Cefamandole Sodium *(BANM, rINNM)*

Cefamandol sódico; Céfamandole Sodique; Cephamandole Sodium; Natrii Cefamandolum.

Натрий Цефамандол

$C_{18}H_{17}N_6NaO_5S_2$ = 484.5.
CAS — 30034-03-8.
ATC — J01DC03.
ATC Vet — QJ01DC03.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

As mentioned under Cefalotin, cephalosporins with an *N*-methylthiotetrazole side-chain such as cefamandole (and possibly those with methylthiadiazolethiol or *N*-methylthiotriazine side-chains as well) may produce bleeding disorders associated with hypoprothrombinaemia and/or platelet disorders.

Sodium content. 1.05 g of cefamandole sodium and 1.11g of cefamandole nafate each contain about 2.2 mmol of sodium.

Interactions

A disulfiram-like interaction with alcohol may occur and has been attributed to the *N*-methylthiotetrazole side-chain of cefamandole; patients should avoid alcohol during, and for at least several days after, cefamandole treatment. Interactions are also possible with preparations containing significant amounts of alcohol.

Cefamandole, and other cephalosporins with an *N*-methylthiotetrazole side-chain, may enhance the hypoprothrombinaemic response to anticoagulants as discussed under Warfarin (p.1428).

Probenecid reduces the renal clearance of cefamandole and many other cephalosporins.

◊ References.

1. Portier H, *et al.* Interaction between cephalosporins and alcohol. *Lancet* 1980; **ii:** 263.
2. Drummer S, *et al.* Antabuse-like effect of β-lactam antibiotics. *N Engl J Med* 1980; **303:** 1417–18.

Antimicrobial Action

Cefamandole is bactericidal and acts similarly to cefalotin, but has a broader spectrum of activity. It generally has similar or less activity against Gram-positive staphylococci and streptococci, but is resistant to some beta-lactamases produced by Gram-negative bacteria. It is more active than cefalotin against many of the Enterobacteriaceae including some strains of *Enterobacter, Escherichia coli*, *Klebsiella*, *Salmonella*, and some *Proteus* spp. However, resistance to cefamandole and other beta lactams has emerged in some species, notably *Enterobacter*, during treatment with cefamandole. Cefamandole is very active *in vitro* against *Haemophilus influenzae* although an inoculum effect has been reported for beta-lactamase-producing strains. Like cefalotin, most strains of *Bacteroides fragilis* are resistant to cefamandole, as are *Pseudomonas* spp.

◊ References.

1. Sabath LD. Reappraisal of the antistaphylococcal activities of first-generation (narrow-spectrum) and second-generation (expanded-spectrum) cephalosporins. *Antimicrob Agents Chemother* 1989; **33:** 407–11.

Pharmacokinetics

Cefamandole is poorly absorbed from the gastrointestinal tract. It is given intramuscularly or intravenously, usually as the nafate which is rapidly hydrolysed to release cefamandole *in vivo*. Peak plasma concentrations for cefamandole of about 13 and 25 micrograms/mL have been achieved 0.5 to 2 hours after intramuscular doses of 0.5 and 1 g respectively; concentrations are very low after 6 hours. About 70% is bound to plasma proteins. The plasma half-life varies from about 0.5 to 1.2 hours depending on the route of injection; it is prolonged in patients with renal impairment.

Cefamandole is widely distributed in body tissues and fluids including bone, joint fluid, and pleural fluid; it diffuses into the CSF when the meninges are inflamed, but concentrations are unpredictable. Cefamandole has also been detected in breast milk. It is rapidly excreted unchanged by glomerular filtration and renal tubular secretion; about 80% of a dose is excreted within 6 hours and high urinary concentrations are achieved. Probenecid competes for renal tubular secretion with cefamandole resulting in higher and prolonged plasma concentrations of cefamandole. Therapeutic concentrations of cefamandole are achieved in bile.

Cefamandole is removed by haemodialysis to some extent.

Uses and Administration

Cefamandole is a second-generation cephalosporin antibacterial used in the treatment of infections due to susceptible bacteria and for surgical infection prophylaxis.

