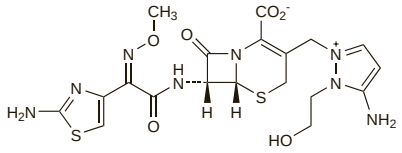
Cefoselis Sulfate *(rINNM)*

Céfosélis, Sulfate de; Cefoselis Sulphate; Cefoselisi Sulfas; FK-037; Sulfato de cefoselís. (−)-5-Amino-2-({(6*R*,7*R*)-7-[2-(2-amino-4-thiazolyl)glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl}methyl)-1-(2-hydroxyethyl)pyrazolium hydroxide, inner salt, 7²-(*Z*)-(*O*-methyloxime) sulfate.

Цефозелиса Сульфат

$C_{19}H_{22}N_8O_6S_2$, H_2SO_4 = 620.6.

CAS — 122841-10-5 (cefoselis); 122841-12-7 (cefoselis sulfate).



(cefoselis)

Profile

Cefoselis sulfate is a cephalosporin antibacterial that has been used in the treatment of susceptible bacterial infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Winceft.

Cefotaxime Sodium *(BANM, USAN, rINNM)*

Cefotaksimo natrio druska; Cefotaksym sodowy; Cefotaxim sodná sůl; Cefotaxima sódica; Céfotaxime sodique; Cefotaximnatrium; Cefotaxim-nátrium; Cefotaximum natricum; CTX; HR-756; Kefotaksiiminatrium; Natrii Cefotaximum; RU-24756; Sefotaksim Sodyum. Sodium (7*R*)-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetamido]cephalosporanate; Sodium (7*R*)-3-acetoxymethyl-7-[(*Z*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetamido]-3-cephem-4-carboxylate.

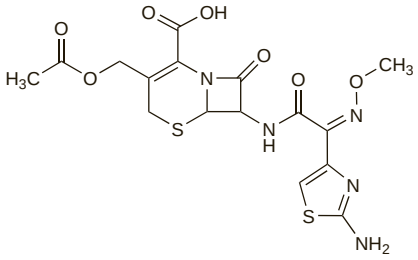
Натрий Цефотаксим

$C_{16}H_{16}N_5NaO_7S_2$ = 477.4.

CAS — 63527-52-6 (cefotaxime); 64485-93-4 (cefotaxime sodium).

ATC — J01DD01.

ATC Vet — QJ01DD01.



(cefotaxime)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefotaxime Sodium). A white or slightly yellow, hygroscopic, powder. Freely soluble in water; sparingly soluble in methyl alcohol. A 10% solution in water has a pH of between 4.5 and 6.5. Store in airtight containers. Protect from light.
USP 31 (Cefotaxime Sodium). An off-white to pale yellow crystalline powder. Freely soluble in water; practically insoluble in organic solvents. pH of a 10% solution in water is between 4.5 and 6.5. Store in airtight containers.

Incompatibility. Cefotaxime sodium has been reported to be incompatible with alkaline solutions such as sodium bicarbonate. Licensed product information recommends that it should be given separately from aminoglycosides.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219. Arrhythmias have been associated with rapid bolus dosage through a central venous catheter in a few cases.

The broad-spectrum third-generation cephalosporins have the potential for colonisation and superinfection with resistant organisms such as *Pseudomonas aeruginosa*, *Enterobacter* spp., *Candida*, and enterococci, at various sites in the body, although the incidence has generally been low with cefotaxime. Changes in bowel flora are a predisposing factor and have been more marked with cefoperazone and ceftriaxone, possibly because of their greater biliary excretion. Pseudomembranous colitis, associated with *Clostridium difficile* infection, may occasionally be seen with any of the third-generation cephalosporins.

◊ Reviews on adverse effects associated with third-generation cephalosporins.

1. Neu HC. Third generation cephalosporins: safety profiles after 10 years of clinical use. *J Clin Pharmacol* 1990; **30:** 396–403.
2. Fekety FR. Safety of parenteral third-generation cephalosporins. *Am J Med* 1990; **88** (suppl 4A): 38S–44S.

