sensitive to cefixime but most strains of staphylococci, enterococci, and *Listeria* spp. are not.

Enterobacter spp., *Pseudomonas aeruginosa*, and *Bacteroides* spp. are resistant to cefixime.

Pharmacokinetics

Only 40 to 50% of an oral dose of cefixime is absorbed from the gastrointestinal tract, whether taken before or after meals, although the rate of absorption may be decreased in the presence of food. Cefixime is better absorbed from oral suspension than from tablets. Absorption is fairly slow; peak plasma concentrations of 2 to 3 micrograms/mL and 3.7 to 4.6 micrograms/mL have been reported between 2 and 6 hours after single doses of 200 and 400 mg, respectively. The plasma half-life is usually about 3 to 4 hours and may be prolonged when there is renal impairment. About 65% of cefixime is bound to plasma proteins.

Information on the distribution of cefixime in body tissues and fluids is limited. It crosses the placenta. Relatively high concentrations may be achieved in bile and urine. About 20% of an oral dose (or 50% of an absorbed dose) is excreted unchanged in the urine within 24 hours. Up to 60% may be eliminated by nonrenal mechanisms; there is no evidence of metabolism but some is probably excreted into the faeces from bile. It is not substantially removed by dialysis.

◊ References.

1. Brittain DC, *et al.* The pharmacokinetic and bactericidal characteristics of oral cefixime. *Clin Pharmacol Ther* 1985; **38:** 590–4.
2. Guay DRP, *et al.* Pharmacokinetics of cefixime (CL-284,635; FK027) in healthy subjects and patients with renal insufficiency. *Antimicrob Agents Chemother* 1986; **30:** 485–90.
3. Faulkner RD, *et al.* Pharmacokinetics of cefixime in the young and elderly. *J Antimicrob Chemother* 1988; **21:** 787–94.
4. Stone JW, *et al.* Cefixime, in-vitro activity, pharmacokinetics and tissue penetration. *J Antimicrob Chemother* 1989; **23:** 221–8.
5. Westphal JF, *et al.* Biliary excretion of cefixime: assessment in patients provided with T-tube drainage. *Antimicrob Agents Chemother* 1993; **37:** 1488–91.
6. Somekh E, *et al.* Penetration and bactericidal activity of cefixime in synovial fluid. *Antimicrob Agents Chemother* 1996; **40:** 1198–1200.

Uses and Administration

Cefixime is generally classified as a third-generation cephalosporin antibacterial and is given orally in the treatment of susceptible infections including gonorrhoea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Cefixime is available as the trihydrate and doses are expressed in terms of anhydrous cefixime; 1.12 g of cefixime trihydrate is equivalent to about 1 g of anhydrous cefixime. It is given orally in adult doses of 200 to 400 mg daily as a single dose or in two divided doses. Children over 6 months and under 50 kg may be given 8 mg/kg daily as an oral suspension, again as a single dose or in two divided doses. For details of reduced dosage of cefixime in patients with moderate to severe renal impairment, see below.

For uncomplicated gonorrhoea, a single oral dose of 400 mg is given.

◊ General references.

1. Leggett NJ, *et al.* Cefixime. *DICP Ann Pharmacother* 1990; **24:** 489–95.
2. Adam D, Wallace RJ, eds. Symposium on cefixime. *Drugs* 1991; **42** (suppl 4): 1–32.
3. Markham A, Brogden RN. Cefixime: a review of its therapeutic efficacy in lower respiratory tract infections. *Drugs* 1995; **49:** 1007–22.

Administration in renal impairment. Doses of cefixime should be reduced in patients with moderate to severe renal impairment. A dose of 200 mg daily should not be exceeded in patients with a creatinine clearance of less than 20 mL/minute.

