CEFIZOX- ceftizoxime injection, powder, lyophilized, for solution
Fujisawa Healthcare, Inc.

Cefizox®
(CEFTIZOXIME FOR INJECTION, USP)

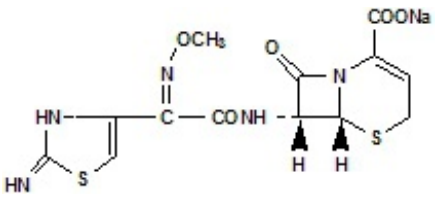
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefizox and other antibacterial drugs, Cefizox should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

For Intravenous Infusion

Description

Cefizox® (ceftizoxime for injection, USP) is a sterile, semisynthetic, broad-spectrum, beta-lactamase resistant cephalosporin antibiotic for parenteral (IV, IM) administration. It is the sodium salt of [6R-[6a,7β(Z)]]-7-[[(2,3-dihydro-2-imino-4- thiazolyl) (methoxyimino) acetyl] amino]-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid. Its sodium content is approximately 60 mg (2.6 mEq) per gram of ceftizoxime activity.

It has the following structural formula:



$C_{13}H_{12}N_5NaO_5S_2$

405.38

Ceftizoxime for injection, USP is a white to pale yellow crystalline powder.

Cefizox is supplied in ADD-vantage® vials as ceftizoxime sodium equivalent to 1 gram or 2 grams ceftizoxime.

Clinical Pharmacology

Following IV administration of 1, 2, and 3 gram doses of Cefizox to normal volunteers, the following serum levels were obtained.

Serum Concentrations After Intravenous Administration

	Serum Concentration (µg/mL)						
Dose	5 min	10 min	30 min	1 hr	2 hr	4 hr	8 hr
1 gram	*	*	60.5	38.9	21.5	8.4	1.4
2 grams	131.8	110.9	77.5	53.6	33.1	12.1	2.0

3 grams	221.1	174.0	112.7	83.9	47.4	26.2	4.8

* Not Done

A serum half-life of approximately 1.7 hours was observed after IV or IM administration.

Cefizox is 30% protein bound.

Cefizox is not metabolized, and is excreted virtually unchanged by the kidneys in 24 hours. This provides a high urinary concentration. Concentrations greater than 6000 µg/mL have been achieved in the urine by 2 hours after a 1 gram dose of Cefizox intravenously. Probenecid slows tubular secretion and produces even higher serum levels, increasing the duration of measurable serum concentrations.

Cefizox achieves therapeutic levels in various body fluids, e.g., cerebrospinal fluid (in patients with inflamed meninges), bile, surgical wound fluid, pleural fluid, aqueous humor, ascitic fluid, peritoneal fluid, prostatic fluid and saliva, and in the following body tissues: heart, gallbladder, bone, biliary, peritoneal, prostatic, and uterine.

In clinical experience to date, no disulfiram-like reactions have been reported with Cefizox.

Microbiology

The bactericidal action of Ceftizoxime results from inhibition of cell-wall synthesis. Ceftizoxime is highly resistant to a broad spectrum of beta-lactamases (penicillinase and cephalosporinase), including Richmond types I, II, III, TEM, and IV, produced by both aerobic and anaerobic gram-positive and gram-negative organisms. Ceftizoxime has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as described in the INDICATIONS AND USAGE section:

Aerobic Gram-Positive Microorganisms

Staphylococcus aureus (including penicillinase producing strains)

NOTE: Methicillinresistant staphylococci are resistant to cephalosporins, including ceftizoxime.

Staphylococcus epidermidis (including penicillinase producing strains)

Streptococcus agalactiae

Streptococcus pneumoniae

Streptococcus pyogenes

NOTE: A streptococcal isolate that is susceptible to penicillin can be considered susceptible to ceftizoxime [4].

NOTE: Ceftizoxime is usually inactive against most strains of *Enterococcus faecalis.*

Aerobic Gram-Negative Microorganisms

Enterobacter spp.

