

CEFUROXIME- cefuroxime injection, powder, for solution
WG Critical Care, LLC

Cefuroxime for Injection, USP

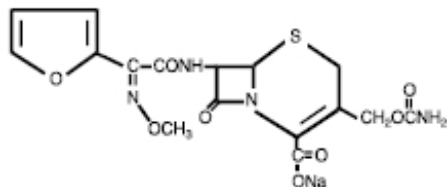
PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION

Rx only

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

DESCRIPTION

Cefuroxime for Injection, USP 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 chemical structure:



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

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

Cefuroxime for Injection, USP in sterile crystalline form is supplied in Pharmacy Bulk Package equivalent to 7.5 g of cefuroxime as cefuroxime sodium. Solutions of Cefuroxime for Injection, USP 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.

A pharmacy bulk package is a container of a sterile powder for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture service and are restricted to the preparation of admixtures for intravenous infusion. FURTHER DILUTION IS REQUIRED BEFORE USE.

CLINICAL PHARMACOLOGY

Following IV doses of 750 mg and 1.5 g, 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 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 urine concentrations.

Intravenous doses of 750 mg and 1.5 g produced urinary levels averaging 1,150 and 2,500 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., *Legionella* 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:

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

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

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

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

<u>Zone Diameter(mm)</u>	<u>Interpretation</u>
≥ 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

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

- 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*.
- Urinary Tract Infections** caused by *Escherichia coli* and *Klebsiella* spp.
- Skin and Skin Structure Infections** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains), *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp.
- Septicemia** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains), *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae* (including ampicillin-resistant strains), and *Klebsiella* spp.
- Meningitis** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (including ampicillin-

resistant strains), *Neisseria meningitidis*, and *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing strains).

6. **Gonorrhea:** 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 for Injection, USP has been used successfully in these mixed infections in which several organisms have been isolated.

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 for Injection 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.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefuroxime for Injection, USP and other antibacterial drugs, Cefuroxime for Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Prevention: The preoperative prophylactic administration of Cefuroxime for Injection, USP 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 for Injection, USP 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 for Injection, USP 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 therapy with Cefuroxime for Injection, USP 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 for Injection, USP is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS

BEFORE THERAPY WITH CEFUROXIME FOR INJECTION, USP 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 FOR INJECTION, USP OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefuroxime for Injection, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

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

Although Cefuroxime for 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 for Injection, USP 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 for Injection, USP 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.

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-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.

Prescribing Cefuroxime for 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.

Information for Patients

Patients should be counseled that antibacterial drugs, including Cefuroxime for Injection, USP should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefuroxime for Injection, USP is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Cefuroxime for Injection, USP or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Drug Interactions

In common with other antibiotics, cefuroxime may affect the gut flora, leading to lower estrogen reabsorption and reduce efficacy of combined estrogen/progesterone oral contraceptives.

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 for Injection, USP.

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 in 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 3,200 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 6,400 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 for Injection, USP 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 1,914 subjects who received cefuroxime in 24 clinical studies of Cefuroxime for Injection, USP, 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 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 DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS

Cefuroxime for Injection, USP 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, USP 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 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.

Immune System Disorders: Cutaneous vasculitis.

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 for Injection, USP, 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.

To report SUSPECTED ADVERSE REACTIONS, contact WG Critical Care, LLC at 1-866-562-4708 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

This insert labeling is for a Pharmacy Bulk Package and is intended for preparing admixtures for intravenous infusion only.

Dosage

Adults: The usual adult dosage range for Cefuroxime for Injection, USP 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 therapy with Cefuroxime for Injection, USP. A course of oral antibiotics was administered when appropriate following the completion of parenteral administration of Cefuroxime for Injection, USP.

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. 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 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 for Injection, USP 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*

* Since Cefuroxime for Injection, USP 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.

$$\text{Males: clearance (mL/min) = } \frac{\text{Weight (kg) x (140 - age)}}{72 \times \text{serum creatinine (mg/dL)}}$$

Females: 0.85 x male value

NOTE: As with antibiotic therapy in general, administration of Cefuroxime for Injection, USP 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 for Injection, USP.

In cases of bacterial meningitis, a larger dosage of Cefuroxime for Injection, USP 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.

Directions for Dispensing

Pharmacy Bulk Package – Not for Direct Infusion: The pharmacy bulk package is for use in a pharmacy admixture service only under a laminar flow hood. Entry into the vial must be made with a sterile

transfer set or other sterile dispensing device, and the contents dispensed in aliquots using aseptic technique, the closure should be penetrated only one time using a suitable sterile dispensing set; which allows measured dispensing of the contents. The use of a syringe and needle is not recommended as it may cause leakage (see DOSAGE AND ADMINISTRATION). AFTER INITIAL WITHDRAWAL USE ENTIRE CONTENTS OF VIAL PROMPTLY. ANY UNUSED PORTION MUST BE DISCARDED WITHIN 4 HOURS.