Preparations

USP 31: Cefixime for Oral Suspension; Cefixime Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Cetaxim†; Novacef; Vixcef; ***Austria:*** Aerocef; Enzine; Exciol; Tricef; Xefotil; Xetinol; ***Braz.:*** Cefnax†; Neo Cefix; Plenax†; ***Canad.:*** Suprax; ***Chile:*** Cefspan†; Tricef; Urotricef; ***Cz.:*** Suprax; ***Fr.:*** Oroken; ***Ger.:*** Cefixdura; Cephoral; InfectoOpticef; Suprax; Uro-Cephoral; ***Gr.:*** Ceftoral; Covocef-N; ***Hung.:*** Suprax; ***India:*** Biotax-O; Cefix; Cefocef-LB; Fixx; Si-Fixim†; Xim; Ziprax; ***Indon.:*** Cefspan; Ceptik; Comsporin; Ethifix; Fixacep; Fixef; Fixiphar; Lanfix; Maxpro; Opixime; Simcef; Sofix; Spancef; Spaxim; Sporetik; Starcef; Tocef; ***Irl.:*** Suprax; ***Israel:*** Supran; ***Ital.:*** Cefixoral; Suprax; Unixime; ***Jpn:*** Cefspan; ***Malaysia:*** Minixime; ***Mex.:*** Denvar; Novaceft; ***Neth.:*** Fixim; ***Philipp.:*** Tergecef; Ultraxime; Zefral; ***Port.:*** Bonoceft; Cefimix; Cefiton; Cefizel; Neocef; Tricef; ***Rus.:*** Suprax (Супракс); ***S.Afr.:*** Fixime; ***Spain:*** Denvar; Necopen; ***Swed.:*** Tricef†; ***Switz.:*** Cephoral; ***Thai.:*** Cefspan; ***Turk.:*** Suprax; Zimaks; ***UK:*** Suprax; ***USA:*** Suprax; ***Venez.:*** Longacef.

Multi-ingredient: ***India:*** Cefix LB.

Cefmenoxime Hydrochloride *(USAN, rINNM)*

Abbott-50192; Cefménoxime, Chlorhydrate de; Cefmenoxime Hemihydrochloride; Cefmenoximi Hydrochloridum; Hidrocloruro de cefmenoxima; SCE-1365 (cefmenoxime). (*Z*)-(7*R*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-3-cephem-4-carboxylic acid hydrochloride.

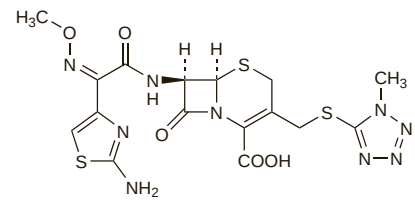
Цефменоксима Гидрохлорид

$(C_{16}H_{17}N_9O_5S_3)_2.HCl$ = 1059.6.

CAS — 65085-01-0 (cefmenoxime); 75738-58-8 (cefmenoxime hydrochloride).

ATC — J01DD05.

ATC Vet — QJ01DD05.



(cefmenoxime)

Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Cefmenoxime Hydrochloride). White to light orange-yellow crystals or crystalline powder. Very slightly soluble in water; practically insoluble in dehydrated alcohol and in ether; freely soluble in formamide; slightly soluble in methyl alcohol. Store in airtight containers.

Profile

Cefmenoxime is a third-generation cephalosporin antibacterial with actions and uses similar to those of cefotaxime (p.228). It has been given as the hydrochloride by intramuscular injection, or intravenously by injection or infusion in the treatment of susceptible infections.

Like cefamandole (p.220), cefmenoxime has an *N*-methylthiotetrazole side-chain and coagulopathy and a disulfiram-like interaction with alcohol have been reported rarely.

Cefmenoxime hydrochloride is also given as eye drops for the treatment of eye infections.

◊ Reviews.

1. Campoli-Richards DM, Todd PA. Cefmenoxime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1987; **34:** 188–221.

Preparations

USP 31: Cefmenoxime for Injection.

Proprietary Preparations (details are given in Part 3)

Gr.: Taceft†; ***Jpn:*** Bestcall; Bestron.

Cefmetazole *(USAN, rINN)*

Cefmetazol; Cefmétazole; Cefmetazolum; U-72791. (6*R*,7*S*)-7-{2-[(Cyanomethyl)thio]acetamido}-7-methoxy-3-{[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl}-8-oxo-5-thia-1-azabicyclo-[4.2.0]oct-2-ene-2-carboxylic acid.

