## Preparations

***USP 31:*** Cefprozil for Oral Suspension; Cefprozil Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Ceprof; ***Austria:*** Procef†; ***Braz.:*** Cefzil; ***Canad.:*** Cefzil; ***Chile:*** Procef†; ***Cz.:*** Cefzil; ***Gr.:*** Cefgram; Cefpro; Gramium; Procef; Zamalin; ***Hong Kong:*** Procef; ***Hung.:*** Cefzil; ***India:*** Refzil-O; ***Indon.:*** Cefzil; Lizor; ***Ital.:*** Cronocef; Procef; Rozicel; ***Malaysia:*** Procef†; ***Mex.:*** Procef; ***Philipp.:*** Procef; ***Pol.:*** Cefzil; ***Port.:*** Procef; Radacefe; ***S.Afr.:*** Prozef; ***Singapore:*** Procef†; ***Spain:*** Arzimol; Brisoral; Precef; ***Switz.:*** Procef; ***Thai.:*** Procef; ***Turk.:*** Serozil; ***UK:*** Cefzil†; ***USA:*** Cefzil; ***Venez.:*** Procef.

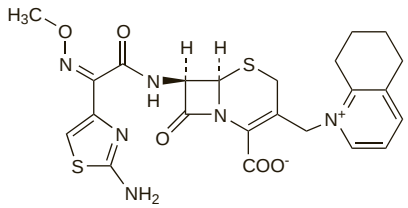
## Cefquinome Sulfate *(USAN, rINNM)*

Cefquinome, Sulfate de; Cefquinome Sulphate *(BANM)*; Cefquinomi Sulfas; HR-111V; Sulfato de cefquinoma. {6*R*-[6α,7β(*Z*)]}-1-[(7-{[(2-amino-4-thiazolyl)-(methoxyimino)acetyl]amino}-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl)methyl]-5,6,7,8,-tetrahydroquinolinium sulfate (1:1).

Цефхинома Сульфат

$C_{23}H_{24}N_6O_5S_2,H_2SO_4$ = 626.7.

*CAS — 84957-30-2 (cefquinome); 118443-89-3 (cefquinome sulfate); 123766-80-3 (cefquinome sulfate).*



*(cefquinome)*

### Profile

Cefquinome is a fourth-generation cephalosporin antibacterial used as the sulfate in veterinary medicine.

# Cefradine *(BAN, rINN)*

Cefradin; Cefradina; Cefradinas; Céfradine; Cefradinum; Cefradyna; Cephradine *(USAN)*; Kefradiini; Sefradin; SKF-D-39304; SQ-11436; SQ-22022 (cefradine dihydrate). (7*R*)-7-(α-D-Cyclohexa-1,4-dienylglycylamino)-3-methyl-3-cephem-4-carboxylic acid.

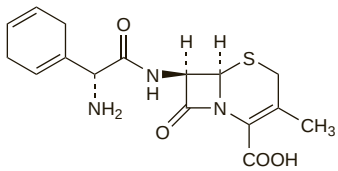
Цефрадин

$C_{16}H_{19}N_3O_4S$ = 349.4.

*CAS — 38821-53-3 (anhydrous cefradine); 31828-50-9 (non-stoichiometric cefradine hydrate); 58456-86-3 (cefradine dihydrate).*

*ATC — J01DB09.*

*ATC Vet — QJ01DB09.*



**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), and *US* (which allows the anhydrous form, the monohydrate, or the dihydrate).
**Ph. Eur. 6.2** (Cefradine). A white or slightly yellow, hygroscopic powder. Sparingly soluble in water; practically insoluble in alcohol and in *n*-hexane. A 1% solution in water has a pH of 3.5 to 6.0. Store at 2° to 8° in airtight containers. Protect from light.
**USP 31** (Cephradine). A white to off-white crystalline powder. Sparingly soluble in water; very slightly soluble in alcohol and in chloroform; practically insoluble in ether. pH of a 1% solution in water is between 3.5 and 6.0. Store in airtight containers.

**Incompatibility and stability.** Commercially available injections contain sodium carbonate or arginine as neutralisers. Injections containing sodium carbonate are incompatible with solutions such as compound sodium lactate injection that contain calcium salts.

References.


1. Wang Y-C J, Monkhouse DC. Solution stability of cephradine neutralized with arginine or sodium bicarbonate. *Am J Hosp Pharm* 1983; **40:** 432.
2. Mehta AC, *et al.* Chemical stability of cephradine injection solutions. *Intensive Therapy Clin Monit* 1988; **9**: 195–6.


