Cefotaxime and desacetylcefotaxime are widely distributed in body tissues and fluids; therapeutic concentrations are achieved in the CSF particularly when the meninges are inflamed. Cefotaxime crosses the placenta and low concentrations have been detected in breast milk.

After partial metabolism in the liver to desacetylcefotaxime and inactive metabolites, elimination is mainly by the kidneys and about 40 to 60% of a dose has been recovered unchanged in the urine within 24 hours; a further 20% is excreted as the desacetyl metabolite. Relatively high concentrations of cefotaxime and desacetylcefotaxime are achieved in bile and about 20% of a dose has been recovered in the faeces.

Probenecid competes for renal tubular secretion with cefotaxime resulting in higher and prolonged plasma concentrations of cefotaxime and its desacetyl metabolite. Cefotaxime and its metabolites are removed by haemodialysis.

When microbiological assays have been used, reported pharmacokinetic values may relate to cefotaxime plus its active metabolite, desacetylcefotaxime.

Hepatic impairment. References.

1. Höffken G, *et al.* Pharmacokinetics of cefotaxime and desacetylcefotaxime in cirrhosis of the liver. *Chemotherapy* 1984; **30:** 7–17.
2. Graninger W, *et al.* Cefotaxime and desacetyl-cefotaxime blood levels in hepatic dysfunction. *J Antimicrob Chemother* 1984; **14** (suppl B): 143–6.
3. Hary L, *et al.* The pharmacokinetics of ceftriaxone and cefotaxime in cirrhotic patients with ascites. *Eur J Clin Pharmacol* 1989; **36:** 613–16.
4. Ko RJ, *et al.* Pharmacokinetics of cefotaxime and desacetylcefotaxime in patients with liver disease. *Antimicrob Agents Chemother* 1991; **35:** 1376–80.

Renal impairment. References.

1. Matzke GR, *et al.* Cefotaxime and desacetyl cefotaxime kinetics in renal impairment. *Clin Pharmacol Ther* 1985; **38:** 31–6.
2. Paap CM, *et al.* Pharmacokinetics of cefotaxime and its active metabolite in children with renal dysfunction. *Antimicrob Agents Chemother* 1991; **35:** 1879–83.
3. Paap CM, *et al.* Cefotaxime and metabolite disposition in two pediatric continuous ambulatory peritoneal dialysis patients. *Ann Pharmacother* 1992; **26:** 341–3.
4. Paap CM, Nahata MC. The relation between type of renal disease and renal drug clearance in children. *Eur J Clin Pharmacol* 1993; **44:** 195–7.

Uses and Administration

Cefotaxime is a third-generation cephalosporin antibacterial used in the treatment of infections due to susceptible organisms, especially serious and life-threatening infections. They include brain abscess, endocarditis, gonorrhoea, intensive care (selective parenteral and enteral antisepsis regimens), Lyme disease, meningitis, peritonitis (primary or spontaneous), pneumonia, septicaemia, and typhoid fever. It is also used for surgical infection prophylaxis. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Administration and dosage. Cefotaxime is given as the sodium salt by deep intramuscular injection or intravenously by slow injection over 3 to 5 minutes or by infusion over 20 to 60 minutes. Doses are expressed in terms of the equivalent amount of cefotaxime; 1.05 g of cefotaxime sodium is equivalent to about 1 g of cefotaxime. It is usually given in doses of 2 to 6 g daily in 2 to 4 divided doses to adults. In severe infections up to 12 g may be given daily by the intravenous route in up to 6 divided doses; pseudomonal infections usually require more than 6 g daily, but a cephalosporin with greater antipseudomonal activity, such as ceftazidime, is preferable. Children may be given 100 to 150 mg/kg (50 mg/kg for neonates) daily in 2 to 4 divided doses, increased in severe infections to 200 mg/kg (150 to 200 mg/kg for neonates) daily if necessary.

For details of reduced doses to be used in patients with severe renal impairment, see below.

In the treatment of gonorrhoea, a single dose of 0.5 or 1 g of cefotaxime is given.

For surgical infection prophylaxis, 1 g is given 30 to 90 minutes before surgery. At caesarean section, 1 g is given intravenously to the mother as soon as the umbilical cord is clamped and two further doses intramuscularly or intravenously 6 and 12 hours later.

Cefotaxime may be used with an aminoglycoside as synergy may occur against some Gram-negative organisms, but the drugs should be given separately. It has sometimes been used with another beta lactam to broaden the spectrum of activity. Cefotaxime has also been used with metronidazole in the treatment of mixed aerobic-anaerobic infections.

◊ General references to third-generation cephalosporins.

1. Neu HC, *et al.*, eds. Third-generation cephalosporins: a decade of progress in the treatment of severe infections. *Am J Med* 1990; **88** (suppl 4A): 1S–45S.

◊ General references to cefotaxime.