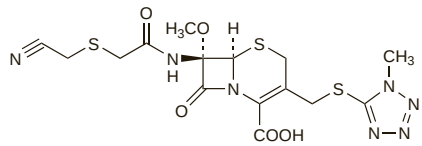
Цефметазол

$C_{15}H_{17}N_7O_5S_3$ = 471.5.

CAS — 56796-20-4.

ATC — J01DC09.

ATC Vet — QJ01DC09.



Pharmacopoeias. In *US*.

USP 31 (Cefmetazole). Store in airtight containers.

Cefmetazole Sodium *(USAN, rINNM)*

Cefmetazol sódico; Cefmétazole Sodique; Cefmetazolnatrium; Cefmetazolum Natricum; CS-1170; Kefmetatsolinatrium; Natrii Cefmetazolum; SKF-83088; U-72791A.

Натрий Цефметазол

$C_{15}H_{16}N_7NaO_5S_3$ = 493.5.

CAS — 56796-39-5.

ATC — J01DC09.

ATC Vet — QJ01DC09.

Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Cefmetazole Sodium). A white solid. Very soluble in water and in methyl alcohol; soluble in acetone; practically insoluble in chloroform. pH of a 10% solution in water is between 4.2 and 6.2. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Cefmetazole contains an *N*-methylthiotetrazole side-chain and has the potential to cause hypoprothrombinaemia and bleeding.

Effects on the blood. References.

1. Breen GA, St Peter WL. Hypoprothrombinemia associated with cefmetazole. *Ann Pharmacother* 1997; **31:** 180–4.

Sodium content. Each g of cefmetazole sodium contains about 2 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Antimicrobial Action

Cefmetazole is a cephamycin antibacterial with a similar spectrum of antibacterial activity to that of cefoxitin (p.230), including the anaerobe *Bacteroides fragilis*.

◊ References.

1. Cornick NA, *et al.* Activity of cefmetazole against anaerobic bacteria. *Antimicrob Agents Chemother* 1987; **31**: 2010–12.

Pharmacokinetics

After cefmetazole sodium 2 g intravenously every 6 hours, peak and trough plasma concentrations of 138 and 6 micrograms/mL have been achieved. Cefmetazole is 65 to 85% bound to plasma proteins, depending on the plasma concentration. A plasma half-life of about 1.1 to 1.5 hours has been reported; it is prolonged in patients with renal impairment. Small amounts have been detected in breast milk. Relatively high concentrations have been achieved in bile.

The majority of a dose is excreted unchanged in the urine resulting in high concentrations; up to 85% of a dose has been recovered within 12 hours. Cefmetazole is partly excreted by renal tubular secretion and probenecid prolongs elimination.

Cefmetazole is removed to some extent by haemodialysis.

Uses and Administration

Cefmetazole is a cephamycin antibacterial generally classified with the second-generation cephalosporins and used similarly to cefoxitin (p.230) in the treatment and prophylaxis of anaerobic and mixed bacterial infections, especially intra-abdominal and pelvic infections. It may also be used in the treatment of gonorrhoea. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Cefmetazole is given intravenously as the sodium salt by infusion over 10 to 60 minutes or by slow injection over 3 to 5 minutes. Cefmetazole sodium is also used intramuscularly in some countries. Doses are expressed in terms of the equivalent amount of cefmetazole; 1.05 g of cefmetazole sodium is equivalent to about 1 g of cefmetazole.

The usual dose is 0.5 to 1 g intramuscularly or intravenously every 12 hours. For severe infections the dose may be increased to 3 to 4 g daily, given in divided doses every 6 to 8 hours.

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

◊ References.

1. Finch R, *et al.* eds. Cefmetazole: a clinical appraisal. *J Antimicrob Chemother* 1989; **23** (suppl D): 1–142.

Administration in renal impairment. Doses of cefmetazole should be reduced in patients with renal impairment. It has been suggested that the interval between doses should be 12, 16, or 24 hours in patients with mild, moderate, or severe renal impairment, respectively; patients with virtually no renal function might be given cefmetazole every 48 hours, after haemodialysis.

