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.

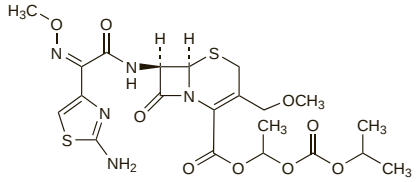
Цефподоксима Проксетил

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

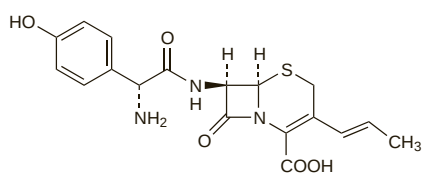
Цефпрозил

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