For infection prophylaxis during surgical procedures, an intravenous dose of 1 or 2 g is given 30 to 60 minutes before surgery or, in caesarean section, as soon as the umbilical cord is clamped.

Administration in renal impairment. Dosage of cefotetan should be reduced in patients with moderate to severe renal impairment. US licensed product information gives the following dosing guidelines based on creatinine clearance (CC):

- CC 10 to 30 mL/minute: the usual dose every 24 hours or one-half the usual dose every 12 hours
- CC less than 10 mL/minute: the usual dose every 48 hours or one-quarter the usual dose every 12 hours

In patients undergoing haemodialysis, one-quarter the usual dose may be given every 24 hours on days between dialysis and one-half the usual dose on the day of dialysis.

Preparations

USP 31: Cefotetan for Injection; Cefotetan Injection.

Proprietary Preparations (details are given in Part 3)

Austral.: Apatef†; ***Belg.:*** Apacef†; ***Canad.:*** Cefotan†; ***Fr.:*** Apacef†; ***Ital.:*** Apatef†; ***Jpn:*** Yamatetan†; ***NZ:*** Apatef†; ***Port.:*** Apatef†; ***USA:*** Cefotan.

Cefotiam Hydrochloride *(BANM, USAN, rINNM)*

Abbott-48999; Céfotiam, Chlorhydrate de; Cefotiami Hydrochloridum; CGP-14221E (cefotiam or cefotiam hydrochloride); Hidrocloruro de cefotiam; SCE-963. 7-[2-(2-Amino-1,3-thiazol-4-yl)acetamido]-3-[1-(2-dimethylaminoethyl)-1*H*-tetrazol-5-ylthiomethyl]-3-cephem-4-carboxylic acid dihydrochloride.

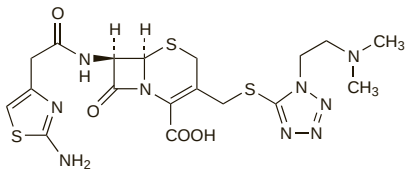
Цефотиама Гидрохлорид

$C_{18}H_{23}N_9O_4S_3,2HCl$ = 598.6.

CAS — 61622-34-2 (cefotiam); 66309-69-1 (cefotiam hydrochloride).

ATC — J01DC07.

ATC Vet — QJ01DC07.



(cefotiam)

Pharmacopoeias. In *Jpn* and *US*. *Jpn* also includes cefotiam hexetil hydrochloride.
USP 31 (Cefotiam Hydrochloride). Store in airtight containers.

Profile

Cefotiam is a third-generation cephalosporin antibacterial with actions and uses similar to those of cefamandole (p.220). It is given intravenously or intramuscularly as the hydrochloride but doses are expressed in terms of the base; 1.14 g of cefotiam hydrochloride is equivalent to about 1 g of cefotiam. The usual dose is the equivalent of up to 6 g of cefotiam daily in divided doses, according to the severity of the infection.

Cefotiam hexetil hydrochloride, a prodrug of cefotiam, is given orally in doses equivalent to 200 to 400 mg of cefotiam twice daily.

◊ References.

1. Brogard JM, *et al.* Clinical pharmacokinetics of cefotiam. *Clin Pharmacokinet* 1989; **17:** 163–74.

Preparations

USP 31: Cefotiam for Injection.

Proprietary Preparations (details are given in Part 3)

Austria: Spizef; ***Fr.:*** Taketiam; Texodil; ***Ger.:*** Spizef; ***Indon.:*** Aspil; Cefradol; Ceradolan; Ethidol; Fodiclo; Fotaram; ***Jpn:*** Pansporin; ***Philipp.:*** Ceradolan; ***Singapore:*** Ceradolan; ***Thai.:*** Ceradolan.