Escherichia coli

Haemophilus influenzae (including ampicillinresistant strains)

Klebsiella pneumoniae

Morganella morganii

Neisseria gonorrhoeae

Proteus mirabilis

Proteus vulgaris

Providencia rettgeri

Pseudomonas aeruginosa

Serratia marcescens

Anaerobic Microorganisms

Bacteroides spp.

Peptococcus spp.

Peptostreptococcus spp.

The following *in vitro* data are available, **but their clinical significance is unknown**. At least 90% of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for ceftizoxime. However, the safety and effectiveness of ceftizoxime in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

Aerobic Gram-Negative Microorganisms

Aeromonas hydrophila

Citrobacter spp.

Moraxellacatarrhalis

Neisseria meningitidis

Providencia stuartii

Susceptibility Testing Methods:

Dilution techniques:

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method[1] (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of ceftizoxime powder. The MIC values should be interpreted according to the following criteria:

For testing non-fastidious aerobic microorganisms other than *Haemophilus* spp., *Neisseria gonorrhoeae*:

MIC (µg/mL)	Interpretation
≤8	Susceptible (S)
16-32	Intermediate (I)
≥64	Resistant (R)

For testing *Haemophilus* spp. *

MIC (µg/mL)	Interpretation †
≤2	Susceptible (S)

For testing *Neisseria gonorrhoeae* ‡

MIC (µg/mL)	Interpretation †
≤0.5	Susceptible (S)

* These interpretative standards are applicable only to broth microdilution susceptibility testing with Haemophilus spp. using Haemophilus Test Medium.[2]

† The current absence of data on resistant strains precludes defining any category other than "susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

‡ These interpretative standards are applicable only to agar dilution susceptibility testing using GC agar base and 1% defined growth supplements.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable, other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Standard ceftizoxime powder should provide the following MIC values:

Microorganism	MIC(µg/mL)
Escherichia coli ATCC 25922	0.03–0.12
Haemophilus influenzae ATCC 49247	0.06-0.5
Neisseria gonorrhoeae ATCC 49226	0.008-0.03
Pseudomonas aeruginosa ATCC 27853	16-64
Staphylococcus aureus ATCC 29213	2–8

Diffusion Techniques:

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2] requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 30-µg ceftizoxime to test the susceptibility of microorganisms to ceftizoxime.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 30-µg ceftizoxime disk should be interpreted according to the following criteria:

Zone diameter interpretative standard for testing non-fastidious aerobic microorganisms other than *Haemophilus* spp. and *Neisseria gonorrhoeae*:

Zone Diameter (mm)	Interpretation
≥ 20	Susceptible (S)
15-19	Intermediate (I)
≤ 14	Resistant (R)

Zone diameter interpretative standard for testing *Haemophilus* spp. *

Zone Diameter (mm)	Interpretation†
≥ 26	Susceptible (S)

Zone diameter interpretative standard for testing *Neisseria gonorrhoeae*. ‡

Zone Diameter (mm)	Interpretation †
≥ 38	Susceptible (S)

* These zone diameter standards are applicable only to susceptibility testing with *Haemophilus* spp. using *Haemophilus* Test Medium.[3]

† The current absence of data on resistant strains precludes defining any category other than "susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

‡ These interpretative standards are applicable only to disk diffusion testing using GC agar base and 1% defined growth supplements incubated at 5% CO_2.

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for ceftizoxime.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms that are used to control the technical aspects of the laboratory procedures. For the diffusion technique, the 30-µg ceftizoxime disk should provide the following zone diameters in these laboratory test quality control strains:

Microorganism	Zone Diameter (mm)
Escherichia coli ATCC 25922	30-36
Haemophilus influenzae ATCC 49247	29-39
Neisseria gonorrhoeae ATCC 49226	42-51
Pseudomonas aeruginosa ATCC 27853	12-17
Staphylococcus aureus ATCC 25923	27-35

Anaerobic Techniques:

For anaerobic bacteria, the susceptibility to ceftizoxime as MICs can be determined by standardized test methods. Agar dilution results can vary widely when using ceftizoxime. It is recommended that broth microdilution method be used when possible.[3] The MIC values obtained should be interpreted according to the following criteria:

MIC(µg/mL)		
Broth dilution	**Agar dilution**	**Interpretation**
≤ 16	≤ 32	Susceptible (S)
32	64	Intermediate (I)
≥ 64	≥ 128	Resistant (R)

Interpretation is identical to that described in Susceptibility Testing: Dilution Techniques.

