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.

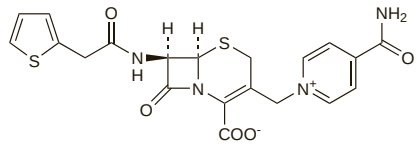
Multi-ingredient: ***India:*** Caceff; Cephadex LB; ***Mex.:*** Arlexen B; Cefabroxil; Cepobrom; Mucocef; Rombox.

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

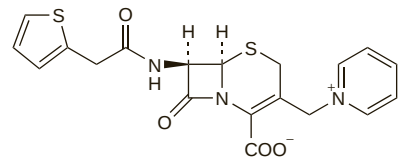
Cefalonium is a cephalosporin antibacterial used in veterinary practice.

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

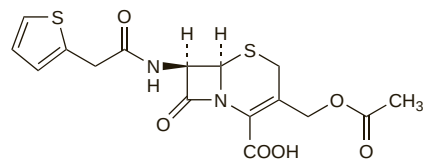
Cefaloridine was one of the first cephalosporin antibacterials to be available clinically. It has properties similar to those of cefalotin (below), but is more nephrotoxic and is seldom used now.

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

cefaclor, 6 of which proved fatal, they had received 12 reports of probable or confirmed cases with cefuroxime axetil and 15 with cefixime, one of them fatal. In clinical trials of cefuroxime axetil and cefixime, diarrhoea and pseudomembranous colitis appeared to be dose-related and therefore the CSM recommended that higher doses should be reserved for severe infections. In any event they advised that treatment should be stopped if symptoms suggestive of pseudomembranous colitis arose.

For further discussion of the management of this condition, see p.171.

1. de Lalla F, *et al.* Third generation cephalosporins as a risk factor for Clostridium difficile-associated disease: a four-year survey in a general hospital. *J Antimicrob Chemother* 1989; **23:** 623–31.
2. Golledge CL, *et al.* Extended spectrum cephalosporins and Clostridium difficile. *J Antimicrob Chemother* 1989; **23:** 929–31.
3. Freiman JP, *et al.* Pseudomembranous colitis associated with single-dose cephalosporin prophylaxis. *JAMA* 1989; **262:** 902.
4. Committee on Safety of Medicines. Pseudomembranous (antibiotic-associated) colitis and diarrhoea with cephalosporins. *Current Problems 32* 1991. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024450&RevisionSelectionMethod=LatestReleased (accessed 04/08/08)

Effects on the blood. References.

1. Lipsky JJ. Antibiotic-associated hypoprothrombinaemia. *J Antimicrob Chemother* 1988; **21:** 281–300.
2. Shearer MJ, *et al.* Mechanism of cephalosporin-induced hypoprothrombinemia: relation to cephalosporin side chain, vitamin K metabolism, and vitamin K status. *J Clin Pharmacol* 1988; **28:** 88–95.
3. Welage LS, *et al.* Comparative evaluation of the pharmacokinetics of N-methylthiotetrazole following administration of cefoperazone, cefotetan, and cefmetazole. *Antimicrob Agents Chemother* 1990; **34:** 2369–74.

Effects on the kidneys. References.

1. Zhanel GG. Cephalosporin-induced nephrotoxicity: does it exist? *DICP Ann Pharmacother* 1990; **24:** 262–5.
2. Tune BM. Nephrotoxicity of beta-lactam antibiotics: mechanisms and strategies for prevention. *Pediatr Nephrol* 1997; **11:** 768–72.

Precautions

Cefalotin should not be given to patients who are hypersensitive to it or to other cephalosporins. Immunological studies have suggested that up to 20% of penicillin-sensitive patients may also be allergic to cephalosporins although clinical studies indicate a lower frequency and the true incidence is uncertain; great care should be taken if cefalotin is to be given to such patients. Care is also necessary in patients with a history of allergy.

Cefalotin should be given with caution to patients with renal impairment; dosage reduction may be necessary. Renal and haematological status should be monitored especially during prolonged and high-dose therapy. Cefalotin and some other cephalosporins and cephamycins (ceforanide, cefotetan, cefoxitin, and cefpirome) may interfere with the Jaffé method of measuring creatinine concentrations and may produce falsely high values; this should be borne in mind when measuring renal function. Positive results to the direct Coombs' test have been found during treatment with cefalotin and these can interfere with blood cross-matching. The urine of patients being treated with cefalotin may give false-positive reactions for glucose using copper-reduction reactions.

