otic; Ceclor; Cloracef; Especlor; Forifek; Medikoncef; Soclor; ***Irl.:*** Cefager; Distaclor; Keftid; Pinaclor; ***Israel:*** Ceclor†; Cefalor; ***Ital.:*** Altaclor; Bacticef; Bactigram; Cefulton; Citiclor†; Clorad; Clorazer; Dorf; Erreclor†; Eurocefix†; Fuclode†; Geniclor; Kliacef; Lafarclor; Macovan; Necloral; Omaspir; Oralcef; Panacef; Performer; Selanir†; Selviclor; Takecef; Tibifor; Valeclor; ***Malaysia:*** Distaclor†; Sifaclor; Soficlor†; Vercef; ***Mex.:*** Arcefal; Cec; Ceclor; Cefalan; Ceflacid; Fasiclor; Fermed; Ranclor; Serviclor; Teraclox; ***Neth.:*** Ceclor; ***NZ:*** Clorotir; ***Philipp.:*** Aczebri; Brelox; Ceclobid; Ceclor; Clorotir; Ephron; Lorcef; Vefarol; Versef; Verzat; Xelent; Xeztron; ***Pol.:*** Ceclor; Cek; Kloracef†; Panclor; Serviclor; Vercef; ***Port.:*** Ceclor; ***Rus.:*** Ceclor (Цеклор); Vercef (Верцеф); ***S.Afr.:*** Cec; Ceclor†; CloraCEF†; Vercef; ***Singapore:*** Cleancef; Distaclor†; Soficlor; Vercef; ***Spain:*** Ceclor; ***Switz.:*** Ceclor; ***Thai.:*** Celco; Clorotir; Distaclor; Kefaclor†; Sifaclor; Tefaclor†; Vercef; ***Turk.:*** Ceclor; Kefsid; Losefar; ***UAE:*** Recocef; ***UK:*** Bacticlor; Distaclor; Keftid; ***USA:*** Ceclor; Raniclor; ***Venez.:*** Ceclor.

Multi-ingredient: *Mex.:* Ceclordox.

Cefadroxil *(BAN, USAN, pINN)*

BL-S578; Cefadroksilis monohidratas; Cefadroksyl jednowodny; Céfadroxil; Cefadroxil monohydrát; Céfadroxil monohydraté; Cefadroxilmonohydrat; Cefadroxilo; Cefadroxilum; Cefadroxilum monohydricum; Cephadroxil; Kefadroksiili; Kefadroksiilimonohydraatti; MJF-11567-3; Sefadroksil. (7*R*)-7-(α-D-4-Hydroxyphenylglycylamino)-3-methyl-3-cephem-4-carboxylic acid monohydrate.

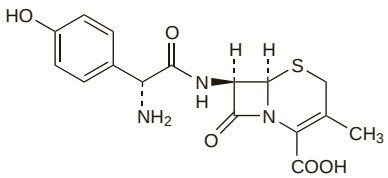
Цефадроксил

$C_{16}H_{17}N_3O_5S,H_2O$ = 381.4.

CAS — 50370-12-2 (anhydrous cefadroxil); 119922-85-9 (cefadroxil hemihydrate); 66592-87-8 (cefadroxil monohydrate).

ATC — J01DB05.

ATC Vet — QJ01DB05.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*. *Jpn* includes the anhydrous substance.

Ph. Eur. 6.2 (Cefadroxil Monohydrate). A white or almost white powder. Slightly soluble in water; very slightly soluble in alcohol. A 5% suspension in water has a pH of 4.0 to 6.0. Protect from light.

USP 31 (Cefadroxil). A white to off-white crystalline powder. Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a 5% suspension in water is between 4.0 and 6.0. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalexin, p.218.

Breast feeding. Although higher concentrations of cefadroxil were reported in breast milk compared with cefalexin, cefalotin, cefapirin, and cefotaxime,[1] no detectable cefadroxil would be expected in breast-fed infants and no adverse effects have been seen in infants whose mothers were receiving cefadroxil. Accordingly, the American Academy of Pediatrics considers[2] that cefadroxil is usually compatible with breast feeding.