As with other susceptibility techniques, the use of laboratory control microorganisms is required to control the technical aspects of the laboratory standardized procedures. Standardized ceftizoxime powder should provide the following MIC values:

Microorganism	**MIC(µg/mL)**	
	Broth dilution	**Agar dilution**
Eubacterium lentum ATCC 43055	16-64	16-64
Bacteriodes thetaiotaomicron ATCC 29741	---	4-16

Susceptibility Testing for Pseu domonas in Urinary Tract Infections

Most strains of *Pseudomonas aeruginosa* are moderately susceptible to ceftizoxime.

Ceftizoxime achieves high levels in the urine (greater than 6000 mcg/mL at 2 hours with 1 gram IV) and, therefore, the following zone sizes should be used when testing ceftizoxime for treatment of urinary tract infections caused by *Pseudomonas aeruginosa*.

Susceptible organisms produce zones of 20 mm or greater, indicating that the test organism is likely to respond to therapy.

Organisms that produce zones of 11 to 19 mm are expected to be susceptible when the infection is confined to the urinary tract (in which high antibiotic levels are attained).

Resistant organisms produce zones of 10 mm or less, indicating that other therapy should be selected.

Indications and Usage

Cefizox (ceftizoxime for injection, USP) is indicated in the treatment of infections due to susceptible strains of the microorganisms listed below.

Lower Respiratory Tract Infections caused by *Klebsiella* spp.; *Proteus mirabilis*; *Escherichia coli; Haemophilus influenzae* including ampicillin‐resistant strains; *Staphylococcus aureus* (penicillinase and nonpenicillinase‐producing); *Serratia* spp.; *Enterobacter* spp.; *Bacteroides* spp.; and *Streptococcus* spp. including *S. pneumoniae*, but excluding enterococci.

Urinary Tract Infections caused by *Staphylococcus aureus* (penicillinase‐ and nonpenicillinase‐ producing); *Escherichia coli*; *Pseudomonas* spp. including *P.aeruginosa*; *Proteus mirabilis*; *P. vulgaris*; *Providencia rettgeri* (formerly *Proteus rettgeri*) and *Morganella morganii* (formerly *Proteus morganii*); *Klebsiella* spp.; *Serratia* spp. including *S. marcescens*; and *Enterobacter* spp.

Gonorrhea including uncomplicated cervical and urethral gonorrhea caused by *Neisseria gonorrhoeae*.

Pelvic Inflammatory Disease caused by *Neisseria gonorrhoeae, Escherichia coli* or *Streptococcus agalactiae*.

NOTE: Ceftizoxime, like other cephalosporins, has no activity against *Chlamydia trachomatis*. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and *C. trachomatis* is one of the suspected pathogens, appropriate antichlamydial coverage should be added.

Intra‐Abdominal Infections caused by *Escherichia coli; Staphylococcusepidermidis; Streptococcus* spp. (excluding enterococci); *Enterobacter* spp.; *Klebsiella* spp.; *Bacteroides* spp. including *B. fragilis*; and anaerobic cocci, including *Peptococcus* spp. and *Peptostreptococcus* spp.

Septicemia caused by *Streptococcus* spp. including *S. pneumoniae* (but excluding enterococci); *Staphylococcus aureus* (penicillinase‐ and nonpenicillinase‐producing); *Escherichia coli; Bacteroides* spp. including *B. fragilis*; *Klebsiella* spp.; and *Serratia* spp.