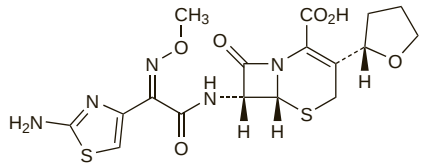
Cefovecin Sodium *(USAN, rINNM)*

Cefovecina sódica; Céfovécine Sodique; Natrii Cefovecinum; UK-287074-02. Sodium (6*R*,7*R*)-7-{[(2*Z*)-(2-aminothiazol-4-yl)(methoxyimino)acetyl]amino}-8-oxo-3-[(2*S*)-tetrahydrofuran-2-yl]-5-thia-1-azabicyclo[4.4.0]oct-2-ene-2-carboxylate.

Натрий Цефовецин

$C_{17}H_{18}N_5NaO_6S_2$ = 475.5.

CAS — 234096-34-5 (cefovecin); 141195-77-9 (cefovecin sodium).



(cefovecin)

Profile

Cefovecin sodium is a third-generation cephalosporin antibacterial used in veterinary medicine.

Cefoxitin Sodium *(BANM, USAN, rINNM)*

Cefoksitino natrio druska; Cefoksytyna sodowa; Cefoxitin sodná sůl; Cefoxitina sódica; Céfoxitine sodique; Cefoxitinnatrium; Cefoxitin-nátrium; Cefoxitinum natricum; Kefoksitiininatrium; L-620388; MK-306; Natrii Cefoxitinum. Sodium 3-carbamoyloxymethyl-7-methoxy-7-[2-(2-thienyl)acetamido]-3-cephem-4-carboxylate.

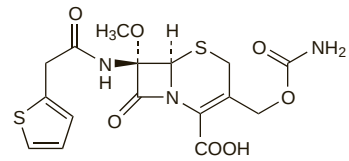
Натрий Цефокситин

$C_{16}H_{16}N_3NaO_7S_2$ = 449.4.

CAS — 35607-66-0 (cefoxitin); 33564-30-6 (cefoxitin sodium).

ATC — J01DC01.

ATC Vet — QJ01DC01.



(cefoxitin)

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Cefoxitin Sodium). A white or almost white, very hygroscopic, powder. Very soluble in water; sparingly soluble in alcohol. A 1% solution in water has a pH between 4.2 and 7.0. Store in airtight containers.
USP 31 (Cefoxitin Sodium). White to off-white, somewhat hygroscopic, granules or powder, having a slight characteristic odour. Very soluble in water; slightly soluble in acetone; insoluble in chloroform and in ether; sparingly soluble in dimethylformamide; soluble in methyl alcohol. pH of a 10% solution in water is between 4.2 and 7.0. Store in airtight containers at a temperature not exceeding 8°.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Cefoxitin may interfere with the Jaffé method of measuring creatinine concentrations to produce falsely high values; this should be borne in mind when measuring renal function.

Breast feeding. Cefoxitin is distributed into breast milk but is detectable only in low concentrations. In a study[1] in which cefoxitin was given prophylactically in doses of 2 to 4 g to 18 women undergoing caesarean section, only one sample of breast milk contained measurable concentrations of cefoxitin, 19 hours after the last dose. No adverse effects have been observed in breast-fed infants whose mothers were receiving cefoxitin, and the American Academy of Pediatrics considers[2] that it is therefore usually compatible with breast feeding.

1. Roex AJM, *et al.* Secretion of cefoxitin in breast milk following short-term prophylactic administration in caesarean section. *Eur J Obstet Gynecol Reprod Biol* 1987; **25:** 299–302.
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)

Effects on the gastrointestinal tract. Marked changes in anaerobic, facultative, and aerobic faecal flora have been noted with cefoxitin.[1]

1. Mulligan ME, *et al.* Alterations in human fecal flora, including ingrowth of Clostridium difficile, related to cefoxitin therapy. *Antimicrob Agents Chemother* 1984; **26:** 343–6.

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

Interactions

Probenecid reduces the renal clearance of cefoxitin.