## Adverse Effects and Precautions

As for Cefalexin, p.218. Intramuscular injections of cefradine can be painful and thrombophlebitis has occurred on intravenous injection.

**Porphyria.** Cefradine is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

## Interactions

As for Cefalexin, p.218.

## Antimicrobial Action

As for Cefalexin, p.218.

## Pharmacokinetics

Cefradine is rapidly and almost completely absorbed from the gastrointestinal tract after oral doses. Doses of 0.25, 0.5, and 1 g given orally have produced peak plasma concentrations of about 9, 17, and 24 micrograms/mL respectively at 1 hour and are similar to those achieved with cefalexin. Absorption is delayed by the presence of food although the total amount absorbed is not appreciably altered. Following intramuscular injection peak plasma concentrations of about 6 and 14 micrograms/mL have been obtained within 1 to 2 hours of doses of 0.5 and 1 g respectively.

Only about 8 to 12% is reported to be bound to plasma proteins. A plasma half-life of about 1 hour has been reported; this is prolonged in patients with renal impairment. Cefradine is widely distributed to body tissues and fluids, but does not enter the CSF in significant quantities. Therapeutic concentrations may be found in the bile. It crosses the placenta into the fetal circulation and is distributed in small amounts into breast milk.

Cefradine is excreted unchanged in the urine by glomerular filtration and tubular secretion, over 90% of an oral dose or 60 to 80% of an intramuscular dose being recovered within 6 hours. Peak urinary concentrations of about 3 mg/mL have been achieved after a 500-mg oral dose. Probenecid delays excretion.

Cefradine is removed by haemodialysis and peritoneal dialysis.

◊ References.


1. Wise R. The pharmacokinetics of the oral cephalosporins—a review. *J Antimicrob Chemother* 1990; **26** (suppl E): 13–20.
2. Schwinghammer TL, *et al.* Pharmacokinetics of cephradine administered intravenously and orally to young and elderly subjects. *J Clin Pharmacol* 1990; **30:** 893–9.


## Uses and Administration

Cefradine is a first-generation cephalosporin antibacterial given orally similarly to cefalexin (p.219) and by the parenteral route similarly to cefazolin (p.222) in the treatment of susceptible infections and in the prophylaxis of infections during surgical procedures.

Cefradine is given orally in doses of 1 to 2 g daily in 2 to 4 divided doses to adults; up to 4 g daily may be given by this route. In severe infections it should be given parenterally, by deep intramuscular injection or intravenously by slow injection over 3 to 5 minutes or by infusion, in doses of 2 to 4 g daily in 4 divided doses; up to 8 g daily may be given parenterally.

In children, the usual daily oral dose is 25 to 50 mg/kg in 2 to 4 divided doses, although 75 to 100 mg/kg daily may be given for otitis media. By injection, 50 to 100 mg/kg daily may be given in 4 divided doses, increasing to 300 mg/kg daily in severe infections.

For surgical infection prophylaxis, 1 to 2 g may be given pre-operatively by intramuscular or intravenous injection; subsequent parenteral or oral doses are given as appropriate.

For details of reduced doses of cefradine in patients with severe renal impairment, see below.

**Administration in renal impairment.** Doses of cefradine should be reduced in patients with severe renal impairment. The following oral and parenteral doses are recommended in UK licensed product information according to creatinine clearance (CC):

- CC more than 20 mL/minute: 500 mg every 6 hours
- CC 5 to 20 mL/minute: 250 mg every 6 hours
- CC less than 5 mL/minute: 250 mg every 12 hours

Patients undergoing chronic intermittent haemodialysis may be given a 250-mg dose at the start of the session, repeated after 6 to 12 hours, then again 36 to 48 hours after the initial dose, and again at the start of the next haemodialysis if more than 30 hours have elapsed since the previous dose.

Further dosage modification may be required in children with renal impairment.