Preparation of Solution

Pharmacy Bulk Package – Not for Direct Infusion: This pharmacy bulk package is designed for use in the pharmacy in preparing admixtures for intravenous infusion only. Use of this product is restricted to a suitable work area, such as a laminar flow hood. The 7.5 grams pharmacy bulk package should be constituted with 77 mL of Sterile Water for Injection; each 8 mL of the resulting solution contains 750 mg of cefuroxime; 16 mL of solution contains 1.5 grams of cefuroxime (approximate cefuroxime concentration equals 95 mg/mL).

THIS PACKAGE IS NOT TO BE DISPENSED AS A UNIT.

Administration

After constitution, the intent of this pharmacy bulk package is for the preparation of solutions for IV infusion only.

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 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 for Injection, USP, it is advisable to temporarily discontinue administration of any other solutions at the same site.

For continuous IV infusion, a solution of Cefuroxime for Injection, USP 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 for Injection, USP, 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 for Injection, USP and an aminoglycoside is indicated, each of these antibiotics can be administered separately to the same patient.

Compatibility and Stability

Intravenous: When the 7.5 g pharmacy bulk package is constituted as directed with Sterile Water for Injection the contents should be withdrawn without delay. However, should this not be possible, a maximum time of 4 hours from initial closure entry is permitted to complete fluid transfer operations. 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, USP 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, USP.

Frozen Stability: Constitute the 7.5 g pharmacy bulk package vial as directed for IV administration. Immediately withdraw 8 mL or 16 mL from the 7.5 g pharmacy bulk package vial and add to a minibag containing 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.

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, USP powder as well as solutions and suspensions tend to darken, depending on storage conditions, without adversely affecting product potency.

The container may be hung by the attached bail band during dispensing of the contents.

HOW SUPPLIED

Store Cefuroxime for Injection, USP at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect From Light. Cefuroxime for Injection, USP is a dry, white to off-white powder supplied in vials and infusion packs as follows:

Cefuroxime for Injection, USP. Cefuroxime sodium equivalent to 7.5 grams of cefuroxime per Pharmacy Bulk Package.

NDC 44567-712-10 7.5 gram vial Pharmacy Bulk Pack (Carton of 10)

Also available:

Cefuroxime for Injection, USP. Cefuroxime sodium equivalent to 750 mg or 1.5 grams cefuroxime per vial or infusion pack.

NDC 44567-710-10 750 mg vial (Carton of 10)

NDC 44567-711-10 1.5 gram vial (Carton of 10)

NDC 44567-720-10 750 mg infusion pack (Carton of 10)

NDC 44567-722-10 1.5 gram infusion pack (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.

CLINITEST® is a registered trademark of Ames Division, Miles Laboratories, Inc.

Manufactured for:

WG Critical Care, LLC

Paramus, New Jersey 07652

Revised: October 2012

SP100476

PRINCIPAL DISPLAY PANEL

100 mL NDC 44567-712-10

Cefuroxime
for Injection, USP

7.5 gram

**PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION**

Equivalent to 7.5 grams of
cefuroxime activity

For IV Use
Rx only

WG CriticalCare

CEFUROXIME FOR INJECTION, USP 7.5 gram

This Pharmacy Bulk Package is intended for preparing IV admixtures only. See insert for complete dosage information and proper use of this container.

USUAL DOSAGE: See package insert.

To prepare solution, add 77 mL of Sterile Water for Injection. Shake well to dissolve. The constituted solution occupies a volume of about 82.5 mL and contains approximately 750 mg of cefuroxime activity per 8 mL.

For use in a pharmacy admixture service only under a laminar flow hood. Entry into the vial must be made with a sterile transfer set or other sterile dispensing device, and the contents dispensed in aliquots using aseptic technique.

AFTER RECONSTITUTION: Use promptly. (DISCARD VIAL WITHIN 4 HOURS AFTER INITIAL ENTRY).

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect From Light.

CONCENTRATION _____
PREPARED ON (date) _____ (time) _____ (AM/PM)
EXPIRES _____

Manufactured for:
WG Critical Care, LLC
Paramus, NJ 07652

SP100477

3 44567 71210 6

NDC 44567-712-10

Cefuroxime for Injection, USP

7.5 gram

Pharmacy Bulk Package

Not for Direct Infusion

Equivalent to 7.5 grams of cefuroxime activity

For IV Use

Rx only

WG Critical Care

CEFUROXIME

cefuroxime injection, powder, for solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:44567-712
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CEFUROXIME SODIUM (UNII: R8A7M9MY61) (CEFUROXIME - UNII:O1R9FJ93ED)	CEFUROXIME	7.5 g in 80 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
---	-----------	---------------------	----------------------	--------------------

1	NDC:44567-712-10	10 in 1 CARTON		
1		80 mL in 1 VIAL		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA064124	10/04/2012	

Labeler - WG Critical Care, LLC (829274633)

Registrant - Steri-Pharma, LLC (169663544)

Establishment

Name	Address	ID/FEI	Business Operations
Steri-Pharma, LLC		169663544	MANUFACTURE(44567-712)

Revised: 10/2012

WG Critical Care, LLC