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

Sodium content. Each g of cefalotin sodium contains about 2.39 mmol of sodium.

Interactions

The use of nephrotoxic drugs such as the aminoglycosides gentamicin and tobramycin may increase the risk of kidney damage with cefalotin. There is also some evidence for enhanced nephrotoxicity with the loop diuretic furosemide, but this is less certain than for furosemide with cefaloridine. As with penicillins, the renal excretion of cefalotin and many other cephalosporins is inhibited by probenecid. There may be antagonism between cefalotin and bacteriostatic antibacterials.

Antimicrobial Action

Cefalotin is a beta-lactam antibacterial. It is bactericidal and acts similarly to benzylpenicillin (p.214) by inhibiting synthesis of the bacterial cell wall. It is most active against Gram-positive cocci, and has moderate activity against some Gram-negative bacilli.

Sensitive Gram-positive cocci include both penicillinase- and non-penicillinase-producing staphylococci, although meticillin-resistant staphylococci are resistant; most streptococci are also sensitive, but not penicillin-resistant *Streptococcus pneumoniae;* enterococci are usually resistant. Some Gram-positive anaerobes are also susceptible. Cefalotin is usually inactive against *Listeria monocytogenes*.

Among Gram-negative bacteria cefalotin has activity against some Enterobacteriaceae including strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Salmonella*, and *Shigella* spp., but not against *Enterobacter*, indole-positive *Proteus*, or *Serratia* spp. It is also active against *Moraxella catarrhalis* (*Branhamella catarrhalis*) and *Neisseria* spp., though *Haemophilus influenzae* is moderately resistant. *Bacteroides fragilis* and *Pseudomonas aeruginosa* are not sensitive and neither are mycobacteria, mycoplasma, and fungi.

Resistance of bacteria to cefalotin may be due to several mechanisms: the drug may be prevented from reaching its site of action, for example in some Gram-negative organisms the cell wall may be a potential barrier; the target penicillin-binding proteins may be altered so that cefalotin cannot bind with these proteins; or, most importantly, the organism may produce beta-lactamases (cephalosporinases). Cefalotin is relatively resistant to hydrolysis by staphylococcal beta-lactamase, but is inactivated by a variety of beta-lactamases produced by Gram-negative organisms; resistance of Gram-negative organisms often depends on more than one factor. Resistance can be chromosomally or plasmid-mediated and may sometimes be inducible by cephalosporins.

Certain strains of bacteria may be inhibited but not killed by cephalosporins or penicillins and in such cases the minimum bactericidal concentration is much greater than the minimum inhibitory concentration; this is known as tolerance.

As well as with other cephalosporins, some cross-resistance may occur between cefalotin and the penicillinase-resistant penicillins.

Pharmacokinetics

Cefalotin is poorly absorbed from the gastrointestinal tract. After intramuscular injection peak plasma concentrations of about 10 and 20 micrograms/mL are achieved within 30 minutes of doses of 0.5 and 1 g, respectively. A concentration of 30 micrograms/mL has been reported 15 minutes after the intravenous injection of a 1-g dose; a range of 14 to 20 micrograms/mL has been achieved by the continuous intravenous infusion of 500 mg/hour.

Cefalotin is widely distributed in body tissues and fluids except the brain and CSF where the concentrations achieved are low and unpredictable. It crosses the placenta and low concentrations have been detected in breast milk. The plasma half-life varies from about 30 to 50 minutes, but may be longer in patients with renal impairment, especially that of the metabolite. About 70% of cefalotin is bound to plasma proteins.

About 20 to 30% of cefalotin is rapidly deacetylated in the liver and about 60 to 70% of a dose is excreted in the urine by the renal tubules within 6 hours as cefalotin and the less active metabolite, desacetylcefalotin. High urine concentrations of 0.8 and 2.5 mg/mL have been observed after intramuscular doses of 0.5 and 1 g, respectively. Probenecid blocks the renal excretion of cefalotin. A very small amount is excreted in bile.

Uses and Administration

Cefalotin is a first-generation cephalosporin antibacterial that has been used in the treatment of infections due to susceptible bacteria, particularly staphylococci, but has generally been replaced by newer cephalosporins.

Cefalotin is given as the sodium salt by slow intravenous injection over 3 to 5 minutes or by intermittent or continuous infusion. It may be given intramuscularly but this route is painful. Doses are expressed in terms of the equivalent amount of cefalotin; 1.06 g of cefalotin sodium is equivalent to about 1 g of cefalotin. The usual dose is 0.5 to 1 g of cefalotin every 4 to 6 hours; up to 12 g daily has been given in severe infections.