Antibiotic-associated colitis. It has been suggested[1] that cefotaxime is associated with an increased risk of *Clostridium difficile* diarrhoea in elderly patients; however, the manufacturer[2] has disputed this, arguing that cefotaxime compares favourably with alternative third-generation cephalosporins.

1. Impallomeni M, *et al.* Increased risk of diarrhoea caused by Clostridium difficile in elderly patients receiving cefotaxime. *BMJ* 1995; **311:** 1345–6.
2. Rothschild E, *et al.* Risk of diarrhoea due to Clostridium difficile during cefotaxime treatment. *BMJ* 1996; **312:** 778.

Breast feeding. Although cefotaxime is excreted in breast milk in small amounts,[1] no adverse effects have been observed in breast-fed infants whose mothers were receiving cefotaxime, and the American Academy of Pediatrics considers[2] that it is therefore usually compatible with breast feeding.

1. Kafetzis DA, *et al.* Passage of cephalosporins and amoxicillin into the breast milk. *Acta Paediatr Scand* 1981; **70:** 285–8.
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)

Sodium content. Each g of cefotaxime sodium contains about 2.09 mmol of sodium.

Interactions

As for many cephalosporins, probenecid reduces the renal clearance of cefotaxime, resulting in higher and prolonged plasma concentrations of cefotaxime and its desacetyl metabolite.

Antibacterials. The total body clearance of cefotaxime has been reduced in patients with normal and reduced renal function by the ureidopenicillins *azlocillin*[1] or *mezlocillin*.[2] Doses of cefotaxime may need to be reduced if either of these penicillins is being given. Encephalopathy with focal motor status and generalised convulsions have been reported in a patient with renal failure given cefotaxime and high doses of azlocillin.[3]

1. Kampf D, *et al.* Kinetic interactions between azlocillin, cefotaxime, and cefotaxime metabolites in normal and impaired renal function. *Clin Pharmacol Ther* 1984; **35:** 214–20.
2. Rodondi LC, *et al.* Influence of coadministration on the pharmacokinetics of mezlocillin and cefotaxime in healthy volunteers and in patients with renal failure. *Clin Pharmacol Ther* 1989; **45:** 527–34.
3. Wroe SJ, *et al.* Focal motor status epilepticus following treatment with azlocillin and cefotaxime. *Med Toxicol* 1987; **2:** 233–4.

Antimicrobial Action

Cefotaxime is a third-generation cephalosporin. It has a bactericidal action similar to cefamandole, but a broader spectrum of activity. It is highly stable to hydrolysis by most beta-lactamases and has greater activity than first- or second-generation cephalosporins against Gram-negative bacteria. Although cefotaxime is generally considered to have slightly less activity than first-generation cephalosporins against Gram-positive bacteria, many streptococci are very sensitive.

Desacetylcefotaxime is an active metabolite of cefotaxime and there may be additive or synergistic effects against some species.

Spectrum of activity. Among Gram-negative bacteria, cefotaxime is active *in vitro* against many Enterobacteriaceae including *Citrobacter* and *Enterobacter* spp., *Escherichia coli*, *Klebsiella* spp., both indole-positive and indole-negative *Proteus*, *Providencia*, *Salmonella*, *Serratia*, *Shigella*, and *Yersinia* spp. Other susceptible Gram-negative bacteria, including penicillin-resistant strains, are *Haemophilus influenzae*, *Moraxella catarrhalis* (*Branhamella catarrhalis*), *Neisseria gonorrhoeae*, and *N. meningitidis*. *Brucella melitensis* is also reported to be moderately sensitive. Some strains of *Pseudomonas* spp. are moderately susceptible to cefotaxime, but most are resistant. Desacetylcefotaxime is active against many of these Gram-negative bacteria, but not against *Pseudomonas* spp.

Among Gram-positive bacteria, cefotaxime is active against staphylococci and streptococci. *Staphylococcus aureus*, including penicillinase-producing strains but not meticillin-resistant *Staph. aureus*, is sensitive. *Staph. epidermidis* is also sensitive but penicillinase-producing strains are resistant. *Streptococcus agalactiae* (group B streptococci), *Str. pneumoniae*, and *Str. pyogenes* (group A streptococci) are all very sensitive although truly penicillin-resistant pneumococci are apparently not sensitive. Enterococci and *Listeria monocytogenes* are resistant.

