Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Cefrom; ***Austria:*** Cedixen; Cefrom; ***Belg.:*** Cefrom†; ***Cz.:*** Cefrom†; ***Fr.:*** Cefrom; ***Gr.:*** Cefrom†; ***India:*** Bacirom†; Ceforth†; Cefrom; Tafrom; ***Indon.:*** Cefir; Cefnos; Cefrin; Cefrom; Lanpirome; Nufirom; Romicef; Sopirom; Xenoprom; ***Irl.:*** Cefrom†; ***Mex.:*** Cefrom; ***Neth.:*** Cefrom; ***NZ:*** Cefrom†; ***Port.:*** Cefrom†; Cipiram; Farmocefe; ***S.Afr.:*** Cefrom; ***Thai.:*** Cefrom; ***UK:*** Cefrom†.

Cefpodoxime Proxetil

(BANM, USAN, rINNM)

Cefpodoxima proxetilo; Cefpodoxime proxétil; Cefpodoxime, Proxétil de; Cefpodoximi Proxetilum; Cefpodoximum proxetili; CS-807; R-3763 (cefpodoxime); U-76252; U-76253 (cefpodoxime). The 1-[(isopropoxycarbonyl)oxy]ethyl ester of (*Z*)-7-[2-(2-amino-1,3-thiazol-4-yl)-2-methoxyiminoacetamido]-3-methoxymethyl-3-cephem-4-carboxylic acid.

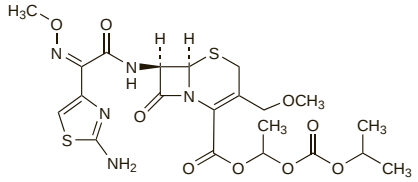
Цефподоксима Проксетил

$C_{21}H_{27}N_5O_9S_2$ = 557.6.

CAS — 80210-62-4 (cefpodoxime); 87239-81-4 (cefpodoxime proxetil).

ATC — J01DD13.

ATC Vet — QJ01DD13.



Pharmacopoeias. In *Jpn* and *US.*

USP 31 (Cefpodoxime Proxetil). A white to light brownish-white powder, odourless or having a faint odour. Very slightly soluble in water; freely soluble in dehydrated alcohol; soluble in acetonitrile and in methyl alcohol; slightly soluble in ether. Store in airtight containers at a temperature not exceeding 25°.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

The most frequently reported adverse effects of cefpodoxime are gastrointestinal disturbances, especially diarrhoea.

Interactions

Absorption of cefpodoxime is decreased by antacids or histamine H_2-receptor antagonists. Probenecid reduces the renal excretion of cefpodoxime.

Antimicrobial Action

As for Cefixime, p.224, but cefpodoxime has greater activity against *Staphylococcus aureus*.

◊ References.

1. Valentini S, *et al.* In-vitro evaluation of cefpodoxime. *J Antimicrob Chemother* 1994; **33:** 495–508.

Pharmacokinetics

Cefpodoxime proxetil is de-esterified in the intestinal epithelium after oral doses, to release active cefpodoxime in the bloodstream. Bioavailability is about 50% in fasting subjects and may be increased in the presence of food. Absorption is decreased in conditions of low gastric acidity. Peak plasma concentrations of about 1.5, 2.5, and 4.0 micrograms/mL have been achieved 2 to 3 hours after oral doses of 100, 200, and 400 mg cefpodoxime respectively. About 20 to 30% of cefpodoxime is bound to plasma proteins. The plasma half-life is about 2 to 3 hours and is prolonged in patients with renal impairment.

Cefpodoxime reaches therapeutic concentrations in the respiratory and genito-urinary tracts and bile. It has been detected in low concentrations in breast milk.

Cefpodoxime is excreted unchanged in the urine. Some is removed by dialysis.

Uses and Administration

Cefpodoxime is a third-generation cephalosporin antibiotic used similarly to cefixime (p.225) in the treatment of susceptible infections. It is given orally as the proxetil ester, which is hydrolysed on absorption to cefpodoxime. Doses are expressed in terms of the equivalent amount of cefpodoxime; 130 mg of cefpodoxime proxetil is equivalent to about 100 mg of cefpodoxime. Absorption may be enhanced if cefpodoxime proxetil is given with food. The usual dose for adults is 100 to 200 mg every 12 hours for respiratory-tract and urinary-tract infections. A dose of 200 or 400 mg every 12 hours may be used for skin and soft-tissue infections. In the USA children aged 2 months and older may be given doses of 5 mg/kg every 12 hours, up to a maximum of 200 mg daily for pharyngitis or tonsillitis or 400 mg daily for acute otitis media or maxillary sinusitis. In the UK cefpodoxime may be given to children and infants aged 15 days and older, in a dose of 4 mg/kg every 12 hours, up to a maximum of 200 mg daily, for infections of the respiratory tract, urinary tract, and skin and soft tissues.

