Cefoperazone Sodium

(BANM, USAN, rINNM)

Cefoperazon sodná sůl; Cefoperazon sodowy; Cefoperazona sódica; Céfopérazone sodique; Cefoperazonnatrium; Cefoperazon-nátrium; Cefoperazono natrio druska; Cefoperazonum natricum; CP-52640-2; CP-52640 (anhydrous cefoperazone); CP-52640-3 (cefoperazone dihydrate); Kefoperatsoninatrium; Natrii Cefoperazonum; Sefoperazon Sodyum; T-1551 (cefoperazone or cefoperazone sodium). Sodium (7*R*)-7-[(*R*)-2-(4-ethyl-2,3-dioxopiperazin-1-ylcarboxamido)-2-(4-hydroxyphenyl)acetamido]-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-3-cephem-4-carboxylate.

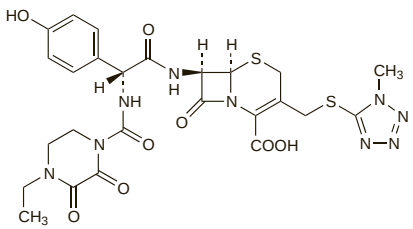
Натрий Цефоперазон

$C_{25}H_{26}N_9NaO_8S_2$ = 667.6.

CAS — 62893-19-0 (cefoperazone); 62893-20-3 (cefoperazone sodium).

ATC — J01DD12.

ATC Vet — QJ01DD12.



(cefoperazone)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefoperazone Sodium). A white or slightly yellow, hygroscopic, powder. If crystalline it exhibits polymorphism. Freely soluble in water; slightly soluble in alcohol; soluble in methyl alcohol. A 25% solution in water has a pH of 4.5 to 6.5. Store in airtight containers at a temperature of 2° to 8°. Protect from light.
USP 31 (Cefoperazone Sodium). A white to pale buff crystalline powder. Freely soluble in water and in methyl alcohol; slightly soluble in dehydrated alcohol; insoluble in acetone, in ether, and in ethyl acetate. pH of a 25% solution in water is between 4.5 and 6.5. Store in airtight containers.

Incompatibility. As with most beta lactams, admixture of cefoperazone sodium with aminoglycosides is not recommended because of the potential for inactivation of either drug.

There have been reports of incompatibility with other drugs including diltiazem,[1] doxorubicin,[2] pentamidine,[3] perphenazine,[4] pethidine,[5] promethazine,[6] and remifentanil.[7]

1. Gayed AA, *et al.* Visual compatibility of diltiazem injection with various diluents and medications during simulated Y-site injection. *Am J Health-Syst Pharm* 1995; **52:** 516–20.
2. Trissel LA, *et al.* Compatibility of doxorubicin hydrochloride liposome injection with selected other drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1997; **54:** 2708–13.
3. Lewis JD, El-Gendy A. Cephalosporin-pentamidine isethionate incompatibilities. *Am J Health-Syst Pharm* 1996; **53:** 1461–2.
4. Gasca M, *et al.* Visual compatibility of perphenazine with various antimicrobials during simulated Y-site injection. *Am J Hosp Pharm* 1987; **44:** 574–5.
5. Nieves-Cordero AL, *et al.* Compatibility of narcotic analgesic solutions with various antibiotics during simulated Y-site injection. *Am J Hosp Pharm* 1985; **42:** 1108–9.
6. Scott SM. Incompatibility of cefoperazone and promethazine. *Am J Hosp Pharm* 1990; **47:** 519.
7. Trissel LA, *et al.* Compatibility of remifentanil hydrochloride with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1997; **54:** 2192–6.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Like cefotaxime (p.228), cefoperazone has the potential for colonisation and superinfection with resistant organisms. Changes in bowel flora may be more marked than with cefotaxime because of the greater biliary excretion of cefoperazone; diarrhoea may occur more often.

Cefoperazone contains an *N*-methylthiotetrazole sidechain, a structure associated with hypoprothrombinaemia. Hypoprothrombinaemia has been reported in patients treated with cefoperazone and has rarely been associated with bleeding episodes. Prothrombin time should be monitored in patients at risk of hypoprothrombinaemia and vitamin K used if necessary.