Skin and Skin Structure Infections caused by *Staphylococcus aureus* (penicillinase‐ and nonpenicillinase‐ producing); *Staphylococcus epidermidis*; *Escherichia coli; Klebsiella* spp.; *Streptococcus* spp. including *Streptococcus pyogenes* (but excluding enterococci); *Proteus mirabilis*; *Serratia* spp.; *Enterobacter* spp.; *Bacteroides* spp. including *B. fragilis*; and anaerobic cocci, including *Peptococcus* spp. and *Peptostreptococcus* spp.

Bone and Joint Infections caused by *Staphylococcus aureus* (penicillinase‐ and nonpenicillinase‐

producing); *Streptococcus* spp. (excluding enterococci); *Proteusmirabilis*; *Bacteroides* spp.; and anaerobic cocci, including *Peptococcus* spp. and *Peptostreptococcus* spp.

Meningitis caused by *Haemophilus influenzae*. Cefizox has also been used successfully in the treatment of a limited number of pediatric and adult cases of meningitis caused by *Streptococcus pneumoniae*.

Cefizox has been effective in the treatment of seriously ill, compromised patients, including those who were debilitated, immunosuppressed, or neutropenic.

Infections caused by aerobic gram‐negative and by mixtures of organisms resistant to other cephalosporins, aminoglycosides, or penicillins have responded to treatment with Cefizox.

Because of the serious nature of some urinary tract infections due to *P. aeruginosa* and because many strains of *Pseudomonas* species are only moderately susceptible to Cefizox, higher dosage is recommended. Other therapy should be instituted if the response is not prompt.

Susceptibility studies on specimens obtained prior to therapy should be used to determine the response of causative organisms to Cefizox. Therapy with Cefizox may be initiated pending results of the studies; however, treatment should be adjusted according to study findings. In serious infections, Cefizox has been used concomitantly with aminoglycosides (see PRECAUTIONS). Before using Cefizox concomitantly with other antibiotics, the prescribing information for those agents should be reviewed for contraindications, warnings, precautions, and adverse reactions. Renal function should be carefully monitored.

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

Contraindications

Cefizox (ceftizoxime for injection, USP) is contraindicated in patients who have known allergy to the drug.

Warnings

BEFORE THERAPY WITH CEFIZOX IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFIZOX, OTHER CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS HYPERSENSITIVITY AMONG BETA‐LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEFIZOX OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTIHISTAMINES, CORTICOSTEROIDS, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

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

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of

clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic‐associated" colitis.

After the diagnosis of pseudomembranous colitis has been established, 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 and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Precautions

General

As with all broad‐spectrum antibiotics, Cefizox (ceftizoxime for injection, USP) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Although Cefizox has not been shown to produce an alteration in renal function, renal status should be evaluated, especially in seriously ill patients receiving maximum dose therapy. As with any antibiotic, prolonged use may result in overgrowth of nonsusceptible organisms. Careful observation is essential; appropriate measures should be taken if superinfection occurs.

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 Cefizox in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Drug Interactions

Although the occurrence has not been reported with Cefizox, nephrotoxicity has been reported following concomitant administration of other cephalosporins and aminoglycosides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long‐term studies in animals to evaluate the carcinogenic potential of ceftizoxime have not been conducted.

In an *in vitro* bacterial cell assay (i.e., Ames test), there was no evidence of mutagenicity at ceftizoxime concentrations of 0.001‐0.5 mcg/plate. Ceftizoxime did not produce increases in micronuclei in the *in vivo* mouse micronucleus test when given to animals at doses up to 7500 mg/kg, approximately six times greater than the maximum human daily dose on a mg/M^2 basis.

Ceftizoxime had no effect on fertility when administered subcutaneously to rats at daily doses of up to 1000 mg/kg/day, approximately two times the maximum human daily dose on a mg/M^2 basis. Ceftizoxime produced no histological changes in the sexual organs of male and female dogs when given intravenously for thirteen weeks at a dose of 1000 mg/kg/day, approximately five times greater than the maximum human daily dose on a mg/M^2 basis.

