

## Cefuroxime

**Introduction:** Cefuroxime for Injection USP and Dextrose Injection USP is a sterile, nonpyrogenic, single use, packaged combination of Cefuroxime Sodium USP (crystalline)

**Mechanism of action:** Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydrolases) while cell wall assembly is arrested.

### Pharmacology:

**Absorption:** Oral (cefuroxime axetil): Increases with food

**Distribution:** Widely to body tissues and fluids; crosses blood-brain barrier; therapeutic concentrations achieved in CSF even when meninges are not inflamed

**Protein binding:** 33% to 50%

**Bioavailability:** Tablet: Fasting: 37%; Following food: 52%

**Half-life elimination:** Children 1-2 hours; Adults: 1-2 hours; prolonged with renal impairment

**Time to peak, serum:** I.M.:15-60 minutes; I.V.: 2-3 minutes; Oral: Children: 3-4 hours; **Adults:** 2-3 hours

**Excretion:** Urine (66% to 100% as unchanged drug)

**Indications:** Cefuroxime is active against both gram positive and gram negative bacteria. It is resistant to beta-lactamases. It is used in meningitis caused by H.influenza, meningococci and pneumococci and for therapy of gonorrhoea.

**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. 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.

### Dosage of Cefuroxime in Adults with Reduced Renal Function

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

**Pediatric Patients Above 3 Months of Age:** Administration of 50 to 100 mg/kg/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/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/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/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.

**Side effects:** 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.

**Hypersensitivity Reactions:** Hypersensitivity reactions have been reported in fewer than 1% of the patients treated with cefuroxime 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 anaphylaxis, 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:** In addition to the adverse events reported during clinical trials, the following events have been observed during clinical practice in patients treated with cefuroxime 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, and hemorrhage.

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

**General:** Although Cefuroxime for Injection USP and Dextrose Injection USP 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, 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 nonsusceptible organisms. Careful observation of the patient is essential. If 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. Neototoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins. As with other therapeutic regimens used in the treatment of

meningitis, mild-to-moderate hearing loss has been reported in a few pediatric patients treated with cefuroxime. Persistence of positive CSF (cerebrospinal fluid) cultures at 18 to 36 hours has also been noted with cefuroxime injection, as well as with other antibiotic therapies; however, the clinical relevance 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. As with other dextrose-containing solutions, Cefuroxime 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 Cefuroxime 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.

**Pregnancy: Teratogenic Effects - Pregnancy Category B.**

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.

**Geriatric Use:** 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

**Contraindications:** Cefuroxime 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.

**How supplied: Customized as per request.**