# Ceftazidime

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## Introduction

Ceftazidime is a parenteral, third-generation cephalosporin antibiotic that is administered by intravenous or intramuscular injection. It is effective against a wide variety of gram-negative organisms, including *Pseudomonas aeruginosa*. Although ceftazidime is active in vitro against gram-positive organisms, clinical use of ceftazidime for gram positive infections is rare. Ceftazidime is used for the treatment of meningitis, lower respiratory infections, febrile neutropenic events, urinary tract infections, pelvic inflammatory disease, and skin and skin structure infections.

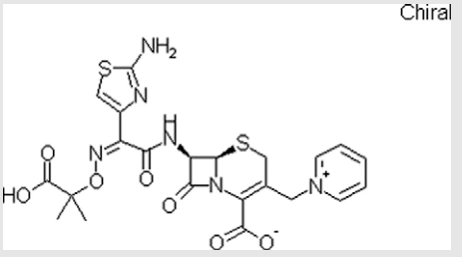
## Nomenclature

| | |
|---|---|
| **Name of the Clinical Form** | Ceftazidime sodium |
| **Related Names** Source: EMTREE | Ceftazidime; 7 [2 (2 aminothiazol 4 yl) 1 (1 carboxy 1methylethoxyimino)acetamido] 3 (1 pyridiniomethyl) 2 cephem 2 carboxylate; 7[2 (2 aminothiazol 4 yl) glyoxylamido] 3 (pyrid 1 ylmethyl) 2 cephem 2 carboxylic acid betaine 7 2 [o(1 carboxy 1 methylethyl)oxime]; ceftazadine; ceftazidime sodium; ceph 2 em 2 carboxylic acid betaine 7 2 [o (1 carboxy 1methylethyl)oxime],7 [2 (2 aminothiazol 4 yl)glyoxylamido] 3 (pyrid 1 ylmethyl); cmi 90; foraz; fortam; fortaz; fortum; glazidim; gr 20263; ly139381; modacin; sn 401; solvetan; tazicef; tazidime; 7 [2 (2 aminothiazol 4 yl) 1 (1 carboxy 1 methylethoxyimino) acetamido] 3 (1 pyridiniomethyl) 2 cephem 2 carboxylate; 7 [2 (2 aminothiazol 4 yl)glyoxylamido] 3 (pyrid 1 ylmethyl) 2 cephem 2 carboxylic acid betaine 7 2 [o (1 carboxy 1 methylethyl)oxime]; ceph 2 em 2 carboxylic acid betaine 7 2 [o (1 carboxy 1 methylethyl)oxime],7 [2 (2 aminothiazol 4 yl) glyoxylamido] 3 (pyrid 1 ylmethyl); cmi90; gr20263; ly 139381; sn401 |
| **Chemical Names** | (Z)-(7R)-7-[2-(2-Aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido]-3-(1-pyridiniomethyl)-3-cephem-4-carboxylate pentahydrate Sweetman (2003) |
| **CAS Number** | 72558-82-8 |

## Basic Chemistry

**Chemical Structure**

**Structure**




| | |
|---|---|
| **Chemical Formula** | C22 H22 N6 O7 S2 |
| **Properties** | |
| **Physical Properties** | Ceftazidime is a white to cream-colored, crystalline powder Sweetman (2003). |
| **Molecular Weight** | 546.583 |
| **Solubility** | Ceftazidime is slightly soluble in water, in dimethylformamide, and in methyl alcohol. It is insoluble in alcohol, in acetone, in chloroform, in dioxan, in ether, in ethyl acetate, and in toluene, and is soluble in alkali and in dimethyl sulfoxide. The pH of a 0.5% aqueous solution is between 3.0 and 4.0 Sweetman (2003). |

**Ionization Constant**

| | Value | Salt | Conditions | Reference | Comments |
|---|---|---|---|---|---|
| pKa | 1.8 | | | Williams (2002) | HA |
| pKa | 2.7 | | | Williams (2002) | HA |
| pKa | 4.1 | | | Williams (2002) | HB+ |

## Human Pharmacokinetics

Because ceftazidime is not absorbed from the gastrointestinal tract it must be administered parenterally. It is widely distributed to body fluids and tissues and is excreted unchanged in urine.

### Pharmacokinetic Properties

| | Value | Units | Prep.and Route of Admin. | Reference | Comments |
|---|---|---|---|---|---|
| **Absorption** | | | | | |
| Bioavailability | | | | | |
| **Distribution** | Ceftazidime is widely distributed to body fluids and tissues. Penetration into the cerebrospinal fluid is good with inflamed meninges. | | | | |
| Volume of Distribution | 0.23 | l/kg | | Balant et al (1985) | The volume of distribution of ceftazidime is increased in aged and burn patients. |

| | | | | | |
|---|---|---|---|---|---|
| Plasma Protein Binding | <10 | % | | Physician's Desk Reference (2003) | |
| **Metabolism** | | | | | |
| Plasma Half-Life | 1.9 | hrs | i.v. | Physician's Desk Reference (2003) | The plasma half-life is 2 hr following i.m. administration and is prolonged if renal function is impaired. |
| Bio Half-Life Clearance | 100 | ml/min | | Physician's Desk Reference (2003) | Renal clearance. |
| **Routes of Elimination** | Approximately 80–90% of an administered dose of ceftazidime is excreted unchanged in urine by glomerular filtration. | | | | |

## Targets-Pharmacodynamics

Ceftazidime is a bactericidal antibiotic that inhibits bacterial cell wall synthesis by binding to one or more penicillin binding proteins of actively dividing cells. It is also proposed that cephalosporins decrease the availability of an inhibitor to murein hydrolase (autolysin), an enzyme involved in cell division.