1. Kafetzis DA, *et al.* Passage of cephalosporins and amoxicillin into the breast milk. *Acta Paediatr Scand* 1981; **70:** 285–8.
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)

Interactions

As for Cefalexin, p.218.

Antimicrobial Action

As for Cefalexin, p.218.

Pharmacokinetics

Cefadroxil is almost completely absorbed from the gastrointestinal tract. After oral doses of 500 mg and 1 g, peak plasma concentrations of about 16 and 30 micrograms/mL respectively are obtained after 1.5 to 2 hours. Although peak concentrations are similar to those of cefalexin, plasma concentrations are more sustained. Dosage with food does not appear to affect the absorption of cefadroxil. About 20% of cefadroxil is reported to be bound to plasma proteins. The plasma half-life of cefadroxil is about 1.5 hours and is prolonged in patients with renal impairment.

Cefadroxil is widely distributed to body tissues and fluids. It crosses the placenta and appears in breast milk.

More than 90% of a dose of cefadroxil may be excreted unchanged in the urine within 24 hours by glomerular filtration and tubular secretion; peak urinary concentrations of 1.8 mg/mL have been reported after a dose of 500 mg. Cefadroxil is removed by haemodialysis.

◊ References.

1. Tanrisever B, Santella PJ. Cefadroxil: a review of its antibacterial, pharmacokinetic and therapeutic properties in comparison with cephalexin and cephradine. *Drugs* 1986; **32** (suppl 3): 1–16.
2. Wise R. The pharmacokinetics of the oral cephalosporins—a review. *J Antimicrob Chemother* 1990; **26** (suppl E): 13–20.
3. Garrigues TM, *et al.* Dose-dependent absorption and elimination of cefadroxil in man. *Eur J Clin Pharmacol* 1991; **41**: 179–83.

Uses and Administration

Cefadroxil is a first-generation cephalosporin antibacterial that is the para-hydroxy derivative of cefalexin (p.219), and is used similarly in the treatment of mild to moderate susceptible infections. It is given orally, and doses are expressed in terms of the anhydrous substance; 1.04 g of cefadroxil monohydrate is equivalent to about 1 g of anhydrous cefadroxil. The usual adult dose is 1 to 2 g daily as a single dose or in two divided doses. The following doses are used in children weighing less than 40 kg: 500 mg twice daily for those over 6 years of age, 250 mg twice daily for those aged 1 to 6 years, and 25 mg/kg daily in divided doses for infants under 1 year. For details of reduced doses of cefadroxil in patients with renal impairment, see below.

Cefadroxil has also been used as the lysine derivative.

Administration in renal impairment. Following an initial loading dose of 0.5 to 1 g, dosage of cefadroxil should be adjusted in patients with renal impairment according to creatinine clearance (CC):

- CC 26 to 50 mL/minute per 1.73 m^2: 0.5 to 1 g every 12 hours
- CC 11 to 25 mL/minute per 1.73 m^2: 0.5 to 1 g every 24 hours
- CC 10 mL/minute per 1.73 m^2 or less: 0.5 to 1 g every 36 hours.