1. Todd PA, Brogden RN. Cefotaxime: an update of its pharmacology and therapeutic use. *Drugs* 1990; **40:** 608–51.
2. Gentry LO. Cefotaxime and prophylaxis: new approaches with a proven agent. *Am J Med* 1990; **88** (suppl 4A): 32S–37S.
3. Davies A, Speller DCE, eds. Cefotaxime—recent clinical investigations. *J Antimicrob Chemother* 1990; **26** (suppl A): 1–83.
4. Brogden RN, Spencer CM. Cefotaxime: a reappraisal of its antibacterial activity and pharmacokinetic properties, and a review of its therapeutic efficacy when administered twice daily for the treatment of mild to moderate infections. *Drugs* 1997; **53:** 483–510.

Administration in renal impairment. Doses of cefotaxime should be reduced in severe renal impairment; after an initial loading dose of 1 g, halving the dose while maintaining the usual frequency of dosing has been suggested.

Preparations

BP 2008: Cefotaxime Injection;
USP 31: Cefotaxime for Injection; Cefotaxime Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Cefacolin; Terasep; Tizoxim†; ***Austral.:*** Claforan†; ***Austria:*** Claforan; Tirotax; ***Belg.:*** Claforan; ***Braz.:*** Cefacolin†; Ceforan; Claforan; Clafordil; Fotax†; Kefoxin†; Taxima; ***Canad.:*** Claforan; ***Chile:*** Grifotaxima†; ***Cz.:*** Cefantral†; Ceftax; Claforan†; Sefotak; Taxcef; ***Denm.:*** Claforan; ***Fin.:*** Claforan; ***Fr.:*** Claforan; ***Ger.:*** Claforan; ***Gr.:*** Ceramil; Ciltiren; Claforan; Flemycin; Letynol; Molelant; Naspor; Phacocef; Solubilax; Spirosine; Stoparen; ***Hong Kong:*** Cetan†; Claforan; Valoran; ***Hung.:*** Cefalekol; Cefotax†; Claforan; Tirotax; ***India:*** Biotax; Claforan; Lyforan; Novatax; Omnatax; Omnicef; Oritaxim; Talcef†; Zetaxim; ***Indon.:*** Baxima; Biocef; Cefor; Cefovell; Cefoxal; Clacef; Claforan; Clatax; Combicef; Efotax; Ethiclaf; Foxim; Goforan; Kalfoxim; Lancef; Lapixime; Procefa; Rycef; Sidaxim; Soclaf; Starclaf; Taxegram; Taximax; Tirdicef; ***Irl.:*** Claforan; ***Israel:*** Claforan; ***Ital.:*** Aximad; Batixim; Cefomit; Centiax; Claforan; Lirgosin; Refotax; Salocef; Spectrocef; Tafocex; Taxime; Xame; Zariviz; Zimanel; ***Malaysia:*** Cetaxima†; Claforan; Claraxim; ***Mex.:*** Benaxima; Biosint; Cefoclin†; Cefotex; Cefradil; Ceftomax; Claforan; Defradil; Fot-Amsa; Fotexina; Sefoxiram; Sepsilem; Taporin; Tebruxim; Tirotax; Viken; Xendin; ***Neth.:*** Claforan; Tirotax; ***Norw.:*** Claforan; ***NZ:*** Claforan; ***Philipp.:*** Cladex; Clafetam; Claforan; Clafoxim; Clavocef; Clinbaxef; Ofetaxim; Pantaxin; Tafoxam; Zefocent; ***Pol.:*** Biotaksym; Rantaksym; Tarcefoksym; Tirotax; ***Port.:*** Antadar; Cefobetox; Forticeporina†; Ralopar; Resibelacta; Totam; ***Rus.:*** Cefosin (Цефосин); Claforan (Клафоран); Intrataxime (Интратаксим); Oritaxim (Оритаксим); Talcef (Талцеф); Tarcefoksym (Тарцефоксим); ***S.Afr.:*** Claforan; Kefotax; Klafotaxim; Reftax; Totam†; ***Singapore:*** Clacef; Claforan; ***Spain:*** Claforan; ***Swed.:*** Claforan; ***Switz.:*** Claforan; ***Thai.:*** Biotaxime†; Cefomic; Ceforan; Cefotax; Ceftaran†; Ceftaxan; Claforan; Claraxim; Fontax; Fortax†; Fotax; Motaxim; Oritaxime†; Valoran†; ***Turk.:*** Betaksim; Claforan; Deforan; Sefagen; Sefoksim; Sefotak; Taxocef; ***UAE:*** Primocef; ***UK:*** Claforan; ***USA:*** Claforan; ***Venez.:*** Baltícina†; Cefam; Cefatox; Cefotas†; Claforan; Novatax; Taxibon†; Tirotax.

Multi-ingredient: ***India:*** Sultax.

Cefotetan *(BAN, USAN, rINN)*

Céfotétan; Cefotetán; Cefotetanum; ICI-156834 (cefotetan or cefotetan disodium); YM-09330 (cefotetan or cefotetan disodium). (7*S*)-7-[(4-Carbamoylcarboxymethylene-1,3-dithietan-2-yl)carboxamido]-7-methoxy-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-3-cephem-4-carboxylic acid.