It is given principally as cefamandole nafate (the sodium salt of cefamandole formyl ester). Doses are expressed in terms of the equivalent amount of cefamandole; 1.05 g of cefamandole sodium and 1.11 g of cefamandole nafate are each equivalent to about 1 g of cefamandole. It is given by deep intramuscular injection, by slow intravenous injection over 3 to 5 minutes, or by intermittent or continuous infusion in doses of 0.5 to 2 g every 4 to 8 hours for adults depending on the severity of the infection. Children over 1 month of age may be given 50 to 100 mg/kg daily in equally divided doses; 150 mg/kg daily may be given in severe infections, but this dose should not be exceeded. For details of reduced doses in patients with renal impairment, see below. If cefamandole is used with an aminoglycoside, the drugs should be given separately.

For surgical infection prophylaxis, a dose of 1 or 2 g intravenously or intramuscularly 30 to 60 minutes before surgical incision, followed by 1 or 2 g every 6 hours for 24 to 48 hours, is recommended. For patients undergoing procedures involving implantation of prosthetic devices, cefamandole should be continued for up to 72 hours. Children over 3 months of age may be treated similarly to adults and given 50 to 100 mg/kg daily in equally divided doses.

Administration in renal impairment. Doses of cefamandole should be reduced for patients with renal impairment. After an initial dose of 1 to 2 g the following maintenance doses have been recommended based on creatinine clearance (CC):

- CC 50 to 80 mL/minute: 0.75 to 2 g every 6 hours
- CC 25 to 50 mL/minute: 0.75 to 2 g every 8 hours
- CC 10 to 25 mL/minute: 0.5 to 1.25 g every 8 hours
- CC 2 to 10 mL/minute: 0.5 to 1 g every 12 hours
- CC less than 2 mL/minute: 0.25 to 0.75 g every 12 hours

Preparations

USP 31: Cefamandole Nafate for Injection.

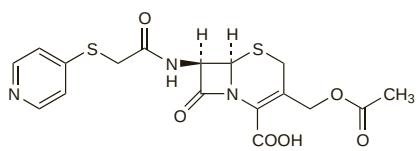
Proprietary Preparations (details are given in Part 3)
Austral.: Mandol; ***Austria:*** Mandokef; ***Belg.:*** Mandol; ***Cz.:*** Mandol†; ***Gr.:*** Acemycin; Cefadin; Mandokef; ***Hong Kong:*** Mandol†; ***Hung.:*** Cefam; Mandokef†; ***Indon.:*** Dardokef; Dofacef; ***Irl.:*** Kefadol†; ***Ital.:*** Cefam; Cemado; Lampomandol; Mancef; Mandokef†; Mandolsan†; Septomandolo†; ***Neth.:*** Mandol; ***NZ:*** Mandol; ***Pol.:*** Tarcefandol; ***Port.:*** Mandokef†; ***Rus.:*** Cefat (Цефат); Mandol (Мандол); ***S.Afr.:*** Kefdole†; Mandokef; ***Switz.:*** Mandokef; ***Thai.:*** Cefadol; Cefmandol; Mandol†.

Cefapirin Sodium *(BANM, plNNM)*

BL-P-1322; Cefapirin sodná sůl; Cefapirina sódica; Céfapirine sodique; Cefapirinnatrium; Cefapirin-nátrium; Cefapirino natrio druska; Cefapirinum natricum; Cephapirin Sodium *(USAN)*; Kefapiriininatrium; Natrii Cefapirinum. Sodium (7*R*)-7-[2-(4-pyridylthio)acetamido]cephalosporanate; Sodium (7*R*)-3-acetoxymethyl-7-[2-(4-pyridylthio)acetamido]-3-cephem-4-carboxylate.

Натрий Цефапирин

$C_{17}H_{16}N_3NaO_6S_2$ = 445.4.
CAS — 21593-23-7 (cefapirin); 24356-60-3 (cefapirin sodium).
ATC — J01DB08.
ATC Vet — QJ01DB08.



(cefapirin)

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
US also includes Cephapirin Benzathine for veterinary use.
Ph. Eur. 6.2 (Cefapirin Sodium). A white or pale yellow powder. Soluble in water; practically insoluble in dichloromethane. A 1% solution in water has a pH of 6.5 to 8.5. Protect from light.
USP 31 (Cephapirin Sodium). A white to off-white crystalline powder, odourless or having a slight odour. Very soluble in water; insoluble in most organic solvents. pH of a solution in water containing the equivalent of cefapirin 1% is between 6.5 and 8.5. Store in airtight containers.