Antimicrobial Action

Cefoxitin is a cephamycin antibacterial which, like the other beta lactams, is bactericidal and is considered to act through the inhibition of bacterial cell wall synthesis.

It has a similar spectrum of activity to cefamandole (p.221) but is more active against anaerobic bacteria, especially *Bacteroides fragilis*.

Cefoxitin can induce the production of beta-lactamases by some bacteria, and use of cefoxitin with other beta lactams have been shown to be antagonistic *in vitro*.

Cefoxitin itself is considered to be resistant to a wide range of beta-lactamases, including those produced by *Bacteroides* spp. However, acquired resistance to cefoxitin has been reported in *B. fragilis* (see Anaerobic Bacterial Infections, p.163) and has been attributed to beta-lactamase as well as to alterations in penicillin-binding proteins or to outer membrane proteins; there may be cross-resistance to other antibacterials.

◊ References.

1. Cuchural GJ, *et al.* Transfer of β-lactamase-associated cefoxitin resistance in Bacteroides fragilis. *Antimicrob Agents Chemother* 1986; **29:** 918–20.
2. Piddock LJV, Wise R. Cefoxitin resistance in Bacteroides species: evidence indicating two mechanisms causing decreased susceptibility. *J Antimicrob Chemother* 1987; **19:** 161–70.
3. Brogan O, *et al.* Bacteroides fragilis resistant to metronidazole, clindamycin and cefoxitin. *J Antimicrob Chemother* 1989; **23:** 660–2.
4. Wexler HM, Halebian S. Alterations to the penicillin-binding proteins in the Bacteroides fragilis group: a mechanism for non-β-lactamase mediated cefoxitin resistance. *J Antimicrob Chemother* 1990; **26:** 7–20.
5. Cherubin CE, Appleman MD. Susceptibility of cefoxitin-resistant isolates of bacteroides to other agents including β-lactamase inhibitor/β-lactam combinations. *J Antimicrob Chemother* 1993; **32:** 168–70.

Pharmacokinetics

Cefoxitin is not absorbed from the gastrointestinal tract; it is given parenterally as the sodium salt. After 1 g by intramuscular injection a peak plasma concentration of up to 30 micrograms/mL at 20 to 30 minutes has been reported whereas concentrations of 125, 72, and 25 micrograms/mL have been achieved after intravenous doses of 1 g over 3, 30, and 120 minutes respectively. Cefoxitin is about 70% bound to plasma proteins. It has a plasma half-life of 45 to 60 minutes which is prolonged in renal impairment. Cefoxitin is widely distributed in the body but there is normally little penetration into the CSF, even when the meninges are inflamed. It crosses the placenta and has been detected in breast milk. Relatively high concentrations are achieved in bile.

The majority of a dose is excreted unchanged by the kidneys, up to about 2% being metabolised to descarbamylcefoxitin which is virtually inactive. Cefoxitin is excreted in the urine by glomerular filtration and tubular secretion and about 85% of a dose is recovered within 6 hours; probenecid slows this excretion. After an intramuscular dose of 1 g, peak concentrations in the urine are usually greater than 3 mg/mL.

Cefoxitin is removed to some extent by haemodialysis.

Uses and Administration

Cefoxitin is a cephamycin antibacterial that differs structurally from the cephalosporins by the addition of a 7-α-methoxy group to the 7-β-aminocephalosporanic acid nucleus.

It is generally classified with the second-generation cephalosporins and can be used similarly to cefamandole (p.221) for the treatment of susceptible infections. However, because of its activity against *Bacteroides fragilis* and other anaerobic bacteria, it is used principally in the treatment and prophylaxis of anaerobic and mixed bacterial infections, especially intra-abdominal and pelvic infections. Indications include endometritis (prophylaxis at caesarean section), pelvic inflammatory disease, and surgical infection (prophylaxis). It may also be used in the treatment of gonorrhoea and