Pregnancy:

Teratogenic Effects:

Pregnancy Category B.

Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to Cefizox. There are, however, no adequate and well‐controlled studies in

pregnant women. Because animal reproduction studies are not always predictive of human effects, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Safety of Cefizox use during labor and delivery has not been established.

Nursing Mothers

Cefizox is excreted in human milk in low concentrations. Caution should be exercised when Cefizox is administered to a nursing woman.

Pediatric Use

Safety and efficacy in pediatric patients from birth to six months of age have not been established. In pediatric patients six months of age and older, treatment with Cefizox has been associated with transient elevated levels of eosinophils, AST (SGOT), ALT (SGPT), and CPK (creatine phosphokinase). The CPK elevation may be related to IM administration.

The potential for the toxic effect in pediatric patients from chemicals that may leach from the single dose IV preparation in plastic has not been determined.

Geriatric Use

Clinical studies of ceftizoxime did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Information for Patients

Patients should be counseled that antibacterial drugs including Cefizox should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefizox 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 Cefizox or other antibacterial drugs in the future.

Adverse Reactions

Cefizox® (ceftizoxime for injection, USP) is generally well tolerated. The *most* frequent adverse reactions (*greater* than 1% but *less* than 5%) are:

Hypersensitivity--Rash, pruritus, fever.

Hepatic--Transient elevation in AST (SGOT), ALT (SGPT), and alkaline phosphatase.

Hematologic--Transient eosinophilia, thrombocytosis. Some individuals have developed a positive Coombs test.

Local--Injection site--Burning, cellulitis, phlebitis with IV administration, pain, induration, tenderness, paresthesia.

The *less* frequent adverse reactions (*less* than 1%) are:

Hypersensitivity--Numbness and anaphylaxis have been reported rarely.

Hepatic--Elevation of bilirubin has been reported rarely.

Renal--Transient elevations of BUN and creatinine have been occasionally observed with Cefizox.

Hematologic--Anemia, including hemolytic anemia with occasional fatal outcome, leukopenia, neutropenia, and thrombocytopenia have been reported rarely.

Urogenital--Vaginitis has occurred rarely.

Gastrointestinal--Diarrhea; nausea and vomiting have been reported occasionally.

Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment (see WARNINGS).

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

Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, serum-sickness like reaction, toxic nephropathy, aplastic anemia, hemorrhage, prolonged prothrombin time, elevated LDH, pancytopenia, and agranulocytosis.

Several cephalosporins 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 occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Dosage and Administration

Note: Cefizox (ceftizoxime for injection, USP) in the ADD-Vantage® vial is intended for intravenous infusion only after dilution with the appropriate volume of ADD-Vantage diluent solution.

The usual adult dosage is 1 or 2 grams of Cefizox (ceftizoxime for injection, USP) every 8 to 12 hours. Proper dosage and route of administration should be determined by the condition of the patient, severity of the infection, and susceptibility of the causative organisms.

General Guidelines for Dosage of Cefizox

Type of Infection	Daily Dose (Grams)	Frequency and Route
Uncomplicated		
Urinary Tract	1	500 mg q12h IM or IV
Other Sites	2-3	1 gram q8-12h IM or IV
Severe or		
Refractory	3-6	1 gram q8h IM or IV
		2 grams q8-12h IM* or IV
PID †	6	2 grams q8h IV
Life-Threatening ‡	9-12	3-4 grams q8h IV

* When administering 2 gram IM doses, the dose should be divided and given in different large muscle masses.

† If *C. trachomatis* is a suspected pathogen, appropriate antichlamydial coverage should be added, because ceftizoxime has no activity against this organism.

‡ In life-threatening infections, dosages up to 2 grams every 4 hours have been given.

Because of the serious nature of urinary tract infections due to *P. aeruginosa* and because many strains of *Pseudomonas* species are only moderately susceptible to Cefizox, higher dosage is recommended. Other therapy should be instituted if the response is not prompt.

