urinary-tract infections. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Administration and dosage. Cefoxitin is given as the sodium salt by deep intramuscular injection, by slow intravenous injection over 3 to 5 minutes, or by intermittent or continuous intravenous infusion.

Doses are expressed in terms of the equivalent amount of cefoxitin; 1.05 g of cefoxitin sodium is equivalent to about 1 g of cefoxitin. The usual adult dose is 1 or 2 g every 8 hours although it may be given more frequently (every 4 or 6 hours). In severe infections up to 12 g daily has been recommended. Children and neonates may be given 20 to 40 mg/kg, every 12 hours for neonates up to 1 week old, every 8 hours for those aged 1 to 4 weeks, and every 6 to 8 hours for older infants and children; in severe infections, up to 200 mg/kg daily may be given, to a maximum of 12 g daily.

For the treatment of uncomplicated urinary-tract infections, cefoxitin 1 g twice daily has been given intramuscularly.

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

For the treatment of uncomplicated gonorrhoea, a single dose of 2 g intramuscularly has been given with probenecid 1 g orally.

For surgical infection prophylaxis, the usual adult dose is cefoxitin 2 g intramuscularly or intravenously 30 to 60 minutes before the procedure and then every 6 hours, not usually for more than 24 hours. Infants and children undergoing surgical procedures can be given doses of 30 to 40 mg/kg, at the same time intervals as adults; neonates may be given 30 to 40 mg/kg, but at intervals of 8 to 12 hours.

At caesarean section a single 2-g dose may be given intravenously to the mother as soon as the umbilical cord is clamped. If necessary, a 3-dose regimen, with further 2-g doses 4 and 8 hours after the initial dose, may be used.

◊ Reviews.

1. DiPiro JT, May JR. Use of cephalosporins with enhanced antianaerobic activity for treatment and prevention of anaerobic and mixed infections. *Clin Pharm* 1988; **7:** 285–302.
2. Goodwin CS. Cefoxitin 20 years on: is it still useful? *Rev Med Microbiol* 1995; **6:** 146–53.

Administration in renal impairment. In renal impairment, dosage of cefoxitin should be reduced according to creatinine clearance (CC). After an initial loading dose of 1 to 2 g, maintenance doses are:

- CC 30 to 50 mL/minute: 1 to 2 g every 8 to 12 hours
- CC 10 to 29 mL/minute: 1 to 2 g every 12 to 24 hours
- CC 5 to 9 mL/minute: 0.5 to 1 g every 12 to 24 hours
- CC below 5 mL/minute: 0.5 to 1 g every 24 to 48 hours

In patients undergoing haemodialysis, the loading dose should be repeated after each dialysis session.

Preparations

BP 2008: Cefoxitin Injection;
USP 31: Cefoxitin for Injection; Cefoxitin Injection.

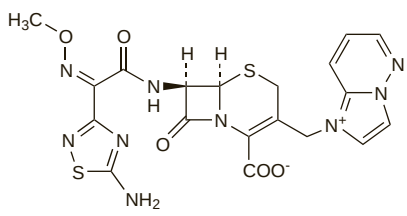
Proprietary Preparations (details are given in Part 3)
Arg.: Mefoxin†; Pluricefo†; ***Austral.:*** Mefoxin; ***Austria:*** Mefoxitin; ***Belg.:*** Mefoxin†; ***Braz.:*** Cefoxan; Cefoxin; Cefton; Foxtil†; Gamacef; Mefoxin; Propoten†; ***Canad.:*** Mefoxin†; ***Cz.:*** Mefoxin†; ***Fin.:*** Mefoxin†; ***Fr.:*** Mefoxin†; ***Ger.:*** Mefoxitin; ***Gr.:*** Destrepen†; Mefoxil; Metaptyl; ***Hong Kong:*** Mefoxin; ***Ital.:*** Cefociclin; Mefoxin; Tifox†; ***Neth.:*** Mefoxin†; ***Norw.:*** Mefoxitin†; ***NZ:*** Mefoxin; ***Philipp.:*** Monowel; Panafox; Zepax; ***Port.:*** Atralxitina; Mefoxin†; Niacef; ***S.Afr.:*** Mefoxin; ***Spain:*** Mefoxitin†; ***Swed.:*** Mefoxitin†; ***Switz.:*** Mefoxitin†; ***Thai.:*** Cefoxin; Cefxitin; Maxotin; Zefin; ***UK:*** Mefoxin†; ***USA:*** Mefoxin; ***Venez.:*** Mefoxitin†.