Administration in renal impairment. Reduced doses are recommended if cefalotin is given to patients with renal impairment. After an intravenous loading dose of 1 to 2 g patients may be given the following maximum doses according to their creatinine clearance (CC):

- CC 50 to 80 mL/minute: 2 g every 6 hours
- CC 25 to 50 mL/minute: 1.5 g every 6 hours
- CC 10 to 25 mL/minute: 1 g every 6 hours
- CC 2 to 10 mL/minute: 500 mg every 6 hours
- CC less than 2 mL/minute: 500 mg every 8 hours

Preparations

USP 31: Cephalothin for Injection; Cephalothin Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Arecamin; Cefade†; Dasuglor; Keflin; Rupecef†; ***Austral.:*** Keflin Neutral; ***Braz.:*** Cefalin; Cefalot†; Cefalotil; Cefariston; Kefalotin†; Keflin; ***Canad.:*** Ceporacin†; ***Denm.:*** Keflin†; ***Fin.:*** Keflin†; ***Indon.:*** Cephation; Moraxine; ***Israel:*** Keflin†; ***Ital.:*** Keflin†; ***Mex.:*** Cefelen; Ceftina; Falot; Keflin; Liroken I; Loriken†; Lotin; ***Neth.:*** Keflin; ***Norw.:*** Keflin; ***Philipp.:*** Fezef; ***S.Afr.:*** Keflin†; ***Singapore:*** Cefadin; ***Thai.:*** Cefadin†; Keflin†; ***Venez.:*** Cefaciclina†; Ceflen; Keflin†.

Cefamandole *(BAN, USAN, rINN)*

83405; Cefamandol; Céfamandole; Cefamandolum; Cephamandole; Compound 83405; Kefamandoli. (7*R*)-7-D-Mandelamido-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid; {6*R*-[6α,7β(R^*)]}-7-[(hydroxyphenylacetyl)amino]-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.

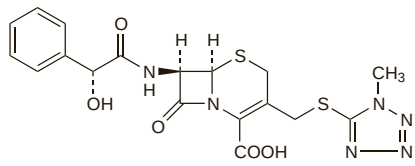
Цефамандол

$C_{18}H_{18}N_6O_5S_2$ = 462.5.

CAS — 34444-01-4.

ATC — J01DC03.

ATC Vet — QJ01DC03.



Cefamandole Nafate *(BAN, USAN, rINNM)*

106223; Cefamandole Formate Sodium; Céfamandole, nafate de; Cefamandoli nafas; Cefamandoli Nafatum; Cefamandolio nafatas; Cefamandolnafat; Cefamandol-nafát; Cefamandolu nafan; Cefmandoli Nafas; Cephamandole Nafate; Kefamandolinafaatti; Nafato de cefamandol. Sodium (7*R*)-7-[(2*R*)-2-formyloxy-2-phenylacetamido]-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylate.

Цефамандола Нафат

$C_{19}H_{17}N_6NaO_6S_2$ = 512.5.

CAS — 42540-40-9.

ATC — J01DC03.

ATC Vet — QJ01DC03.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Cefamandole Nafate). A white, or almost white powder. Freely soluble in water; sparingly soluble in methyl alcohol. A 10% solution in water has a pH, measured after 30 minutes, of 6.0 to 8.0. Store in airtight containers. Protect from light.

USP 31 (Cefamandole Nafate). A white, odourless, crystalline solid. Soluble in water and in methyl alcohol; practically insoluble in chloroform, in cyclohexane, in ether, and in benzene. pH of a 10% solution in water is between 3.5 and 7.0. Store in airtight containers.

Incompatibility and stability. Cefamandole nafate has been reported to be incompatible with aminoglycosides and with metronidazole. Formulations of cefamandole nafate available for injection contain sodium carbonate and are incompatible with solutions containing calcium or magnesium salts. When reconstituted with water the sodium carbonate rapidly hydrolyses about 30% of the ester to cefamandole sodium; during storage of the reconstituted solution at room temperature carbon dioxide is produced.

References.

1. Frable RA, *et al.* Stability of cefamandole nafate injection with parenteral solutions and additives. *Am J Hosp Pharm* 1982; **39:** 622–7. Correction. *ibid.*; 1479.