Preparations

BP 2008: Cefadroxil Capsules; Cefadroxil Oral Suspension;
USP 31: Cefadroxil Capsules; Cefadroxil for Oral Suspension; Cefadroxil Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Cefabiot†; Cefacar; Cefacilina; Cefadrox; Cefamar; Cefasin; Cefatenk; Droxil; Kandicin; Klonadroxil†; Versatic; ***Austria:*** Biodroxil; Duracef; ***Belg.:*** Duracef; Moxacef†; ***Braz.:*** Cefadroxon; Cefamox; Celoxin†; Drofaxil†; Neo Cefadril; ***Canad.:*** Duricef; ***Chile:*** Adroxef; Biodroxil†; Cefamox; Sedafex; ***Cz.:*** Biodroxil; Cedrox†; Cefadrox†; Duracef; ***Fin.:*** Duracef; ***Fr.:*** Oracefal; ***Ger.:*** Cedrox†; Gruncef; ***Gr.:*** Cefalom†; Kleotrat†; Moxacef; Nefalox†; ***Hong Kong:*** Amben; Androxyl; Biodroxil; Duracef; Qualidrox; Sofidrox†; ***Hung.:*** Biodroxil†; Duracef; ***India:*** Cefadrox; Cefadur; Lactocef; Lydroxil; Odoxil; Pendrox; Vepan; Vistadrox; ***Indon.:*** Alxil; Ancefa; Bidicef; Biodroxil; Cefat; Dexacef; Doxef; Duricef; Erphadrox; Ethicef; Kelfex; Lapicef; Librocef; Longcef; Opicef; Osadrox; Pyricef; Q Cef; Qidrox; Renasistin; Roksicap; Sedrofen; Stafonin; Tisacef; Widrox; ***Irl.:*** Ultracef; ***Israel:*** Biodroxil; Duracef†; ***Ital.:*** Cefadril; Ceoxil†; Cephos; Foxil; Oradroxil; ***Malaysia:*** Kefloxin; Sofidrox†; ***Mex.:*** Cefamox; Cepotec; Duracef; Teroxina; ***Philipp.:*** Drolex; Drozid; Lexipad; ***Pol.:*** Biodroxil; Duracef; ***Port.:*** Biofaxil†; Cefacile; Ceforal; Cefra†; ***S.Afr.:*** Cipadur; Dacef; Duracef; ***Singapore:*** Duricef; Sofidrox; ***Spain:*** Duracef; ***Swed.:*** Cefamox; ***Thai.:*** Cefadril†; ***Turk.:*** Cefradur; Duricef; ***UK:*** Baxan; ***USA:*** Duricef†; ***Venez.:*** Bidroxyl; Cedroxim; Cefadril†; Cefaval; Cefonax; Drocef; Droxifan; Grunicef; Sanodril.

Multi-ingredient: *Arg.:* Cefacar Mucolitico†; Cefacilina Bronquial; ***Mex.:*** Duracef Expec.

Cefalexin *(BAN, pINN)*

66873; Cefaleksinas monohidratas; Cefaleksyna; Cefalexin monohydrát; Cefalexina; Céfalexine; Céfalexine monohydratée; Cefalexinmonohydrat; Cefalexinum; Cefalexinum monohydricum; Cephalexin *(USAN)*; Kefaleksiini; Kefaleksiinimonohydraatti; Sefaleksin. (7*R*)-3-Methyl-7-(α-D-phenylglycylamino)-3-cephem-4-carboxylic acid monohydrate.

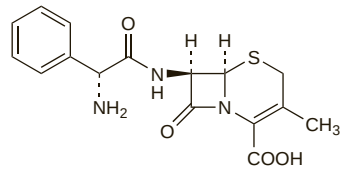
Цефалексин

$C_{16}H_{17}N_3O_4S,H_2O$ = 365.4.

CAS — 15686-71-2 (anhydrous cefalexin); 23325-78-2 (cefalexin monohydrate).

ATC — J01DB01.

ATC Vet — QJ01DB01; QJ51DA01.



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

Ph. Eur. 6.2 (Cefalexin Monohydrate). A white or almost white crystalline powder. Sparingly soluble in water; practically insoluble in alcohol. A 0.5% solution in water has a pH of 4.0 to 5.5. Protect from light.

USP 31 (Cephalexin). A white to off-white crystalline powder. Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a 5% suspension in water is between 3.0 and 5.5. Store in airtight containers.

Cefalexin Hydrochloride *(BANM, pINNM)*

Céfalexine, Chlorhydrate de; Cefalexini Hydrochloridum; Cephalexin Hydrochloride *(USAN)*; Hidrocloruro de cefalexina; LY-061188.

Цефалексина Гидрохлорид

$C_{16}H_{17}N_3O_4S,HCl,H_2O$ = 401.9.

CAS — 105879-42-3.

ATC — J01DB01.

ATC Vet — QJ01DB01.

Pharmacopoeias. In *US*.

