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.

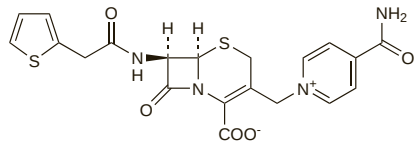
Multi-ingredient: ***India:*** Caceff; Cephadex LB; ***Mex.:*** Arlexen B; Cefabroxil; Cepobrom; Mucocef; Rombox.

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

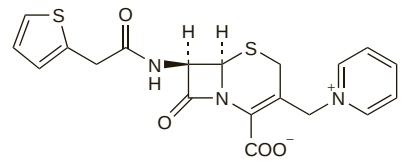
Cefalonium is a cephalosporin antibacterial used in veterinary practice.

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

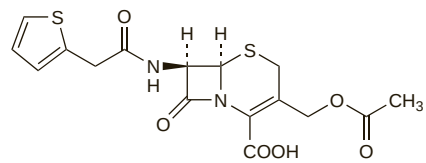
Cefaloridine was one of the first cephalosporin antibacterials to be available clinically. It has properties similar to those of cefalotin (below), but is more nephrotoxic and is seldom used now.

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