Sodium content. Each g of cefoperazone sodium contains about 1.5 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Unlike many other cephalosporins, probenecid has no effect on the renal clearance of cefoperazone.

Antimicrobial Action

Cefoperazone has antimicrobial activity similar to that of ceftazidime (p.234), although it is slightly less active against some Enterobacteriaceae. It has good activity against *Pseudomonas aeruginosa*, but is less active than ceftazidime.

Cefoperazone is more susceptible than cefotaxime to hydrolysis by certain beta-lactamases.

Activity, particularly against Enterobacteriaceae and *Bacteroides* spp. has been enhanced in the presence of the beta-lactamase inhibitor sulbactam; resistant *Ps. aeruginosa* are not sensitive to the combination.

◊ References.

1. Fass RJ, *et al.* In vitro activities of cefoperazone and sulbactam singly and in combination against cefoperazone-resistant members of the family Enterobacteriaceae and nonfermenters. *Antimicrob Agents Chemother* 1990; **34:** 2256–9.
2. Clark RB, *et al.* Multicentre study on antibiotic susceptibilities of anaerobic bacteria to cefoperazone-sulbactam and other antimicrobial agents. *J Antimicrob Chemother* 1992; **29:** 57–67.

Pharmacokinetics

Cefoperazone is given parenterally as the sodium salt. With intramuscular doses equivalent to cefoperazone 1 or 2 g, peak plasma concentrations of 65 and 97 micrograms/mL have been reported after 1 to 2 hours. The plasma half-life of cefoperazone is about 2 hours, but may be prolonged in neonates and in patients with hepatic or biliary-tract disease. Cefoperazone is 82 to 93% bound to plasma proteins, depending on the concentration.

Cefoperazone is widely distributed in body tissues and fluids, although penetration into the CSF is generally poor. It crosses the placenta, and low concentrations have been detected in breast milk.

Cefoperazone is excreted mainly in the bile where it rapidly achieves high concentrations. Urinary excretion is primarily by glomerular filtration. Up to 30% of a dose is excreted unchanged in the urine within 12 to 24 hours; this proportion may be increased in patients with hepatic or biliary disease. Cefoperazone A, a degradation product less active than cefoperazone, has been found only rarely *in vivo*.

Uses and Administration

Cefoperazone is a third-generation cephalosporin antibiotic used similarly to ceftazidime (p.235) in the treatment of susceptible infections, especially those due to *Pseudomonas* spp. It is not recommended for the treatment of meningitis because of poor penetration into the CSF.

Cefoperazone is given as the sodium salt by deep intramuscular injection or intravenously by intermittent or continuous infusion. Doses are expressed in terms of the equivalent amount of cefoperazone; 1.03 g of cefoperazone sodium is equivalent to about 1 g of cefoperazone. The usual dose is 2 to 4 g daily in 2 divided doses. In severe infections, up to 12 g daily in 2 to 4 divided doses may be given.

For details of dosage in patients with hepatic and renal impairment, see below.

If cefoperazone is used with an aminoglycoside, the drugs should be given separately.

Cefoperazone has also been given with the beta-lactamase inhibitor sulbactam.

Administration in hepatic and renal impairment. In general, the dose of cefoperazone should not exceed 4 g daily in patients with liver disease or biliary obstruction or 1 to 2 g daily in those with both hepatic and renal impairment; if higher doses are used plasma concentrations of cefoperazone should be monitored.