USP 31 (Cephalexin Hydrochloride). A white to off-white crystalline powder. Soluble 1 in 100 in water, in acetone, in acetonitrile, in alcohol, in dimethylformamide, and in methyl alcohol; practically insoluble in chloroform, in ether, in ethyl acetate, and in isopropyl alcohol. pH of a 1% solution in water is between 1.5 and 3.0. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

The most common adverse effects of cefalexin and other oral cephalosporins are generally gastrointestinal disturbances and hypersensitivity reactions. Pseudomembranous colitis has been reported.

◊ References.

1. Dave J, *et al.* Cephalexin induced toxic epidermal necrolysis. *J Antimicrob Chemother* 1991; **28**: 477–8.
2. Baran R, Perrin C. Fixed-drug eruption presenting as an acute paronychia. *Br J Dermatol* 1991; **125**: 592–5.
3. Clark RF. Crystalluria following cephalexin overdose. *Pediatrics* 1992; **89**: 672–4.
4. Murray KM, Camp MS. Cephalexin-induced Stevens-Johnson syndrome. *Ann Pharmacother* 1992; **26:** 1230–3.
5. Czechowicz RT, *et al.* Bullous pemphigoid induced by cephalexin. *Australas J Dermatol* 2001; **42:** 132–5.
6. Longstreth KL, *et al.* Cephalexin-induced acute tubular necrosis. *Pharmacotherapy* 2004; **24:** 808–11.
7. Skoog SM, *et al.* Cephalexin-induced cholestatic hepatitis. *J Clin Gastroenterol* 2004; **38:** 833.
8. Penttilä J, *et al.* Delirium in an adolescent patient during treatment with cephalexin. *J Adolesc Health* 2006; **39:** 782–3.

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

Interactions

The renal excretion of cefalexin, and many other cephalosporins, is delayed by probenecid.

Hormonal contraceptives. There have been isolated reports of cefalexin decreasing the efficacy of oestrogen-containing oral contraceptives.[1] For a discussion of decreased efficacy of oral contraceptives and the need for additional contraceptive methods in patients taking broad-spectrum antibacterials, see under Hormonal Contraceptives, p.2068.

1. Friedman M, *et al.* Cephalexin and Microgynon-30 do not go well together. *J Obstet Gynaecol* 1982; **2**: 195–6.

Antimicrobial Action

As for Cefalotin Sodium, p.220, although cefalexin is generally less potent. Some strains of Gram-negative bacteria may be inhibited only by the high concentrations achievable in the urinary tract. *Haemophilus influenzae* is moderately resistant to cefalexin.

Pharmacokinetics

Cefalexin is almost completely absorbed from the gastrointestinal tract and produces a peak plasma concentration of about 18 micrograms/mL 1 hour after a 500-mg oral dose. If cefalexin is taken with food, absorption may be delayed, but the total amount absorbed is

not appreciably altered. Up to 15% of a dose is bound to plasma proteins. The plasma half-life is about 1 hour; it increases with reduced renal function.

Cefalexin is widely distributed in the body but does not enter the CSF in significant quantities. It crosses the placenta and small quantities are found in breast milk. Cefalexin is not metabolised. About 80% or more of a dose is excreted unchanged in the urine in the first 6 hours by glomerular filtration and tubular secretion; urinary concentrations greater than 1 mg/mL have been achieved after a dose of 500 mg. Probenecid delays urinary excretion. Therapeutically effective concentrations may be found in the bile and some may be excreted by this route.

Cefalexin 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.

Uses and Administration

Cefalexin is a first-generation cephalosporin antibacterial. It is given orally for the treatment of susceptible infections including those of the respiratory and urinary tracts and of the skin (see under Choice of Antibacterial, p.162). For severe infections, treatment with parenteral cephalosporins is to be preferred.

Cefalexin is usually given as the monohydrate although the hydrochloride is sometimes used. Doses are expressed in terms of the equivalent amount of anhydrous cefalexin; 1.05 g of cefalexin monohydrate and 1.16 g of cefalexin hydrochloride are each equivalent to about 1 g of anhydrous cefalexin.

The usual dose for adults is 1 to 2 g daily given in divided doses at 6-, 8-, or 12-hourly intervals; in severe or deep-seated infections the dose can be increased to up to 6 g daily but when high doses are required the use of a parenteral cephalosporin should be considered. Children may be given 25 to 100 mg/kg daily in divided doses to a maximum of 4 g daily.

