted solution may be further diluted with Sodium Chloride Injection 0.9% w/v, or 5% w/v Dextrose Injection.

7.5 g Pharmacy Bulk Vial

THE AVAILABILITY OF THE PHARMACY BULK VIAL IS RESTRICTED TO HOSPITALS WITH A RECOGNIZED INTRAVENOUS ADMIXTURE PROGRAM.

Cefuroxime for Injection does not contain any preservatives. The Pharmacy Bulk Vial is intended for multiple dispensing for intravenous use only, employing a single puncture. Constitute with 77 mL Sterile Water for Injection.

Vial Size	Diluent to be added to Vial	Volume to be With-drawn	Approximate Cefuroxime Concentration
7.5 g	77 mL	Amount needed*	95 mg/mL
*8 mL of solution contains 750 mg of cefuroxime; 16 mL of solution contains 1.5 g of cefuroxime. Shake well until dissolved.			

Following constitution with Sterile Water for Injection, the solution should be dispensed for further dilution within four hours. Any unused portion of the constituted solution should be discarded.

As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitate, discoloration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discoloration or leakage should not be used.

STABILITY AND STORAGE RECOMMENDATIONS

Storage

Cefuroxime for Injection, USP in the dry state should be stored between 15 and 30°C and protected from light.

Constituted solution for intravenous injection should be used within 4 hours if kept between 15 and 30°C or 48 hours if stored under refrigeration.

The further diluted solutions (1 - 30 mg/mL) for intravenous infusion should be used immediately after dilution or stored for up to 36 hours under refrigeration in the dark. Some increase in colour intensity may occur on storage.

Note: The pH of 2.74% w/v Sodium Bicarbonate Injection considerably affects the colour of the solution, therefore, this solution is not recommended for the dilution of Cefuroxime for Injection, USP. However, if needed, for patients receiving Sodium Bicarbonate Injection by infusion, the cefuroxime dose may be introduced into the tube of the set.

Incompatibility

Cefuroxime for Injection, USP should not be mixed in the syringe with aminoglycoside antibiotics (e.g., gentamicin sulfate, tobramycin sulfate, amikacin sulfate) due to potential interaction.

AVAILABILITY OF DOSAGE FORMS

Cefuroxime for Injection, USP (sterile cefuroxime sodium) is available as follows:

PF327013 15 mL vials containing cefuroxime sodium powder equivalent to 750 mg of cefuroxime in packages of 25 vials.

PF327014 50 mL vials containing cefuroxime sodium powder equivalent to 1.5 g of cefuroxime, in packages of 10 vials.

PF327015 100 mL Pharmacy Bulk Vials containing cefuroxime sodium powder equivalent to 7.5 g of cefuroxime, in packages of 10 vials.

*Delayed sterilization of cerebral spinal fluid has been reported in a few children treated with cefuroxime for bacterial meningitis. Hearing impairment has occasionally occurred as a complication of meningitis in children treated with cefuroxime.

PHARMACEUTICAL PARTNERS OF CANADA INC.
Richmond Hill, ON L4B 3P6
☎ 1-877-821-7724