## Preparations

***BP 2008:*** Cefradine Capsules; Cefradine Oral Suspension;
***USP 31:*** Cephradine Capsules; Cephradine for Injection; Cephradine for Oral Suspension; Cephradine Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Belg.:*** Velosef; ***Chile:*** Velosef†; ***Fr.:*** Dexef; Kelsef†; Zeefra; ***Gr.:*** Tracilarin†; Vethisel†; ***Hong Kong:*** Qualisef; Velosef; Zeefra; ***Indon.:*** Dynacef; Lovecef; Velosef; ***Irl.:*** Velosef; ***Ital.:*** Cefrabiotic†; Ecosporina; Lisacef; Planocid†; ***Malaysia:*** Sephros†; ***Mex.:*** Veracef; ***Neth.:*** Velosef; ***NZ:*** Velosef†; ***Philipp.:*** Cefralon; Gramcep; Racep; Sedinef; Senadex; Solphride; Tolzep; Vamosef; Velodyne; Yudinef; Zepdril; ***Pol.:*** Tafril; ***Port.:*** Biocefra; Cefalmin; Cefradur; Novacefrex†; Velosef†; ***S.Afr.:*** Bactocef†; Cefril; Ranfradin†; ***Spain:*** Septacef; Velocef; ***UAE:*** Eskacef; Julphacef; ***UK:*** Nicef; Velosef; ***USA:*** Velosef†; ***Venez.:*** Cefracin†; Veracef.

## Cefsulodin Sodium *(BANM, USAN, rINNM)*

Abbott-46811; Cefsulodina sódica; Cefsulodine Sodique; Cefsulodinnatrium; Cefsulodinum Natricum; CGP-7174E; Kefsulodiinatrium; Natrii Cefsulodinum; SCE-129; Sulcephalosporin Sodium. Sodium 3-(4-carbamoylpyridiniomethyl)-7-[(2*R*)-2-phenyl-2-sulphoacetamido]-3-cephem-4-carboxylate.

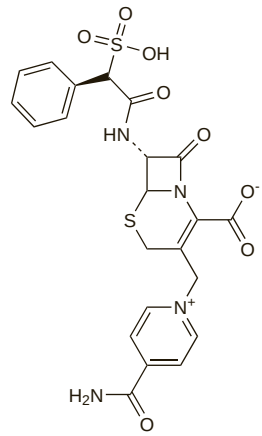
Натрий Цефсулодин

$C_{22}H_{19}N_4NaO_8S_2$ = 554.5.

*CAS — 62587-73-9 (cefsulodin); 52152-93-9 (cefsulodin sodium).*

*ATC — J01DD03.*

*ATC Vet — QJ01DD03.*



*(cefsulodin)*

**Pharmacopoeias.** In *Jpn.*

### Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

**Sodium content.** Each g of cefsulodin sodium contains about 1.8 mmol of sodium.

### Antimicrobial Action

Cefsulodin is a bactericidal antibiotic with activity against *Pseudomonas aeruginosa* as great as that of ceftazidime (p.234), but no significant activity against other Gram-negative bacteria. Gram-positive bacteria and anaerobes are not very susceptible. Its activity against *Ps. aeruginosa* may be enhanced by aminoglycosides.

Cefsulodin is stable to hydrolysis by many beta-lactamases, but emergence of resistant *Ps. aeruginosa* has been reported.

### Pharmacokinetics

Cefsulodin is given parenterally as the sodium salt. It has a plasma half-life of about 1.6 hours, which is prolonged in renal impairment. Up to 30% of cefsulodin in the circulation is bound to plasma proteins. Therapeutic concentrations have been reported in a wide range of body tissues and fluids. The major route of excretion of cefsulodin is via the urine, mainly by glomerular filtration. Clearance may be enhanced in cystic fibrosis, although there have been conflicting reports.

◊ References.


1. Granneman GR, *et al.* Cefsulodin kinetics in healthy subjects after intramuscular and intravenous injection. *Clin Pharmacol Ther* 1982; **31:** 95–103.
2. Reed MD, *et al.* Single-dose pharmacokinetics of cefsulodin in patients with cystic fibrosis. *Antimicrob Agents Chemother* 1984; **25:** 579–81.
3. Hedman A, *et al.* Increased renal clearance of cefsulodin due to higher glomerular filtration rate in cystic fibrosis. *Clin Pharmacokinet* 1990; **18:** 168–75.

### Uses and Administration

Cefsulodin is a third-generation cephalosporin antibiotic with a narrow spectrum of activity that has been used similarly to ceftazidime (p.235) for the treatment of infections caused by susceptible strains of *Pseudomonas aeruginosa*.

It is given as the sodium salt by intravenous injection. Doses are expressed in terms of the equivalent amount of cefsulodin; 1.04 g of cefsulodin sodium is equivalent to about 1 g of cefsulodin. The usual adult dose is 6 g daily in 4 divided doses; in less severe infections daily doses of 3 to 4 g may be given. Children may be given a usual dose of 100 mg/kg daily; 50 mg/kg daily may be given in less severe infections.