For the prophylaxis of recurrent urinary-tract infection, cefalexin may be given in a dose of 125 mg at night.

Cefalexin sodium or cefalexin lysine have been used parenterally.

The dose of cefalexin may need to be reduced in renal impairment, see below.

Administration in renal impairment. Doses of cefalexin may need to be reduced in patients with renal impairment. The *BNF* recommends the following maximum daily doses according to creatinine clearance (CC):

- CC 40 to 50 mL/minute: maximum 3 g daily
- CC 10 to 40 mL/minute: maximum 1.5 g daily
- CC less than 10 mL/minute: maximum 750 mg daily

Preparations

BP 2008: Cefalexin Capsules; Cefalexin Oral Suspension; Cefalexin Tablets; ***USP 31:*** Cephalexin Capsules; Cephalexin for Oral Suspension; Cephalexin Tablets; Cephalexin Tablets for Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Arg.: Beliam; Cefalexi†; Cefapoten; Cefarinol; Cefasporina; Cefosporen; Ceporexin; Fabotop; Keforal; Lars; Lexin; Lorbicefax; Novalexin; Pectorina†; Permvastat; Sanibiotic; Septilisin; Trexina; Triblix; Velexina; ***Austral.:*** Cilex; Ialex; Ibilex; Keflex; Rancef; Sporahexal; ***Austria:*** Cepexin; Cephalobene; Keflex; Ospexin; Sanaxin; ***Belg.:*** Ceporex†; Keforal; ***Braz.:*** Betacef†; Cefaben; Cefagel; Cefagon†; Cefagran; Cefalexan†; Cefanal; Cefaxon; Cefexina; Ceflexin†; Celen; Celexin; Celinax†; Ceporexin†; Falexin†; Kefalexin†; Keflaxina†; Keflex; Keforal; Kiflexin†; Lexin; Lifalexin†; Neo Ceflex; Neoceflex; Primacef; Profalexina; Todexin†; Valflex; ***Canad.:*** Apo-Cephalex; Novo-Lexin; Nu-Cephalex; ***Cz.:*** Cefaclen; Oraceft; Ospexin; Sporidex; ***Denm.:*** Keflex; ***Fin.:*** Kefalex; Kefexin; Orakef†; ***Fr.:*** Cefacet; Ceporexine; Keforal; ***Ger.:*** Cephalex; Ceporexin†; Oraceft; ***Hong Kong:*** Anxer; Cefacin-M; Cefacure; Ceporex; Felexin; Keflex†; Medolexin; Ospexin; Sofilex; Solulexin; ***Hung.:*** Keflex†; Pyassan; Servispor†; ***India:*** Alexin†; Betaspore†; Cefmix; Cephadex; Cephaxin; Nufex; Phexin; Rofex†; Sepexin; Sporidex; ***Indon.:*** Cefabiotic; Madlexin; Ospexin; Pralexin; Tepaxin; Theralexin; ***Irl.:*** Ceporex†; Kefexin†; Keflex; ***Israel:*** Cefalin†; Ceforal; Cefovit; Keflex†; ***Ital.:*** Ceporex; Keforal; Lafarin; ***Jpn:*** Larixin; ***Malaysia:*** Cefax†; Celexin; Ceporex†; Felexin; Kefexin†; Medolexin; Ospexin; Refex†; Sofilex†; Sporidex; Uphalexin; ***Mex.:*** Acacin; Arlexen; Cefalver; Ceporex; Facelit; Falexol†; Fleximin; Flextinol; Keflex; Nafacil; Nixelaf-C; Optocef; Paferxin; Quimosporina; Servicef; ***Neth.:*** Keforal; ***Norw.:*** Keflex; ***NZ:*** Keflex†; ***Philipp.:*** Airex; Bacilexin; Bandax; Bloflex; Canelin; Cefalin; Cendalex; Ceporex; Civalex; Eliphorin; Forexine; Halcepin; Infexin; Keflex; Lewimycin; Lexum; Lonarel; Lyceplix; Madexin; Medilexin; Medoxine; Montralex; Nefadon; Neolecsin; Nerfalex; Oneflex; Respinal; Selzef; Servispor; Sorlex; Sporidex; Xinflex; Zepharyl; Zeporin; Zucoflaxin; ***Pol.:*** Keflex; ***Port.:*** Ceflax†; Ceporex; Keflex†; ***S.Afr.:*** Fexin†; Keflex; Lenocef; Ranceph; ***Singapore:*** Celexin; Cephalen; Cephanmycin; Ceporex†; Felexin†; Ospexin; Sofilex; Sporidex; Uphalexin; ***Spain:*** Bioscefal†; Cefalexgobens; Defaxina†; Kefloridina; Lexincef; Sulquipen; Torlasporin; ***Swed.:*** Keflex; ***Thai.:*** Anxer†; Cefexin; Cefxin†; Celex; Celexin; Cephalexyl; Cephin; Ceporex†; Farmalex; Felexin; Ibilex; Keflex; Pondnacef; Sefasin; Sialexin; Sporicef; Sporidex; Toflex; Ulflex; Zeplex; ***Turk.:*** Maksipor; Sef; ***UAE:*** Cefrin; ***UK:*** Ceporex; Keflex; ***USA:*** Biocef†; Cefanex; Keflex; Keftab†; ***Venez.:*** Bidocef; Cefaloga†; Keforal; Stricef.