A single, 1 gram IM dose is the usual dose for treatment of uncomplicated gonorrhea.

The IV route may be preferable for patients with bacterial septicemia, localized parenchymal abscesses (such as intraabdominal abscess), peritonitis, or other severe or life-threatening infections.

In those with normal renal function, the IV dosage for such infections is 2 to 12 grams of Cefizox (ceftizoxime for injection, USP) daily. In conditions such as bacterial septicemia, 6 to 12 grams/day may be given initially by the IV route for several days, and the dosage may then be gradually reduced according to clinical response and laboratory findings.

Pediatric Dosage Schedule

	Unit Dose	Frequency
Pediatric patients 6 months or older	50 mg/kg	q6-8h

Dosage may be increased to a total daily dose of 200 mg/kg (not to exceed the maximum adult dose for serious infection).

Impaired Renal Function

Modification of Cefizox dosage is necessary in patients with impaired renal function. Following an initial loading dose of 500 mg-1 gram IM or IV, the maintenance dosing schedule shown below should be followed. Further dosing should be determined by therapeutic monitoring, severity of the infection, and susceptibility of the causative organisms.

When only the serum creatinine level is available, creatinine clearance may be calculated from the following formula. The serum creatinine level should represent current renal function at the steady state.

Males

$$\text{Clcr} = \frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/100 mL)}}$$

Females are 0.85 of the calculated clearance values for males.

In patients undergoing hemodialysis, no additional supplemental dosing is required following hemodialysis; however, dosing should be timed so that the patient receives the dose (according to the table below) at the end of the dialysis.

Dosage in Adults with Reduced Renal Function

Creatinine Clearance mL/min	Renal Function	Less Severe Infections	Life-Threatening Infections
79-50	Mild Impairment	500 mg q8h	0.75-1.5 grams q8h
49-5	Moderate to severe impairment	250-500 mg q12h	0.5-1 gram q12h
4-0	Dialysis Patients	500 mg q48h or 250 mg q24h	0.5-1 gram q48h or 0.5 gram q24h

Reconstitution

Cefizox in the ADD-Vantage vial is intended for use with ADD-Vantage diluent containers only, available in 50 mL and 100 mL sizes of Sodium Chloride Injection 0.9% and Dextrose Injection 5%.

Ordinarily, the ADD-Vantage vials should be reconstituted only when it is certain that the patient is ready to receive the drug. However, reconstitued Cefizox is stable for 24 hours at room temperature or 96 hours under refrigeration 5°C (41°F).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

To Open ADD-Vantage ® Diluent Containers

Peel overwrap at corner and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually.

To Assemble Vial and Flexible Diluent Container (Use Aseptic Technique)

1. Remove the protective covers from the top of the vial and the vial port on the diluent container as follows:

a. To remove the breakaway vial cap, swing the pull ring over the top of the vial and pull down far enough to start the opening (SEE FIGURE 1.), then pull straight up to remove the cap. (SEE FIGURE 2.)

NOTE: Once the breakaway cap has been removed, do not access vial with syringe.

Fig. 1

Fig. 2

b. To remove the vial port cover, grasp the tab on the pull ring, pull up to break the three tie strings, then pull further to remove the cover. (SEE FIGURE 3.)

2. Screw the vial into the vial port until it will go no further. THE VIAL MUST BE SCREWED IN TIGHTLY TO ASSURE A SEAL. This occurs approximately ½ turn (180°) after the first audible click. (SEE FIGURE 4.) The clicking sound does not assure a seal; the vial must be turned as far as it will go. NOTE: Once vial is sealed, do not attempt to remove. (SEE FIGURE 4.)