Profile

Cefapirin is a first-generation cephalosporin antibacterial with actions and uses very similar to those of cefalotin (p.219). It is used as the sodium salt but doses are expressed in terms of cefapirin base; 1.05 g of cefapirin sodium is equivalent to about 1 g of cefapirin. The usual dose is the equivalent of 0.5 to 1 g of cefapirin every 4 to 6 hours by intramuscular injection or intravenously. In severe infections up to 12 g daily may be given, preferably intravenously.

Administration in renal impairment. Reduced doses of cefapirin sodium may be necessary in patients with renal impairment. One regimen, based on creatinine clearance (CC), that has been suggested is:

- CC 5 to 20 mL/minute: 1 g every 12 hours
- CC less than 5 mL/minute: 1 g every 24 hours

Patients undergoing haemodialysis may receive 7.5 to 15 mg/kg after each dialysis.

Sodium content. Each g of cefapirin sodium contains about 2.2 mmol of sodium.

Preparations

USP 31: Cephapirin for Injection.

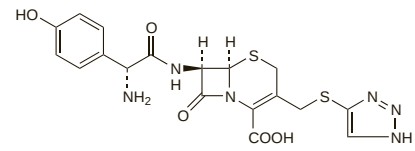
Proprietary Preparations (details are given in Part 3)
Cz.: Cefatrexyl†; ***Fr.:*** Cefaloject; ***Gr.:*** Cefatrex†; ***Spain:*** Brisfirina.

Cefatrizine *(BAN, USAN, plNN)*

BL-S640; Cefatrizina; Céfatrizine; Cefatrizinum; SKF-60771; S-640P. (7*R*)-7-(α-D-4-Hydroxyphenylglycylamino)-3-(1*H*-1,2,3-triazol-4-ylthiomethyl)-3-cephem-4-carboxylic acid.

Цефатризин

$C_{18}H_{18}N_6O_5S_2$ = 462.5.
CAS — 51627-14-6.
ATC — J01DB07.
ATC Vet — QJ01DB07.



Cefatrizine Propylene Glycol *(BANM, plNNM)*

Cefatrizina propilenglicol; Cefatrizinas propilenglikolis; Céfatrizine propylèneglycol; Cefatrizin-propilénglikol; Cefatrizinpropylenglykol; Cefatrizin-propylenglykol; Cefatrizinum propylen glycolum; Cefatrizinum Propylenglycolum; Kefatritsiinipropyleeniglykoli. (7*R*)-7-(α-D-4-Hydroxyphenylglycylamino)-3-(1*H*-1,2,3-triazol-4-ylthiomethyl)-3-cephem-4-carboxylate propylene glycol.

Цефатризин Пропиленгликол

$C_{18}H_{18}N_6O_5S_2$, $(C_3H_8O_2)_n$.
CAS — 64217-62-5.
ATC — J01DB07.
ATC Vet — QJ01DB07.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*.
Ph. Eur. 6.2 (Cefatrizine Propylene Glycol). A white or almost white powder. Slightly soluble in water; practically insoluble in alcohol and in dichloromethane.

Profile

Cefatrizine is a cephalosporin antibacterial with actions and uses similar to those of cefalexin (p.218), although it might be more active *in vitro*. It is given orally as the base or, more often, as a compound with propylene glycol, in usual doses equivalent to 500 mg twice daily of cefatrizine.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Cefaperos; ***Fr.:*** Cefaperos†; ***Gr.:*** Anfagladin; Axelorax; Banadroxin†; Ceftazin; Cetrizin; Clomin†; Fica-F; Gertemycin; Izerin; Kentacef; Klevasin; Liamycin; Liferost; Lingopen; Mekan†; Nibocin; Northiron; Phacobiotic†; Relyovix; Specicef-N; Trixilan; ***Ital.:*** Biotrixina†; Cefatrix†; Cetrazil†; Cetrinox†; Faretrizin; Ipatrizina†; Ketrizin; Miracef†; Novacef†; Tamyl†; Tricef†; Trizina; ***Port.:*** Macropen; Supracefa.