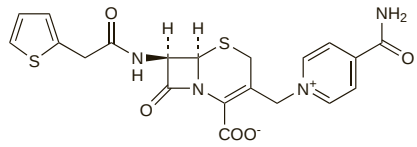
Multi-ingredient: ***India:*** Caceff; Cephadex LB; ***Mex.:*** Arlexen B; Cefabroxil; Cepobrom; Mucocef; Rombox.

Cefalonium *(BAN, pINN)*

41071; Carbamoylcefaloridine; Cefalonio; Céfalonium; Cephalonium. (7*R*)-3-(4-Carbamoyl-1-pyridiniomethyl)-7-[2-(2-thienyl)-acetamido]-3-cephem-4-carboxylate.

Цефалоний

$C_{20}H_{18}N_4O_5S_2$ = 458.5.
CAS — 5575-21-3.
ATC Vet — QJ51DA90.



Pharmacopoeias. *BP(Vet)* includes the dihydrate.
BP(Vet) 2008 (Cefalonium). The dihydrate is a white or almost white crystalline powder. Very slightly soluble in water and in methyl alcohol; insoluble in alcohol, in dichloromethane, and in ether; soluble in dimethyl sulfoxide. It dissolves in dilute acids and in alkaline solutions. Store at temperature not exceeding 30°. Protect from light.

Profile

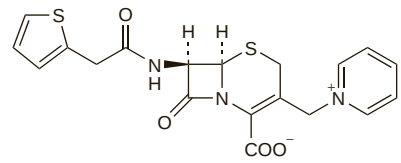
Cefalonium is a cephalosporin antibacterial used in veterinary practice.

Cefaloridine *(BAN, pINN)*

40602; Cefaloridin; Cefaloridina; Céfaloridine; Cefaloridinum; Cephaloridine *(USAN)*; Kefaloridiini. (7*R*)-3-(1-Pyridiniomethyl)-7-[(2-thienyl)acetamido]-3-cephem-4-carboxylate.

Цефалоридин

$C_{19}H_{17}N_3O_4S_2$ = 415.5.
CAS — 50-59-9.
ATC — J01DB02.
ATC Vet — QJ01DB02.



Profile

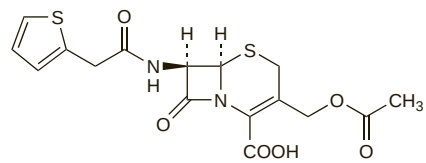
Cefaloridine was one of the first cephalosporin antibacterials to be available clinically. It has properties similar to those of cefalotin (below), but is more nephrotoxic and is seldom used now.