3. Recheck the vial to assure that it is tight by trying to turn it further in the direction of assembly.

4. Label appropriately.

Fig. 3

Fig. 4

To Prepare Admixture

1. Squeeze the bottom of the diluent container gently to inflate the portion of the container surrounding the end of the drug vial.
2. With the other hand, push the drug vial down into the container telescoping the walls of the container. Grasp the inner cap of the vial through the walls of the container. (SEE FIGURE 5.)
3. Pull the inner cap from the drug vial. (SEE FIGURE 6.) Verify that the rubber stopper has been pulled out, allowing the diluent to enter the drug vial and thoroughly dissolve the powder.
4. Mix container contents thoroughly by inverting several times, and use within the specified time.

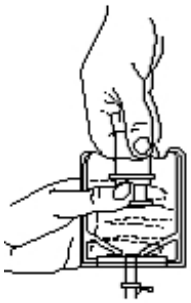


Fig. 5

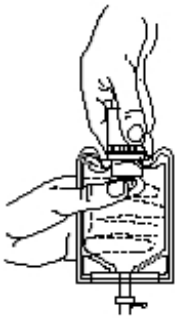


Fig. 6

Preparation for Administration (Use Aseptic Technique)

1. Confirm the activation and admixture of vial contents.
2. Check for leaks by squeezing container firmly. If leaks are found, discard unit as sterility may be impaired.
3. Close flow control clamp of administration set.
4. Remove cover from outlet port at bottom of container.
5. Insert piercing pin of administration set into port with a twisting motion until the pin is firmly seated. NOTE: See full directions on administration set carton.
6. Lift the free end of the hanger loop on the bottom of the vial, breaking the two tie strings. Bend the loop outward to lock it in the upright position, then suspend container from hanger.
7. Squeeze and release drip chamber to establish proper fluid level in chamber.
8. Open flow control clamp and clear air from set. Close clamp.
9. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.
10. Regulate rate of administration with flow control clamp.

WARNING: Do not use flexible container in series connections.

How Supplied

Cefizox® (ceftizoxime for injection, USP) in ADD-Vantage® Vials

NDC 0469-7271-01 equivalent to 1 gram ceftizoxime, packaged in tens	Product No. 727101
NDC 0469-7272-02 equivalent to 2 grams ceftizoxime, packaged in tens	Product No. 727202

Unreconstituted Cefizox should be protected from excessive light, and stored at controlled room temperature 15°-30°C (59°-86°F) in the original package until used.

ADD-Vantage® is registered trademark of Abbott Laboratories.

U.S. Patent 4,427,674

Product of Japan

REFERENCES

1. National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically – Fifth Edition. Approved Standard NCCLS Document M7-A5, Vol. 20, No. 2, NCCLS, Wayne, PA, January 2000.
2. National Committee for Clinical Laboratory Standards. Performance Standards for Antimicrobial Disk Susceptibility Tests – Seventh Edition. Approved Standard NCCLS Document M2-A7, Vol. 20, No. 1, NCCLS, Wayne, PA, January 2000.
3. National Committee for Clinical Laboratory Standards. Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria – Fourth Edition. Approved Standard NCCLS Document M11-A4, Vol. 17, No. 22, NCCLS, Wayne, PA, December 1997.
4. National Committee for Clinical Laboratory Standards. MIC Testing Supplemental Tables. NCCLS Document M100-S10 (M7), NCCLS, Wayne, PA, January 2000.

Rx only

Manufactured for Fujisawa Healthcare, Inc.

Deerfield, IL 60015-2548 by GlaxoSmithKline, Philadelphia, PA 19101

CEFIZOX

ceftizoxime injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0469-7271
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ceftizoxime sodium (UNII: 26337D5X88) (ceftizoxime - UNII:C43C467DPE)		1 g

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**

1	NDC:0469-7271-01	10 in 1 PACKAGE		
1		1 in 1 VIAL		

CEFIZOX

ceftizoxime injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0469-7272
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ceftizoxime sodium (UNII: 26337D5X88) (ceftizoxime - UNII:C43C467DPE)		2 g

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0469-7272-02	10 in 1 PACKAGE		
1		1 in 1 VIAL		

Labeler - Fujisawa Healthcare, Inc.

Revised: 6/2006 Fujisawa Healthcare, Inc.