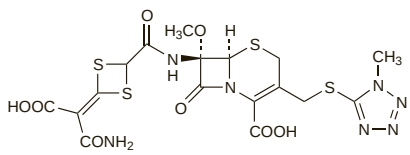
Цефотетан

$C_{17}H_{17}N_7O_8S_4$ = 575.6.

CAS — 69712-56-7.

ATC — J01DC05.

ATC Vet — QJ01DC05.



Pharmacopoeias. In *Jpn* and *US.*
USP 31 (Cefotetan). Store in airtight containers.

Cefotetan Disodium *(BANM, USAN, rINNM)*

Cefotetán disódico; Céfotétan Disodique; Cefotetanum Dinatricum; ICI-156834 (cefotetan or cefotetan disodium); YM-09330 (cefotetan or cefotetan disodium). (7*S*)-7-[(4-Carbamoylcarboxymethylene-1,3-dithietan-2-yl)carboxamido]-7-methoxy-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-3-cephem-4-carboxylic acid, disodium salt.

Динатрий Цефотетан

$C_{17}H_{15}N_7Na_2O_8S_4$ = 619.6.

CAS — 74356-00-6.

ATC — J01DC05.

ATC Vet — QJ01DC05.

Pharmacopoeias. In *US.*
USP 31 (Cefotetan Disodium). pH of a 10% solution in water is between 4.0 and 6.5. Store in airtight containers.

Incompatibility and stability. There may be incompatibility with aminoglycosides. Precipitation has been reported with promethazine hydrochloride.

References.

1. Das Gupta V, *et al.* Chemical stability of cefotetan disodium in 5% dextrose and 0.9% sodium chloride injections. *J Clin Pharm Ther* 1990; **15:** 109–14.
2. Erickson SH, Ulici D. Incompatibility of cefotetan disodium and promethazine hydrochloride. *Am J Health-Syst Pharm* 1995; **52:** 1347.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Cefotetan contains an *N*-methylthiotetrazole side-chain and has the potential to cause hypoprothrombinaemia and bleeding.

Cefotetan, especially at high doses, may interfere with the Jaffé method of measuring creatinine concentrations to produce falsely elevated values; this should be borne in mind when measuring renal function.

Effects on the blood. Reviews[1,2] and a case report[3] of haemolytic anaemia associated with cefotetan.

1. Moes GS, MacPherson BR. Cefotetan-induced hemolytic anemia: a case report and review of the literature. *Arch Pathol Lab Med* 2000; **124:** 1344–6.
2. Viraraghavan R, *et al.* Cefotetan-induced haemolytic anaemia: a review of 85 cases. *Adverse Drug React Toxicol Rev* 2002; **21:** 101–7.
3. Robinson HE, *et al.* Cefotetan-induced life-threatening haemolysis. *Med J Aust* 2006; **184:** 251.

Sodium content. Each g of cefotetan disodium contains about 3.2 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Antimicrobial Action

Cefotetan is a cephamycin antibiotic with a mode of action and spectrum of activity similar to those of cefoxitin (p.230). It is generally much more active *in vitro* than cefoxitin against the Gram-negative Enterobacteriaceae, but has similar activity against *Bacteroides fragilis* and may be less active against some other *Bacteroides* spp.

Pharmacokinetics

On intramuscular injection of cefotetan, peak plasma concentrations of about 70 micrograms/mL at 1 hour and 90 micrograms/mL at 3 hours have been reported after doses of 1 and 2 g, respectively. The plasma half-life of cefotetan is usually in the range of 3.0 to 4.6 hours and is prolonged in patients with renal impairment. About 88% of cefotetan may be bound to plasma proteins, depending on the plasma concentration.

Cefotetan is widely distributed in body tissues and fluids. It crosses the placenta and low concentrations have been detected in breast milk. High concentrations are achieved in bile.

Cefotetan is excreted in the urine, primarily by glomerular filtration, as unchanged drug; 50 to 80% of a dose has been recovered in the urine in 24 hours and high concentrations are achieved. Small amounts of the tautomeric form of cefotetan have been detected in both plasma and urine.

Biliary excretion of cefotetan probably accounts for nonrenal clearance.

Some cefotetan is removed by dialysis.

◊ References.

1. Martin C, *et al.* Clinical pharmacokinetics of cefotetan. *Clin Pharmacokinet* 1994; **26:** 248–58.

Uses and Administration

Cefotetan is a cephamycin antibacterial generally classified with the second-generation cephalosporins and used similarly to cefoxitin (p.230) in the treatment and prophylaxis of anaerobic and mixed bacterial infections, especially intra-abdominal and pelvic infections.

It is given as the disodium salt by deep intramuscular injection or intravenously by slow injection over 3 to 5 minutes or by infusion. Doses are expressed in terms of the equivalent amount of cefotetan; 1.08 g of cefotetan disodium is equivalent to about 1 g of cefotetan. The usual dose is 1 or 2 g every 12 hours. For the treatment of life-threatening infections, 3 g every 12 hours may be given intravenously. Doses of cefotetan should be reduced in patients with moderate to severe renal impairment (see below).