Preparations

USP 31: Cefmetazole for Injection; Cefmetazole Injection.

Proprietary Preparations (details are given in Part 3)

Hong Kong: Cefmetazon†; ***Ital.:*** Metacaf†; Metafar; Metasal†; Metax; Metazol†; ***Jpn:*** Cefmetazon†; ***USA:*** Zefazone†.

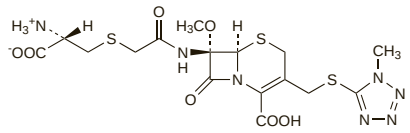
Cefminox Sodium *(pINNM)*

Cefminox sódico; Cefminox Sodique; MT-141; Natrii Cefminoxum. Sodium 7-{2-[(*S*)-2-amino-2-carboxyethyl]thioacetamido}-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylate.

Натрий Цефминокс

$C_{16}H_{20}N_7NaO_7S_3$ = 541.6.

CAS — 75481-73-1 (cefminox).



(cefminox)

Pharmacopoeias. *Jpn* includes the heptahydrate.

Profile

Cefminox sodium is a cephamycin antibacterial with properties similar to those of cefoxitin (p.230) but with an *N*-methylthiotetrazole side-chain like cefamandole (p.220). It is given intravenously as the sodium salt but doses are expressed in terms of cefminox; 1.04 g of cefminox sodium is equivalent to about 1 g of cefminox. A usual dose is 2 to 4 g daily given in divided doses.

◊ References.

1. Watanabe S, Omoto S. Pharmacology of cefminox, a new bactericidal cephamycin. *Drugs Exp Clin Res* 1990; **16:** 461–7.
2. Soriano F, *et al.* Comparative susceptibility of cefminox and cefoxitin to β-lactamases of Bacteroides spp. *J Antimicrob Chemother* 1991; **28:** 55–60.
3. Aguilar L, *et al.* Cefminox: correlation between in-vitro susceptibility and pharmacokinetics and serum bactericidal activity in healthy volunteers. *J Antimicrob Chemother* 1994; **33:** 91–101.
4. Mayama T, *et al.* Postmarketing surveillance on side-effects of cefminox sodium (Meicelin). *Int J Clin Pharmacol Ther* 1995; **33:** 149–55.
5. Hoellman DB, *et al.* In vitro activities of cefminox against anaerobic bacteria compared with those of nine other compounds. *Antimicrob Agents Chemother* 1998; **42:** 495–501.
6. Torres AJ, *et al.* Cefminox versus metronidazole plus gentamicin in intra-abdominal infections: a prospective randomized controlled clinical trial. *Infection* 2000; **28:** 318–22.

Sodium content. Each g of cefminox sodium contains about 1.84 mmol of sodium.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Meicelin; ***Port.:*** Tencef; ***Spain:*** Tencef; ***Thai.:*** Meicelin.

Cefodizime Sodium *(BANM, rINNM)*

Cefodizima sódica; Céfodizime Sodique; HR-221; Natrii Cefodizimum; S-771221B; Sefodizim Disodyum; THR-221; TRH-221. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(5-carboxymethyl-4-methylthiazol-2-ylthiomethyl)-3-cephem-4-carboxylic acid, disodium salt.

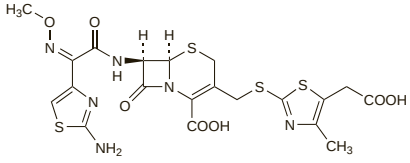
Натрий Цефодизим

$C_{20}H_{18}N_6Na_2O_7S_4$ = 628.6.

CAS — 69739-16-8 (cefodizime); 86329-79-5 (cefodizime sodium).

ATC — J01DD09.

ATC Vet — QJ01DD09.



(cefodizime)

Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

As for Cefotaxime, p.228.

Sodium content. Each g of cefodizime sodium contains about 3.2 mmol of sodium.

Interactions

Probenecid reduces the renal clearance of cefodizime.

Antimicrobial Action

Cefodizime has similar antimicrobial activity to that of cefotaxime (p.228) although cefodizime has no active metabolite. It has variable activity against *Citrobacter* spp., and *Pseudomonas aeruginosa* and *Bacteroides fragilis* are generally resistant.