◊ References.


1. Smith BR. Cefsulodin and ceftazidime, two antipseudomonal cephalosporins. *Clin Pharm* 1984; **3:** 373–85.
2. Wright DB. Cefsulodin. *Drug Intell Clin Pharm* 1986; **20:** 845–9.


**Administration in renal impairment.** The dosage of cefsulodin given intravenously should be adjusted in patients with renal impairment according to creatinine clearance (CC):

- CC 20 to 50 mL/minute: a loading dose of 1.5 g then 1 g every 8 hours
- CC 5 to 20 mL/minute: a loading dose of 1.5 g then 1 g every 12 hours
- CC less than 5 mL/minute: a loading dose of 1.5 g then 1 g every 24 hours

In patients undergoing haemodialysis, 1 g is given before and after dialysis.

### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Fr.:*** Pyocefal; ***Jpn:*** Takesulin.

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## Ceftazidime *(BAN, USAN, rINN)*

Ceftazidim; Ceftazidim pentahydrát; Ceftazidima; Ceftazidimas; Ceftazidimum; Ceftazidimum Pentahydricum; Ceftazydym; GR-20263; Keftatsidiimi; LY-139381; Seftazidim. (*Z*)-(7*R*)-7-[2-(2-Aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido]-3-(1-pyridiniomethyl)-3-cephem-4-carboxylate pentahydrate.

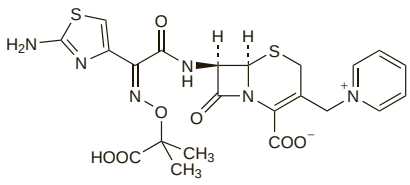
Цефтазидим

$C_{22}H_{22}N_6O_7S_2,5H_2O$ = 636.7.

*CAS — 72558-82-8 (anhydrous ceftazidime); 78439-06-2 (ceftazidime pentahydrate).*

*ATC — J01DD02.*

*ATC Vet — QJ01DD02.*



**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

**Ph. Eur. 6.2** (Ceftazidime). A white or almost white crystalline powder. Slightly soluble in water and in methyl alcohol; practically insoluble in alcohol and in acetone; it dissolves in acid and alkali solutions. A 0.5% solution in water has a pH of 3.0 to 4.0. Store in airtight containers.

**USP 31** (Ceftazidime). A white to cream-coloured crystalline powder. Slightly soluble in water, in dimethylformamide, and in methyl alcohol; insoluble in alcohol, in acetone, in chloroform, in dioxan, in ether, in ethyl acetate, and in toluene; soluble in alkali and in dimethyl sulfoxide. pH of a 0.5% solution in water is between 3.0 and 4.0. Store in airtight containers.

**Formulation.** Ceftazidime for injection is available as a dry powder containing ceftazidime with sodium carbonate. When reconstituted ceftazidime sodium is formed with the evolution of carbon dioxide. An alternative formulation, ceftazidime with arginine, appears to overcome the problems associated with effervescence.[1] In some countries a frozen injection containing ceftazidime sodium is also used.


1. Stiles ML, *et al.* Gas production of three brands of ceftazidime. *Am J Hosp Pharm* 1991; **48:** 1727–9.


**Incompatibility.** It has been reported that ceftazidime does not cause decreased activity when incubated in solution with *gentamicin*[1] or *tobramycin*[2] at 37°, or when mixed with tobramycin in serum.[3] Ceftazidime and tobramycin[4] were also stable for up to 16 hours at room temperature when combined in a glucose-containing dialysis solution, and for a further 8 hours at 37°. However, licensed product information recommends that ceftazidime, like most other beta lactams, should not be mixed with an aminoglycoside in the same giving set or syringe because of the potential for inactivation of either drug.

Ceftazidime is generally considered to be compatible with *metronidazole*, but degradation of ceftazidime has been reported.[5] Precipitation has occurred with *vancomycin*[6] and therefore the product information considers it prudent to flush giving sets and intravenous lines between giving the two drugs. However, in one study[7] ceftazidime and/or vancomycin were stable in a glucose-containing peritoneal dialysis solution when kept for 6 days in a refrigerator or 48 to 72 hours at room temperature, and in a further study[8] the two drugs were stable when combined in similar solutions containing 1.5% or 4.25% glucose for up to 12 hours when stored at 37° and for 24 hours when stored at 4° and 24°. Ceftazidime and *teicoplanin*[9] were stable in combination in a peritoneal dialysis solution at 37° for 8 hours when it had been previously stored at 4°, but not when previously stored at 25°. Ceftazidime was not stable when mixed in solution with *aminophylline*.[10] There was some evidence of possible incompatibility with *pentamidine*.[11]