Preparations

USP 31: Cefoperazone for Injection; Cefoperazone Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Cefobid†; ***Austria:*** Cefobid; ***Braz.:*** Cefazone†; Neoperazona†; ***Chile:*** Cefobid; ***Cz.:*** Cefobid; ***Hong Kong:*** Cefobid; ***Hung.:*** Cefobid; ***India:*** Cefomycin; Magnamycin; ***Indon.:*** Bifotik; Cefobid; Cefophar; Ceropid; Cerozon; Ferzobat; Logafox; Stabixin; ***Ital.:*** Bioperazone; Cefoneg†; Cefoper; Dardum; Farecef; Ipazone†; Novobiocyl†; Tomabef†; Zonceft; ***Jpn:*** Cefobid†; Cefoperazin; ***Malaysia:*** Cefobid; Medocef; Shinfomycin; ***Mex.:*** Cefobid; ***Philipp.:*** Bactizon; ***Pol.:*** Biocefazon; Cefobid; Dardum; ***Rus.:*** Cefobid (Цефобид); Medocef (Медоцеф); ***Singapore:*** Cefobid; Cefozone; Dardum; ***Spain:*** Cefobid†; ***Thai.:*** Cefobid; Cefozone†; Medocef; ***Turk.:*** Cefobid; ***USA:*** Cefobid†; ***Venez.:*** Cefobid†; Ortosep†.

Multi-ingredient: ***Arg.:*** Sulperazon†; ***Chile:*** Sulperazon; ***Cz.:*** Sulperazon; ***Hong Kong:*** Sulperazon; ***India:*** Lactagard; Sulbacef; Zosul; ***Indon.:*** Fosular; Stabactam; Sulperazon; ***Malaysia:*** Sulperazon; ***Philipp.:*** Sulperazone; ***Pol.:*** Sulperazon; ***Rus.:*** Sulcef (Сульцеф); Sulperason (Сульперазон); ***Thai.:*** Cebactam; Cefper; Sulcef; Sulperazon; ***Turk.:*** Primasef; Sulperazon; ***Venez.:*** Sulperazon.

Ceforanide *(BAN, USAN, rINN)*

BL-S786; Ceforanida; Céforanide; Ceforanidum. 7-[2-(α-Amino-*o*-tolyl)acetamido]-3-(1-carboxymethyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid.

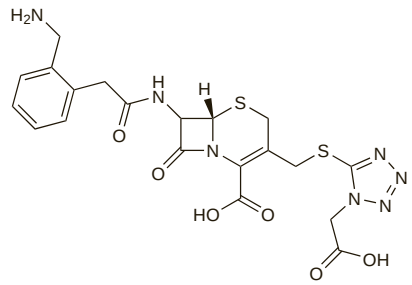
Цефоранид

$C_{20}H_{21}N_7O_6S_2$ = 519.6.

CAS — 60925-61-3.

ATC — J01DC11.

ATC Vet — QJ01DC11.



Pharmacopoeias. In *US*.
USP 31 (Ceforanide). A white to off-white powder. Practically insoluble in water, in chloroform, in ether, and in methyl alcohol; very soluble in 1N sodium hydroxide. pH of a 5% suspension in water is between 2.5 and 4.5. Store in airtight containers.

Profile

Ceforanide is a second-generation cephalosporin antibacterial with actions and uses similar to those of cefamandole (p.220), although it is reported to be less active *in vitro* against some bacteria, including staphylococci and *Haemophilus influenzae*. It is used in the treatment of susceptible infections and for surgical infection prophylaxis.

It is given as the lysine salt ($C_{26}H_{35}N_9O_8S_2$ = 665.7) but doses are expressed in terms of the equivalent amount of ceforanide; 1.28 g of ceforanide lysine is equivalent to about 1 g of ceforanide. It is given by deep intramuscular injection, or intravenously by slow injection over 3 to 5 minutes or by infusion. The usual adult dose is 1 to 2 g every 12 hours. Children may be given 20 mg/kg daily in 2 divided doses. For surgical infection prophylaxis, a dose of 1 to 2 g intravenously 1 hour before surgical incision is used in adults.

Ceforanide contains a substituted *N*-methylthiotetrazole sidechain, a structure associated with hypoprothrombinaemia and alcohol intolerance. Probenecid does not affect the renal excretion of ceforanide.

◊ References.

1. Campoli-Richards DM, *et al.* Ceforanide: a review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. *Drugs* 1987; **34:** 411–37.

Preparations

USP 31: Ceforanide for Injection.

Proprietary Preparations (details are given in Part 3)

Belg.: Precef†; ***Gr.:*** Radacef.