Pharmacokinetics

Cefodizime is given by injection as the sodium salt. Intramuscular injection of 1 g cefodizime produces peak plasma concentrations of about 60 to 75 micrograms/mL at about 1 to 1.5 hours. Immediately after intravenous doses of 1 or 2 g cefodizime mean peak plasma concentrations of 215 and 394 micrograms/mL, respectively, have been achieved. Cefodizime is about 80% bound to plasma proteins and is widely distributed into body tissues and fluids. It crosses the placenta and small amounts have been detected in breast milk. Plasma elimination is reported to be triphasic with a terminal elimination half-life of about 4 hours. The half-life is prolonged by renal impairment.

The majority of a dose is excreted unchanged in the urine; up to 80% of a dose has been recovered within 24 hours. Cefodizime is mainly excreted by glomerular filtration with some tubular secretion. Probenecid delays excretion. Cefodizime is removed by dialysis.

Uses and Administration

Cefodizime is a third-generation cephalosporin antibacterial with uses similar to those of cefotaxime (p.229).

Cefodizime is given as the disodium salt by intramuscular injection or intravenously by injection or infusion in the treatment of susceptible infections. Doses are expressed in terms of the equivalent amount of cefodizime; 1.08 g of cefodizime sodium is equivalent to about 1 g of cefodizime. Adults are usually given 1 to 2 g every 12 or 24 hours for lower respiratory-tract infections and upper and lower urinary-tract infections. Doses up to 4 g daily may be given in severe infection. In women with uncomplicated lower urinary-tract infections a single dose of 1 to 2 g may be sufficient. For gonorrhoea a single dose of 0.25 to 0.5 g may be given. Doses may need to be reduced in patients with renal impairment (see below).

◊ References.

1. Finch RG, *et al.*, eds. Cefodizime: a third generation cephalosporin with immunomodulating properties. *J Antimicrob Chemother* 1990; **26** (suppl C): 1–134.
2. Barradell LB, Brogden RN. Cefodizime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1992; **44:** 800–834.
3. Thalhammer F, *et al.* Single-dose cefodizime as infection prophylaxis in abdominal surgery: a prospective multicenter study. *Infection* 1998; **26:** 136–8.
4. Matsumoto T, *et al.* Single dose of cefodizime completely eradicated multidrug-resistant strain of Neisseria gonorrhoeae in urethritis and uterine cervicitis. *J Infect Chemother* 2006; **12:** 97–9.
5. Matsumoto T, *et al.* Multiple doses of cefodizime are necessary for the treatment of Neisseria gonorrhoeae pharyngeal infection. *J Infect Chemother* 2006; **12:** 145–7.

Administration in renal impairment. Doses of cefodizime should be reduced in patients with renal impairment according to creatinine clearance (CC):

- CC 10 to 30 mL/minute: 1 to 2 g daily
- CC less than 10 mL/minute: 0.5 to 1 g daily

In patients undergoing dialysis, 0.5 to 1 g daily is given after dialysis.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Timecef; ***Ital.:*** Diezime; Modivid; Timecef; ***Jpn:*** Kenicef; ***Mex.:*** Modivid†; ***NZ:*** Timecef; ***Port.:*** Modivid; ***Turk.:*** Modivid.

Cefonicid Sodium *(BANM, USAN, rINNM)*

Cefonicid sódico; Cefonicide sodique; Céfonicide Sodique; Cefonicidum natricum; Natrii Cefonicidum; SKF-D-75073-Z_2; SKF-D-75073-Z (cefonicid monosodium). 7-[(*R*)-Mandelamido]-3-(1-sulphomethyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid, disodium salt.

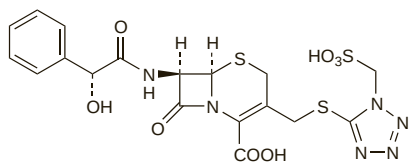
Натрий Цефоницид

$C_{18}H_{16}N_6Na_2O_8S_3$ = 586.5.

CAS — 61270-58-4 (cefonicid); 61270-78-8 (cefonicid disodium); 71420-79-6 (cefonicid monosodium).