The interval between doses of cefpodoxime may need to be extended in patients with renal impairment (see below).

For uncomplicated gonorrhoea, a single dose of 200 mg may be given.

◊ References.

1. Moore EP, *et al.*, eds. Cefpodoxime proxetil: a third-generation oral cephalosporin. *J Antimicrob Chemother* 1990; **26** (suppl E): 1–101.
2. Adam D, *et al.*, eds. Cefpodoxime proxetil: a new third generation oral cephalosporin. *Drugs* 1991; **42** (suppl 3): 1–66.
3. Frampton JE, *et al.* Cefpodoxime proxetil: a review of its antibacterial activity, pharmacokinetic properties and therapeutic potential. *Drugs* 1992; **44:** 889–917.
4. Chocas EC, *et al.* Cefpodoxime proxetil: a new, broad-spectrum, oral cephalosporin. *Ann Pharmacother* 1993; **27:** 1369–77.
5. Fulton B, Perry CM. Cefpodoxime proxetil: a review of its use in the management of bacterial infections in paediatric patients. *Paediatr Drugs* 2001; **3:** 137–58.

Administration in renal impairment. The interval between doses of cefpodoxime should be extended in patients with renal impairment to every 24 hours in those with creatinine clearance of 10 to 39 mL/minute, and to every 48 hours when the creatinine clearance is less than 10 mL/minute. In patients on haemodialysis the dose should be given after each dialysis session.

Preparations

USP 31: Cefpodoxime Proxetil for Oral Suspension; Cefpodoxime Proxetil Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Biocef; Celiol; Cintalux; Otreon; ***Braz.:*** Orelox; ***Chile:*** Cefirax; ***Cz.:*** Orelox†; ***Fr.:*** Orelox; ***Ger.:*** Orelox; Podomexef; ***Hong Kong:*** Banan; ***India:*** Cefoprox; Cepodem; Kefpod; Monocef-O; Monotax-O; Tambac; ***Indon.:*** Banan; ***Irl.:*** Cefodox; ***Ital.:*** Cefodox; Orelox; Otreon; ***Jpn:*** Banan; ***Mex.:*** Orelox; ***Neth.:*** Orelox; Otreon; ***Philipp.:*** Banan; Zudem; ***Port.:*** Orelox; ***S.Afr.:*** Cepodem; Orelox; ***Spain:*** Garia; Instana; Kelbium; Otreon; ***Swed.:*** Orelox; ***Switz.:*** Orelox; Podomexef; ***Thai.:*** Banan; ***UK:*** Orelox; ***USA:*** Vantin.

Cefprozil *(BAN, USAN, rINN)*

BMY-28100-03-800; BMY-28100 (*cis*-isomer); BMY-28167 (*trans*-isomer); Cefprozilo; Cefprozilum; Kefprotsiili; Sefprozil. (6*R*,7*R*)-7-[(*R*)-2-Amino-2-(*p*-hydroxyphenyl)acetamido]-8-oxo-3-(1-propenyl)-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate; 7-(D-4-Hydroxyphenylglycylamino)-3-[(*E*)prop-1-enyl]cephem-4-carboxylic acid monohydrate.

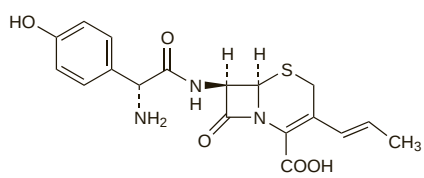
Цефпрозил

$C_{18}H_{19}N_3O_5S,H_2O$ = 407.4.

CAS — 92665-29-7 (anhydrous cefprozil); 121123-17-9 (cefprozil monohydrate).

ATC — J01DC10.

ATC Vet — QJ01DC10.



Pharmacopoeias. In *US.*

USP 31 (Cefprozil). pH of a 0.5% solution in water is between 3.5 and 6.5. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalexin, p.218.

Breast feeding. A study[1] in 9 healthy women found that concentrations of cefprozil in breast milk corresponded to no more than 0.3% of a dose and concluded that cefprozil could be given safely during breast feeding. The American Academy of Pediatrics[2] states that there have been no reports of any clinical effect on the infant associated with the use of cefprozil in breast-feeding mothers, and that it may be considered to be usually compatible with breast feeding.

