

Ceftazidime

Introduction: Ceftazidime is a semisynthetic, broad-spectrum, beta-lactam antibiotic for parenteral administration.

Mechanism of action: Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibit 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:

Distribution: Widely throughout the body including bone, bile, skin, CSF (higher concentrations achieved when meninges are inflamed), endometrium, heart, pleural and lymphatic fluids

Protein binding: 17%

Half-life elimination: 1-2 hours, prolonged with renal impairment; Neonates <23 days: 2.2-4.7 hours

Time to peak, serum: I.M.: 1 hour

Excretion: Urine (80% to 90% as unchanged drug)

Indications:

- **Lower Respiratory Tract Infections**, including pneumonia, caused by *Pseudomonas aeruginosa* and other *Pseudomonas* spp.; *Haemophilus influenzae*, including ampicillin-resistant strains; *Klebsiella* spp.; *Enterobacter* spp.; *Proteus mirabilis*; *Escherichia coli*; *Serratia* spp.; *Citrobacter* spp.; *Streptococcus pneumoniae*; and *Staphylococcus aureus* (methicillin-susceptible strains).
- **Skin and Skin-Structure Infections** caused by *Pseudomonas aeruginosa*; *Klebsiella* spp.; *Escherichia coli*; *Proteus* spp.; including *Proteus mirabilis* and indole-positive *Proteus*; *Enterobacter* spp.; *Serratia* spp.; *Staphylococcus aureus* (methicillin-susceptible strains); and *Streptococcus pyogenes* (group A beta-hemolytic streptococci).
- **Urinary Tract Infections**, both complicated and uncomplicated, caused by *Pseudomonas aeruginosa*; *Enterobacter* spp.; *Proteus* spp., including *Proteus mirabilis* and indole-positive *Proteus*; *Klebsiella* spp.; and *Escherichia coli*.
- **Bacterial Septicemia** caused by *Pseudomonas aeruginosa*, *Klebsiella* spp., *Haemophilus influenzae*, *Escherichia coli*, *Serratia* spp., *Streptococcus pneumoniae*, and *Staphylococcus aureus* (methicillin-susceptible strains).
- **Bone and Joint Infections** caused by *Pseudomonas aeruginosa*; *Klebsiella* spp.; *Enterobacter* spp., and *Staphylococcus aureus* (methicillin-susceptible strains).

- **Gynecologic Infections**, including endometritis, pelvic cellulitis, and other infections of the female genital tract caused by *Escherichia coli*.
- **Intra-abdominal Infections**, including peritonitis caused by *Escherichia coli*, *Klebsiella* spp., and *Staphylococcus aureus* (methicillin-susceptible strains) and polymicrobial infections caused by aerobic and anaerobic organisms and *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).
- **Central Nervous System Infections**, including meningitis, caused by *Haemophilus influenzae* and *Neisseria meningitidis*. Ceftazidime has also been used successfully in a limited number of cases of meningitis due to *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*.

Dosage: The usual adult dosage is 1 gram administered intravenously or intramuscularly every 8 to 12 hours. The dosage and route should be determined by the susceptibility of the causative organisms, the severity of infection, and the condition and renal function of the patient.

Recommended Dosage Schedule

	Dose	Frequency
Patients 12 years and older*		
Usual recommended dosage	1 gram IV or IM	q8-12hr
Uncomplicated urinary tract infections	250 mg IV or IM	q12hr
Bone and joint infections	2 grams IV	q12hr
Complicated urinary tract infections	500 mg IV or IM	q8-12hr
Uncomplicated pneumonia; mild skin and skin-structure infections	500 mg-1 gram IV or IM	q8hr
Serious gynecologic and intra-abdominal infections	2 grams IV	q8hr
Meningitis	2 grams IV	q8hr
Very severe life-threatening infections, especially in immunocompromised patients	2 grams IV	q8hr
Lung infections caused by <i>Pseudomonas</i> spp. in patients with cystic fibrosis with normal renal function [†]	30-50 mg/kg IV to a maximum of 6 grams per day	q8hr

Impaired Renal Function: Ceftazidime is excreted by the kidneys, almost exclusively by glomerular filtration. Therefore, in patients with impaired renal function (glomerular filtration rate [GFR] < 50 mL/min), it is recommended that the dosage of ceftazidime be reduced to compensate for its slower excretion.

Side effects: Ceftazidime is generally well-tolerated. The most common were local reactions following IV injection and allergic and gastrointestinal reactions. Other adverse reactions were encountered infrequently. Local Effects, were phlebitis and inflammation at the site of injection.

Hypersensitivity Reactions, reported are pruritus, rash and fever. Toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme have also been reported. Angioedema and anaphylaxis (bronchospasm and/or hypotension) have been reported very rarely.

Gastrointestinal Symptoms, reported were diarrhea, nausea, vomiting and abdominal pain. The onset of pseudomembranous colitis symptoms may occur during or after treatment.

Central Nervous System Reactions include headache, dizziness and paresthesia. Seizures have been reported. In addition, encephalopathy, asterixis and neuromuscular excitability have been reported in renally impaired patients treated with unadjusted dosage regimens of ceftazidime .

Precautions:

General: The total daily dosage should be reduced when ceftazidime is administered to patients with renal insufficiency. Elevated levels of ceftazidime in these patients can lead to seizures, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms. Ceftazidime should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. Distal necrosis can occur after inadvertent intra-arterial administration of ceftazidime.

Pregnancy: There are no adequate and well-controlled studies in pregnant women; this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Ceftazidime is excreted in human milk in low concentrations. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety of the arginine component of Ceftazidime in neonates, infants, and children has not been established. This product is for use in patients 12 years and older. If treatment with ceftazidime is indicated for neonates, infants, or children, a sodium carbonate formulation should be used.

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: Ceftazidime is contraindicated in patients who have shown hypersensitivity to ceftazidime or the cephalosporin group of antibiotics.

How supplied: Customized as per request.