1. Elliott TSJ, *et al.* Stability of gentamicin in combination with selected new β-lactam antibiotics. *J Antimicrob Chemother* 1984; **14:** 668–9.
2. Elliott TSJ, *et al.* Stability of tobramycin in combination with selected new β-lactam antibiotics. *J Antimicrob Chemother* 1986; **17:** 680–1.
3. Pennell AT, *et al.* Effect of ceftazidime, cefotaxime, and cefoperazone on serum tobramycin concentrations. *Am J Hosp Pharm* 1991; **48:** 520–2.
4. Mason NA, *et al.* Stability of ceftazidime and tobramycin sulfate in peritoneal dialysis solution. *Am J Hosp Pharm* 1992; **49:** 1139–42.
5. Messerschmidt W. Pharmazeutische kompatibilität von ceftazidim und metronidazol. *Pharm Ztg* 1990; **135:** 36–8.
6. Cairns CJ, Robertson J. Incompatibility of ceftazidime and vancomycin. *Pharm J* 1987; **238:** 577.
7. Vaughan LM, Poon CY. Stability of ceftazidime and vancomycin alone and in combination in heparinized and nonheparinized peritoneal dialysis solution. *Ann Pharmacother* 1994; **28:** 572–6.
8. Stamatakis MK, *et al.* Stability of high-dose vancomycin and ceftazidime in peritoneal dialysis solutions. *Am J Health-Syst Pharm* 1999; **56:** 246–8.
9. Manduru M. *et al.* Stability of ceftazidime sodium and teicoplanin sodium in a peritoneal dialysis solution. *Am J Health-Syst Pharm* 1996; **53:** 2731–4.
10. Pleasants RA, *et al.* Compatibility of ceftazidime and aminophylline admixtures for different methods of intravenous infusion. *Ann Pharmacother* 1992; **26:** 1221–6.
11. Lewis JD. El-Gendy A. Cephalosporin-pentamidine isethionate incompatibilities. *Am J Health-Syst Pharm* 1996; **53:** 1462–3.


**Stability.** References.


1. Richardson BL, *et al.* The pharmacy of ceftazidime. *J Antimicrob Chemother* 1981; **8** (suppl B): 233–6.
2. Brown AF, *et al.* Freeze thaw stability of ceftazidime. *Br J Parenter Ther* 1985; **6:** 43, 45, 50.
3. Walker SE, Dranitsaris G. Ceftazidime stability in normal saline and dextrose in water. *Can J Hosp Pharm* 1988; **41:** 65–6, 69–71.
4. Wade CS, *et al.* Stability of ceftazidime and amino acids in parenteral nutrient solutions. *Am J Hosp Pharm* 1991; **48:** 1515–19.
5. Stiles ML, *et al.* Stability of ceftazidime (with arginine) and of cefuroxime sodium in infusion-pump reservoirs. *Am J Hosp Pharm* 1992; **49:** 2761–4.
6. Stewart JT, *et al.* Stability of ceftazidime in plastic syringes and glass vials under various storage conditions. *Am J Hosp Pharm* 1992; **49:** 2765–8.
7. Nahata MC, *et al.* Stability of ceftazidime (with arginine) stored in plastic syringes at three temperatures. *Am J Hosp Pharm* 1992; **49:** 2954–6.
8. Bednar DA, *et al.* Stability of ceftazidime (with arginine) in an elastomeric infusion device. *Am J Health-Syst Pharm* 1995; **52:** 1912–14.
9. van Doorne H, *et al.* Ceftazidime degradation rates for predicting stability in a portable infusion-pump reservoir. *Am J Health-Syst Pharm* 1996; **53:** 1302–5.
10. Stendal TL, *et al.* Drug stability and pyridine generation in ceftazidime injection stored in an elastomeric infusion device. *Am J Health-Syst Pharm* 1998; **55:** 683–5.
11. Servais H, Tulkens PM. Stability and compatibility of ceftazidime administered by continuous infusion to intensive care patients. *Antimicrob Agents Chemother* 2001; **45:** 2643–7.


### Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Like cefotaxime (p.228), ceftazidime has the potential for colonisation and superinfection with resistant organisms. The risk of superinfection with, for example, *Staphylococcus aureus* may be higher than with cefotaxime, since ceftazidime is less active against staphylococci.