1. Shyu WC, *et al.* Excretion of cefprozil into human breast milk. *Antimicrob Agents Chemother* 1992; **36:** 938–41.
2. 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)

Hypersensitivity. Serum sickness-like reactions were reported in 4 patients, 3 of them children, given cefprozil.[1] Such reactions have been associated with cefaclor (p.217), but whether they represent a class-related hypersensitivity reaction is not clear.

1. Lowery N, *et al.* Serum sickness-like reactions associated with cefprozil therapy. *J Pediatr* 1994; **125:** 325–8.

Interactions

As for Cefalexin, p.218.

Antimicrobial Action

Cefprozil is bactericidal and has a similar but wider range of antimicrobial activity than cefaclor (p.217).

Pharmacokinetics

Cefprozil is well absorbed from the gastrointestinal tract with a reported bioavailability of 90 to 95%. Oral doses of 0.25, 0.5, and 1 g produce peak plasma concentrations of about 6, 10, and 18 micrograms/mL respectively at 1 to 2 hours. The presence of food is reported to have little or no effect on the absorption of cefprozil. A plasma half-life of 1 to 1.4 hours has been reported; it is increased in patients with renal impairment, up to about 6 hours in those with end-stage renal failure. About 35 to 45% of cefprozil is bound to plasma proteins.

Cefprozil is widely distributed in the body tissues. Concentrations of cefprozil in tonsillar and adenoidal tissue are reported to be about 40 to 50% of those in plasma, and less than 0.3% of a 1-g dose has been recovered in breast milk in 24 hours. About 60% of a dose is excreted unchanged in the urine in the first 8 hours by glomerular filtration and tubular secretion. High concentrations of cefprozil are achieved in the urine; concentrations of 700, 1000, and 2900 micrograms/mL have been reported within 4 hours of doses of 0.25, 0.5, and 1 g respectively. Some cefprozil is removed by haemodialysis.

Uses and Administration

Cefprozil is a cephalosporin antibacterial consisting of *cis*- and *trans*- isomers in a ratio of about 90:10. It is used similarly to cefaclor (p.217) in the treatment of susceptible infections, including upper and lower respiratory-tract infections and skin and soft-tissue infections, and should probably be classified as a second-generation cephalosporin.

Cefprozil is given orally as the monohydrate. Doses are expressed in terms of the equivalent amount of anhydrous cefprozil; 523 mg of cefprozil monohydrate is equivalent to about 500 mg of anhydrous cefprozil. The usual adult dose is 500 mg daily (as a single dose or in two divided doses), increased to 500 mg twice daily if necessary. Children may be given up to 20 mg/kg once or twice daily (to a maximum of 500 mg once daily, or twice daily if necessary for otitis media).

For details of reduced dosage of cefprozil in patients with renal impairment, see below.

◊ Reviews.

1. Wiseman LR, Benfield P. Cefprozil: a review of its antibacterial activity, pharmacokinetic properties, and therapeutic potential. *Drugs* 1993; **45:** 295–317.
2. Barriere SL. Review of in vitro activity, pharmacokinetic characteristics, safety, and clinical efficacy of cefprozil, a new oral cephalosporin. *Ann Pharmacother* 1993; **27:** 1082–9.

Administration in renal impairment. Doses of cefprozil should be reduced in patients with renal impairment; half the standard dose should be given to patients with a creatinine clearance of less than 30 mL/minute.

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.

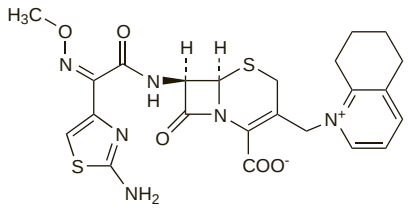
Cefquinome Sulfate *(USAN, rINNM)*

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.

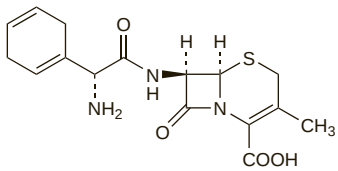
Цефрадин

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

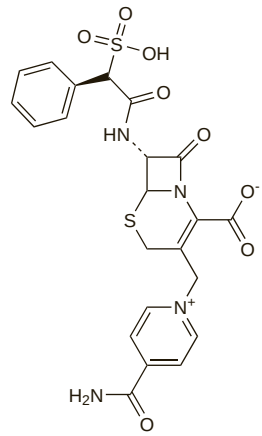
Натрий Цефсулодин

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