Cefozopran Hydrochloride *(rINNM)*

Céfozopran, Chlorhydrate de; Cefozoprani Hydrochloridum; Hidrocloruro de cefozoprán. (–)-1-{[(6*R*,7*R*)-7-[2-(5-Amino-1,2,4-thiadiazol-3-yl)glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl}-1*H*-imidazo[1,2-*b*]pyridazin-4-ium hydroxide inner salt, 7²-(*Z*)-(*O*-methyloxime), hydrochloride.

Цефозопрана Гидрохлорид

$C_{19}H_{17}N_9O_5S_2,HCl$ = 552.0.
CAS — 113359-04-9 (cefozopran); 113981-44-5 (cefozopran hydrochloride).



(cefozopran)

Pharmacopoeias. In *Jpn.*

Profile
Cefozopran is a cephalosporin antibacterial used parenterally as the hydrochloride.

◊ References.

1. Iwahi T, *et al.* In vitro and in vivo activities of SCE-2787, a new parenteral cephalosporin with a broad antibacterial spectrum. *Antimicrob Agents Chemother* 1992; **36:** 1358–66.
2. Paulfeuerborn W, *et al.* Comparative pharmacokinetics and serum bactericidal activities of SCE-2787 and ceftazidime. *Antimicrob Agents Chemother* 1993; **37:** 1835–41.
3. Fujii R, *et al.* Pharmacokinetics and clinical effects of cefozopran in pediatric patients. *Jpn J Antibiot* 1996; **49:** 17–33.

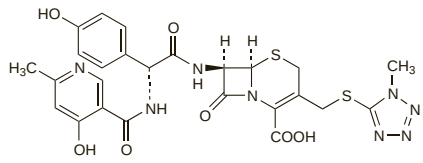
Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Firstcin.

Cefpiramide *(USAN, rINN)*

Cefpiramida; Cefpiramidum; SM-1652; Wy-44635. (7*R*)-7-[(*R*)-2-(4-Hydroxy-6-methylnicotinamido)-2-(4-hydroxyphenyl)acetamido]-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid.

Цефпирамид

$C_{25}H_{24}N_8O_7S_2$ = 612.6.
CAS — 70797-11-4.
ATC — J01DD11.
ATC Vet — QJ01DD11.



Pharmacopoeias. In *US.*
USP 31 (Cefpiramide). Store in airtight containers. pH of a 0.5% suspension in water is between 3.0 and 5.0.

Cefpiramide Sodium *(USAN, rINNM)*

Cefpiramida sódica; Cefpiramide Sodique; Natrii Cefpiramidum.

Натрий Цефпирамид

$C_{25}H_{23}N_8NaO_7S_2$ = 634.6.
CAS — 74849-93-7.
ATC — J01DD11.
ATC Vet — QJ01DD11.

Pharmacopoeias. In *Jpn.*

Profile
Cefpiramide is a third-generation cephalosporin antibacterial related to cefoperazone (p.227) and with similar activity against *Pseudomonas aeruginosa*, but possibly less active against Enterobacteriaceae. Cefpiramide is also active against staphylococci and streptococci and marginal activity against enterococci *in vitro* has been reported. Like cefamandole (p.220), cefpiramide contains an *N*-methylthiotetrazole side-chain, a structure associated with hypoprothrombinaemia, alcohol intolerance, and potentiation of anticoagulants.

Cefpiramide is given by intravenous injection or infusion as the sodium salt in the treatment of susceptible infections but doses are expressed in terms of cefpiramide; 1.04 g of cefpiramide sodium is equivalent to about 1 g of cefpiramide. The usual dose is 1 to 2 g daily in 2 divided doses.

◊ References.

1. Wang H, *et al.* In-vitro antibacterial activities of cefpiramide and other broad-spectrum antibiotics against 440 clinical isolates in China. *J Infect Chemother* 2000; **6:** 81–5.

Sodium content. Each g of cefpiramide sodium contains about 1.6 mmol of sodium.

Preparations
USP 31: Cefpiramide for Injection.

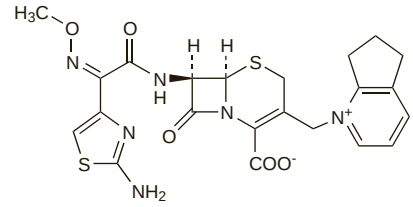
Proprietary Preparations (details are given in Part 3)
Jpn: Sepatren.