**Breast feeding.** No adverse effects have been seen in breast-fed infants whose mothers were receiving ceftazidime, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.


1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)


**Effects on the blood.** References.


1. Hui CH, Chan LC. Agranulocytosis associated with cephalosporin. *BMJ* 1993; **307:** 484.


**Effects on the nervous system.** References.


1. Al-Zahawi MF, *et al.* Hallucinations in association with ceftazidime. *BMJ* 1988; **297:** 858.
2. Jackson GD, Berkovic SF. Ceftazidime encephalopathy: absence status and toxic hallucinations. *J Neurol Neurosurg Psychiatry* 1992; **55:** 333–4.
3. Chow KM, *et al.* Retrospective review of neurotoxicity induced by cefepime and ceftazidime. *Pharmacotherapy* 2003; **23:** 369–73.


**Effects on the skin.** References.


1. Vinks SATMM, *et al.* Photosensitivity due to ambulatory intravenous ceftazidime in cystic fibrosis patient. *Lancet* 1993; **341:** 1221–2.


### Interactions

Unlike many other cephalosporins, probenecid has little effect on the renal clearance of ceftazidime.

◊ References.


1. Verhagen CA, *et al.* The renal clearance of cefuroxime and ceftazidime and the effect of probenecid on their tubular excretion. *Br J Clin Pharmacol* 1994; **37:** 193–7.


### Antimicrobial Action

Ceftazidime has a bactericidal action and broad spectrum of activity similar to that of cefotaxime (p.228), but increased activity against *Pseudomonas* spp.; it is less active against staphylococci and streptococci. Unlike cefotaxime it has no active metabolite.

Ceftazidime is highly stable to hydrolysis by most beta-lactamases. It is active *in vitro* against many Gram-negative bacteria including *Pseudomonas aeruginosa*, *Burkholderia pseudomallei* (*Pseudomonas pseudomallei*), and Enterobacteriaceae including *Citrobacter* and *Enterobacter* spp., *Escherichia coli*, *Klebsiella* spp., both indole-positive and indole-negative *Proteus*, *Providencia*, *Salmonella*, *Serratia*, and *Shigella* spp. and *Yersinia enterocolitica*. Other susceptible Gram-negative bacteria include *Haemophilus influenzae*, *Moraxella catarrhalis* (*Branhamella catarrhalis*), and *Neisseria* spp. Among Gram-positive bacteria it is active against some staphylococci and streptococci, but meticillin-resistant staphylococci, enterococci, and *Listeria monocytogenes* are generally resistant. Ceftazidime is active against some anaerobes, although most strains of *Bacteroides fragilis* and *Clostridium difficile* are resistant.

The activity of ceftazidime against *Ps. aeruginosa* and some Enterobacteriaceae may be enhanced by aminoglycosides. Antagonism has been reported *in vitro* between ceftazidime and chloramphenicol.

*Resistance.* As with cefotaxime, resistance may develop during treatment due to the derepression of chromosomally mediated beta-lactamases. It has been noted particularly in *Pseudomonas* spp. and in Enterobacteriaceae including *Citrobacter*, *Enterobacter* spp. and *Proteus vulgaris*. Resistance may also occur due to the production of plasmid-mediated extended-spectrum beta-lactamases, particularly in *Klebsiella* spp. and *E. coli*.

### Pharmacokinetics

Ceftazidime is given by injection as the sodium salt or in solution with arginine. Mean peak plasma concentrations of 17 and 39 micrograms/mL have been reported about 1 hour after intramuscular doses of 0.5 and 1 g of ceftazidime, respectively. Five minutes after intravenous bolus injections of 0.5, 1, and 2 g of ceftazidime, mean plasma concentrations of 45, 90, and 170 micrograms/mL, respectively, have been reported. The plasma half-life of ceftazidime is about 2 hours, but this is prolonged in patients with renal impairment and in neonates. Clearance may be enhanced in patients with cystic fibrosis. It is about 10% bound to plasma proteins.

Ceftazidime is widely distributed in body tissues and fluids; therapeutic concentrations are achieved in the CSF when the meninges are inflamed. It crosses the placenta and is distributed into breast milk.

Ceftazidime is passively excreted in bile, although only a small proportion is eliminated by this route. It is mainly excreted by the kidneys, almost exclusively by glomerular filtration; probenecid has little effect on the excretion. About 80 to 90% of a dose appears un-