Cefalotin Sodium *(BANM, pINNM)*

38253; Cefalotin sodná sůl; Cefalotina sódica; Céfalotine sodique; Cefalotinnatrium; Cefalotin-nátrium; Cefalotino natrio druska; Cefalotinum natricum; Cefalotyna sodowa; Cephalothin Sodium *(USAN)*; Kefalotiininatrium; Natrii Cefalotinum; Sodium Cephalothin. Sodium (7*R*)-7-[2-(2-thienyl)acetamido]cephalosporanate; Sodium (7*R*)-3-acetoxymethyl-7-[2-(2-thienyl)acetamido]-3-cephem-4-carboxylate.

Натрий Цефалотин

$C_{16}H_{15}N_2NaO_6S_2$ = 418.4.
CAS — 153-61-7 (cefalotin); 58-71-9 (cefalotin sodium).
ATC — J01DB03.
ATC Vet — QJ01DB03.



(cefalotin)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefalotin Sodium). A white or almost white powder. Freely soluble in water; slightly soluble in dehydrated alcohol. A 10% solution in water has a pH of 4.5 to 7.0. Protect from light.
USP 31 (Cephalothin Sodium). A white to off-white, practically odourless, crystalline powder. Freely soluble in water, in sodium chloride 0.9%, and in glucose solutions; insoluble in most organic solvents. pH of a 25% solution in water is between 4.5 and 7.0. Store in airtight containers.

Incompatibility and stability. Cefalotin sodium has been reported to be incompatible with aminoglycosides and with many other drugs. Precipitation may occur in solutions with a pH of less than 5.

Adverse Effects

The adverse effects associated with cefalotin and other cephalosporins are broadly similar to those described for penicillins (see Benzylpenicillin, p.213). The most common are hypersensitivity reactions, including skin rashes, urticaria, eosinophilia, fever, reactions resembling serum sickness, and anaphylaxis.

There may be a positive response to the Coombs' test although haemolytic anaemia rarely occurs. Neutropenia and thrombocytopenia have occasionally been reported. Agranulocytosis has been associated rarely with some cephalosporins. Bleeding complications related to hypoprothrombinaemia and/or platelet dysfunction have occurred especially with cephalosporins and cephamycins having an *N-methylthiotetrazole* side-chain, including

- cefamandole
- cefbuperazone
- cefmenoxime
- cefmetazole
- cefonicid
- cefoperazone
- ceforanide
- cefotetan
- cefpiramide
- latamoxef.

The presence of a *methylthiadiazolethiol* side-chain, as in cefazolin, or an *N-methylthiotriazine* ring, as in ceftriaxone, might also be associated with such bleeding disorders. Hypoprothrombinaemia which is usually reversible with vitamin K, was once thought to be due to an alteration in intestinal flora but interference with prothrombin synthesis now seems more likely.

Nephrotoxicity has been reported with cefalotin although it is less toxic than cefaloridine. Acute renal tubular necrosis has followed excessive dosage and has also been associated with its use in older patients or those with pre-existing renal impairment, or when used with nephrotoxic drugs such as aminoglycosides. Acute interstitial nephritis is also a possibility as a manifestation of hypersensitivity.

Transient increases in liver enzyme values have been reported. Hepatitis and cholestatic jaundice have occurred rarely with some cephalosporins.

Convulsions and other signs of CNS toxicity have been associated with high doses, especially in patients with severe renal impairment.

Gastrointestinal adverse effects such as nausea, vomiting, and diarrhoea have been reported rarely. Prolonged use may result in overgrowth of non-susceptible organisms and, as with other broad-spectrum antibiotics, pseudomembranous colitis may develop (see also below).

There may be pain at the injection site after intramuscular use, and thrombophlebitis has occurred on intravenous infusion of cephalosporins. Cefalotin appears to be more likely to cause such local reactions than other cephalosporins.

Antibiotic-associated colitis. Pseudomembranous colitis has occurred with many antibacterials, including broad-spectrum cephalosporins.[1-3] In 1991 the UK CSM warned[4] of the dangers of pseudomembranous colitis with the newer, as well as the older, oral cephalosporins. In addition to 33 reports of pseudomembranous colitis associated with cefalexin, cefradine, cefadroxil, and