ATC — J01DC06.

ATC Vet — QJ01DC06.



(cefonicid)

Pharmacopoeias. In *US.*

USP 31 (Cefonicid Sodium). A white to off-white solid. Freely soluble in water, in sodium chloride 0.9%, and in glucose 5%; very slightly soluble in dehydrated alcohol; soluble in methyl alcohol. pH of a 5% solution in water is between 3.5 and 6.5. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Cefonicid contains a substituted *N*-methylthiotetrazole side-chain, a structure associated with hypoprothrombinaemia.

Effects on the blood. References.

1. Riancho JA, *et al.* Life-threatening bleeding in a patient treated with cefonicid. *Ann Intern Med* 1995; **123:** 472–3.

Effects on the liver. References.

1. Famularo G, *et al.* Eosinophilic hepatitis associated with cefonicid therapy. *Ann Pharmacother* 2001; **35:** 1669–71.

Sodium content. Each g of cefonicid sodium contains about 3.4 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Antimicrobial Action

Cefonicid sodium has an antimicrobial action and pattern of resistance similar to those of cefamandole (p.221), although it is generally less active against Gram-positive cocci.

Pharmacokinetics

Cefonicid is given parenterally as the sodium salt. Peak plasma concentrations ranging from 67 to 126 micrograms/mL have been achieved 1 to 2 hours after a 1-g intramuscular dose. Cefonicid is more than 90% bound to plasma proteins. It has a plasma half-life of about 4.5 hours, which is prolonged in patients with renal impairment.

Therapeutic concentrations of cefonicid have been reported in a wide range of body tissues and fluids.

Up to 99% of a dose of cefonicid is excreted unchanged in the urine within 24 hours. Probenecid reduces excretion of cefonicid.

Uses and Administration

Cefonicid is a second-generation cephalosporin antibacterial used similarly to cefamandole (p.221) in the treatment of susceptible infections and for surgical infection prophylaxis.

It is given as the sodium salt by deep intramuscular injection, or intravenously by slow injection over 3 to 5 minutes or by infusion. Doses are expressed in terms of the equivalent amount of cefonicid; 1.08 g of cefonicid sodium is equivalent to about 1 g of cefonicid. The usual dose is cefonicid 1 g once daily. For uncomplicated urinary-tract infections, a dose of 500 mg once daily is recommended; up to 2 g once daily has been given in severe infections. More than 1 g should not be injected intramuscularly into a single site.

For surgical infection prophylaxis, a single dose of 1 g given 1 hour before surgical incision is usually sufficient, but may be given daily for a further 2 days in prosthetic arthroplasty or open-heart surgery.

◊ References.

1. Saltiel E, Brogden RN. Cefonicid: a review of its antibacterial activity, pharmacological properties and therapeutic use. *Drugs* 1986; **32:** 222–59.

Administration in renal impairment. For patients with renal impairment a loading dose equivalent to cefonicid 7.5 mg/kg is recommended, followed by reduced maintenance doses according to the creatinine clearance and the severity of the infection. A dose supplement is not required after dialysis.

Preparations

USP 31: Cefonicid for Injection.

Proprietary Preparations (details are given in Part 3)
Belg.: Monocid†; ***Israel:*** Monocef; ***Ital.:*** Abiocef†; Auricid†; Bacid†; Biocil; Bioticic; Cefobacter; Cefodie; Cefoger†; Cefok; Cefoplus; Cefosporin†; Chefir; Clastidin†; Daycef; Delsacid†; Diespor; Emidoxin; Epicef†; Fonexel†; Fonicef†; Fonicid; Fonisal†; Framecef; Ipacid†; Krucef; Lampocef†; Lisa; Maxid; Microcid†; Modicef; Modiem; Monobios; Monobiotic; Monocid†; Necid; Nokid; Pantacid†; Parecid; Praticef; Raikocef; Renbiocid†; Rocid†; Silverce†; Sintocef; Sofarcid; Unicid†; Valecid; ***Port.:*** Monocid; ***Spain:*** Monocid; Unidie; ***USA:*** Monocid†.