Cefpirome Sulfate *(USAN, rINNM)*

Cefpirome, sulfate de; Cefpirome Sulphate *(BANM)*; Cefpiromi sulfas; Cefpiromsulfat; HR-810 (cefpirome or cefpirome sulfate); Kefpiromisulfaatti; Sulfato de cefpiroma. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(1-pyrindiniomethyl)-3-cephem-4-carboxylate sulphate.

Цефпирома Сульфат

$C_{22}H_{22}N_6O_5S_2,H_2SO_4$ = 612.7.
CAS — 84957-29-9 (cefpirome); 98753-19-6 (cefpirome sulfate).
ATC — J01DE02.
ATC Vet — QJ01DE02.



(cefpirome)

Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions
As for Cefalotin, p.219.

Cefpirome is reported to interfere with the Jaffé method of measuring creatinine concentrations to determine renal function.

◊ References.

1. Rubinstein E, *et al.* A review of the adverse events profile of cefpirome. *Drug Safety* 1993; **9:** 340–5.

Interactions
Probenecid reduces the renal clearance of cefpirome.

Antimicrobial Action
Cefpirome is a fourth-generation cephalosporin that is stable to a wide range of beta-lactamases. It has a spectrum of activity similar to that of the third-generation cephalosporin cefotaxime (p.228), but it appears to be more active *in vitro* against staphylococci, some enterococci, some Enterobacteriaceae, and *Pseudomonas aeruginosa*. Cefpirome may be less active than ceftazidime (p.234) against *Ps. aeruginosa*.

Pharmacokinetics
Cefpirome is given by injection as the sulfate. Mean peak serum concentrations of 80 to 90 micrograms/mL are attained after a single intravenous 1-g dose. The elimination half-life is about 2 hours and is prolonged in patients with renal impairment. Cefpirome is less than 10% bound to plasma proteins.

Cefpirome is widely distributed into body tissues and fluids and appears in breast milk. It is mainly excreted by the kidneys and 80 to 90% of a dose is recovered unchanged in the urine. Significant amounts are removed by haemodialysis.

Uses and Administration
Cefpirome is a fourth-generation cephalosporin antibacterial used in the treatment of infections due to susceptible organisms. They include infections of the urinary tract, respiratory tract, and skin, and also septicaemia and infections in immunocompromised patients. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Cefpirome is given by intravenous injection over 3 to 5 minutes or infusion over 20 to 30 minutes as the sulfate, but doses are expressed in terms of the base; 1.19 g of cefpirome sulfate is equivalent to about 1 g of cefpirome. The usual dose is the equivalent of 1 or 2 g of cefpirome every 12 hours. For details of reduced doses to be used in renal impairment, see below.

◊ References.

1. Brown EM, *et al.* eds. Cefpirome: a novel extended spectrum cephalosporin. *J Antimicrob Chemother* 1992; **29** (suppl A): 1–104.
2. Wiseman LR, Lamb HM. Cefpirome: a review of its antibacterial activity, pharmacokinetic properties and clinical efficacy in the treatment of severe nosocomial infections and febrile neutropenia. *Drugs* 1997; **54:** 117–40.

Administration in renal impairment. Dosage of cefpirome should be modified in renal impairment; after a loading dose of 1 or 2 g depending on the severity of infection, the maintenance dosage should be adjusted according to creatinine clearance (CC) and the severity of infection:

- CC 20 to 50 mL/minute: 0.5 or 1 g twice daily
- CC 5 to 20 mL/minute: 0.5 or 1 g once daily
- CC 5 mL/minute or less (in haemodialysis patients): 0.5 or 1 g once daily plus a half-dose after each dialysis session.

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.

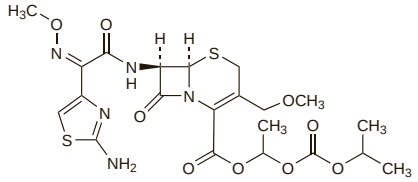
Цефподоксима Проксетил

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

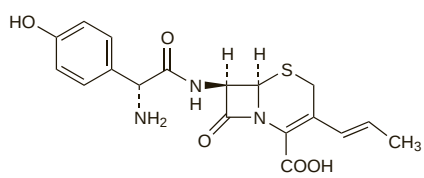
Цефпрозил

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