### Target Name(s):

**Penicillin binding proteins**

## Therapeutics

Ceftazidime is active against a wide range of gram-negative organisms, including *Pseudomonas aeruginosa*. Although ceftazidime is active in vitro against gram-positive bacteria, it is rarely used for these infections. Ceftazidime is used for the treatment of meningitis, lower respiratory infections, febrile neutropenic events, urinary tract infections, pelvic inflammatory disease, and skin structure and skin infections.

### Indications

| | Value | Units | Prep.and Route of Admin. | Reference | Comments |
|---|---|---|---|---|---|
| **Pneumonia** | | | | | |
| Dosage | 500–2,000 | mg | i.v. or i.m. every 8 hrs | Physician's Desk Reference (2003) | For pseudomonal or severe, life threatening infections 2 g of ceftazidime should be given i.v. every 8 hrs. Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Intraabdominal Infection** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Dosage | 2 | g | i.v. every 8 hrs | Physician's Desk Reference (2003) | Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Urinary Tract Infection** | | | | | |
| Dosage | 250–500 | mg | i.v. or i.m. every 8–12 hrs | Physician's Desk Reference (2003) | Complicated urinary tract infections should be treated with higher doses and, possibly, a more frequent dosing interval. Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Skin and Skin Structure, Mild** | | | | | |
| Dosage | 500–1,000 | mg | i.v. or i.m. every 8 hrs | Physician's Desk Reference (2003) | Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Bone and Joint Infection** | | | | | |
| Dosage | 2 | G | i.v. every 12 hrs | Physician's Desk Reference (2003) | Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Meningitis** | | | | | |
| Dosage | 2 | g | i.v. every 8 hrs | Physician's Desk Reference (2003) | Doses must be reduced in those with renal insufficiency based on creatinine clearance. |
| **Infections, Pediatrics** | | | | | |
| Dosage | 30–50 | mg/kg | i.v. every 8 hrs | Physician's Desk Reference (2003) | Maximum of 6 g/day. Doses must be reduced in those with renal insufficiency based on creatinine clearance. |

## Contraindications

Ceftazidime is contraindicated in patients with a history of allergic reactions to cephalosporin antibiotics. Ceftazidime should be avoided in those with anaphylactic reactions to penicillins and should be used with caution in patients with delayed hypersensitivity reactions such as rash, fever, or eosinophilia AHFS (2001).

## Adverse Effects

Hypersensitivity reactions occur in approximately 5% or less of patients receiving cephalosporin antibiotics. These include urticaria, pruritis, rash, fever, eosinophilia, angioedema, hypotension, Stevens-Johnson Syndrome, erythema multiforme, toxic epidermal necrolysis, and exfoliative dermatitis. Positive direct and indirect antiglobulin (Coombs') test have been reported in 3% or more of patients receiving cephalosporins. Rarely, cephalosporins cause neutropenia, thrombocytopenia, leukocytosis, granulocytosis, monocytosis, lymphocytopenia, basophilia, reversible leukopenia, aplastic anemia, pancytopenia, and hemolytic anemia. Transient increases in BUN and serum creatinine, renal dysfunction and nephrotoxicity have occurred with cephalosporin use, as have transient increases in AST, ALT, GGT, and alkaline phosphotase. Clostridium difficile colitis can occur with cephalosporin use AHFS (2001).

### Agent-Agent Interactions

| Agent Name | Mode of Interaction |
|---|---|
| Aminoglycoside antibiotics | Aminoglycoside antibiotics (e.g., **gentamicin**, **tobramycin**, **amikacin**). There is an increased risk of nephrotoxicity associated with the concurrent use of ceftazidime and aminoglycoside antibiotics. |

## Pre-Clinical Research

### Pharmacokinetics
### Potency

| | Value | Units | Organ/ Tissue | Prep. and Route of Admin. | Cell Line/ Type | Effects | Exp. End Point | Reference | Comments |
|---|---|---|---|---|---|---|---|---|---|
| **Rat** | | | | | | | | | |
| LD50 | 5800 | mg/kg | | i.v. | | | | Poisindex (2003) | |
| LD50 | >20 | g/kg | | p.o. | | | | Poisindex (2003) | |
| **Mouse** | | | | | | | | | |
| LD50 | 6300 | mg/kg | | i.v. | | | | Poisindex (2003) | |
| LD50 | >20 | g/kg | | p.o. | | | | Poisindex (2003) | |
| **Rabbit** | | | | | | | | | |
| LD50 | >2 | g/kg | | i.v. | | | | Poisindex (2003) | |

## Journal Citations

Balant, L., Dayer, P., Auckenthaler, R., 1985. Clinical pharmacokinetics of third generation cephalosporins. *Clin. Pharmacokinet.*, 10, 101–143.

## Book Citations

Sweetman, S., 2003. Martindale: The Complete Drug Reference. Sweetman, S. (Ed.), *Micromedex, Electronic Version*. Pharmaceutical Press, Greenwood Village, Colorado.
Williams, D., 2002. pKa Values for Some Drugs and Miscellaneous Organic Acids and Bases. Williams, D.A., Lemke, T.L. (Ed.), *Foye's Principles of Medicinal Chemistry*, Edition 5, p. 1071, Lippincott Williams and Wilkins, Philadelphia.
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AHFS, 2001, Drug Monographs. McEvoy, G. (Ed.), *American Hospital Formulary System*, pp. 128–253, American Society of Health-System Pharmacists, Inc., Bethesda, Maryland.
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