Cefotaxime is active against some anaerobic bacteria. *Bacteroides fragilis* may be moderately sensitive, but many strains are resistant; synergy has been demonstrated with desacetylcefotaxime *in vitro*. *Clostridium perfringens* is sensitive, but most *Cl. difficile* are resistant.

Other organisms sensitive to cefotaxime include the spirochaete *Borrelia burgdorferi* and *Haemophilus ducreyi*.

Activity with other antimicrobials. In addition to possible synergy or additive effects with desacetylcefotaxime, the activity of cefotaxime may be enhanced by aminoglycosides such as gentamicin; synergy has been demonstrated *in vitro* against Gram-negative bacteria including *Pseudomonas aeruginosa*. There have also been reports of enhanced activity *in vitro* with other antibacterials including fosfomycin and ciprofloxacin and variable results with penicillins.

Resistance may develop during treatment with cefotaxime due to derepression of chromosomally mediated beta-lactamases, and has been reported particularly in *Enterobacter* spp., with multiresistant strains emerging during treatment. This type of resistance has also developed in other bacteria including *Citrobacter*, *Serratia*, and *Pseudomonas* spp. Another mechanism of cefotaxime resistance is the development of plasma-mediated, extended-spectrum beta-lactamases, and this has occurred in *Klebsiella* spp. and also other Enterobacteriaceae. Resistance in *Str. pneumoniae* is due to the production of altered penicillin-binding proteins.

◊ References to the antimicrobial activity of cefotaxime and other third-generation cephalosporins, including the problem of bacterial resistance.

1. Neu HC. Pathophysiologic basis for the use of third-generation cephalosporins. *Am J Med* 1990; **88** (suppl 4A): 3S–11S.
2. Chow JW, *et al.* Enterobacter bacteremia: clinical features and emergence of antibiotic resistance during therapy. *Ann Intern Med* 1991; **115:** 585–90.
3. Sanders CC. New β-lactams: new problems for the internist. *Ann Intern Med* 1991; **115:** 650–1.
4. Thomson KS, *et al.* High-level resistance to cefotaxime and ceftazidime in Klebsiella pneumoniae isolates from Cleveland, Ohio. *Antimicrob Agents Chemother* 1991; **35:** 1001–3.
5. Piddock LJV, *et al.* Prevalence and mechanism of resistance to 'third-generation' cephalosporins in clinically relevant isolates of Enterobacteriaceae from 43 hospitals in the UK, 1990-1991. *J Antimicrob Chemother* 1997; **39:** 177–87.
6. Gums JG, *et al.* Differences between ceftriaxone and cefotaxime: microbiological inconsistencies. *Ann Pharmacother* 2008; **42:** 71–9.

Pharmacokinetics

Cefotaxime is given by injection as the sodium salt. It is rapidly absorbed after intramuscular injection and mean peak plasma concentrations of about 12 and 20 micrograms/mL have been reported 30 minutes after doses of 0.5 and 1 g of cefotaxime, respectively. Immediately after intravenous injection of 0.5, 1, or 2 g of cefotaxime, mean peak plasma concentrations of 38, 102, and 215 micrograms/mL, respectively, have been achieved with concentrations ranging from about 1 to 3 micrograms/mL after 4 hours. The plasma half-life of cefotaxime is about 1 hour and that of the active metabolite desacetylcefotaxime about 1.5 hours; half-lives are increased in neonates and in patients with severe renal impairment, especially those of the metabolite, and a reduction in dosage may be necessary. The effects of liver disease on clearance of cefotaxime and its metabolite have been variable, but in general dosage adjustment has not been considered necessary. About 40% of cefotaxime is reported to be bound to plasma proteins.

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.

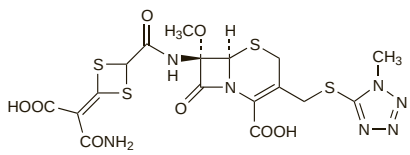
Цефотетан

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