lin-resistant *Staphylococcus aureus*. It is given as the medocaril derivative.

◊ References.

1. Noel GJ. Clinical profile of ceftobiprole, a novel beta-lactam antibiotic. *Clin Microbiol Infect* 2007; **13** (suppl 2): 25–9.
2. Murthy B, Schmitt-Hoffmann A. Pharmacokinetics and pharmacodynamics of ceftobiprole, an anti-MRSA cephalosporin with broad-spectrum activity. *Clin Pharmacokinet* 2008; **47:** 21–33.
3. Zhanel GG, *et al.* Ceftobiprole: a review of a broad-spectrum and anti-MRSA cephalosporin. *Am J Clin Dermatol* 2008; **9:** 245–54.
4. Deresinski SC. The efficacy and safety of ceftobiprole in the treatment of complicated skin and skin structure infections: evidence from 2 clinical trials. *Diagn Microbiol Infect Dis* 2008; **61:** 103–9.
5. Anderson SD, Gums JG. Ceftobiprole: an extended-spectrum anti-methicillin-resistant Staphylococcus aureus cephalosporin. *Ann Pharmacother* 2008; **42:** 806–16.

Ceftriaxone Sodium *(BANM, USAN, rINNM)*

Ceftriakson sodowy; Ceftriaksono natrio druska; Ceftriaxon sodná sůl trihemihydrát; Ceftriaxona sódica; Ceftriaxone sodique; Ceftriaxonnatrium; Ceftriaxon-nátrium; Ceftriaxonum natricum; Ceftriaxonum Natricum Trihemihydricum; Keftriaksoninatrium; Natrii Ceftriaxonum; Ro-13-9904; Ro-13-9904/000 (ceftriaxone); Seftriakson Sodyum. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[(2,5-dihydro-6-hydroxy-2-methyl-5-oxo-1,2,4-triazin-3-yl)thiomethyl]-3-cephem-4-carboxylic acid, disodium salt, sesquaterhydrate.

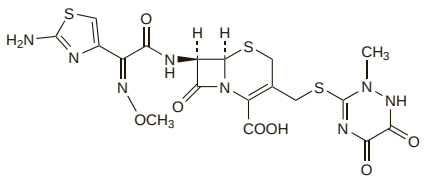
Натрий Цефтриаксон

$C_{18}H_{16}N_8Na_2O_7S_3,3H_2O$ = 661.6.

CAS — 73384-59-5 (ceftriaxone); 74578-69-1 (anhydrous ceftriaxone sodium); 104376-79-6 (ceftriaxone sodium sesquaterhydrate).

ATC — J01DD04.

ATC Vet — QJ01DD04.



(ceftriaxone)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Ceftriaxone Sodium). A semi-synthetic product derived from a fermentation product. An almost white to yellowish, slightly hygroscopic, crystalline powder. Freely soluble in water; very slightly soluble in dehydrated alcohol; sparingly soluble in methyl alcohol. A 12% solution in water has a pH of 6.0 to 8.0. Store in airtight containers. Protect from light.

USP 31 (Ceftriaxone Sodium). A white to yellowish-orange crystalline powder. Freely soluble in water; very slightly soluble in alcohol; sparingly soluble in methyl alcohol. pH of a 10% solution in water is between 6.0 and 8.0. Store in airtight containers.

Incompatibility. UK licensed product information warns of incompatibility if ceftriaxone sodium is mixed with calcium-containing solutions or with aminoglycosides, amsacrine, fluconazole, labetalol, or vancomycin. Published reports of incompatibility have included that between ceftriaxone and vancomycin[1] or pentamidine.[2]

1. Pritts D, Hancock D. Incompatibility of ceftriaxone with vancomycin. *Am J Hosp Pharm* 1991; **48:** 77.
2. Lewis JD, El-Gendy A. Cephalosporin-pentamidine isethionate incompatibilities. *Am J Health-Syst Pharm* 1996; **53:** 1461–2.

Stability. References.

1. Nahata MC. Stability of ceftriaxone sodium in peritoneal dialysis solutions. *DICP Ann Pharmacother* 1991; **25:** 741–2.
2. Canton E, Esteban MJ. Stability of ceftriaxone solution. *J Antimicrob Chemother* 1992; **30:** 397–8.
3. Bailey LC, *et al.* Stability of ceftriaxone sodium in injectable solutions stored frozen in syringes. *Am J Hosp Pharm* 1994; **51:** 2159–61.
4. Plumridge RJ, *et al.* Stability of ceftriaxone sodium in polypropylene syringes at −20, 4, and 20°C. *Am J Health-Syst Pharm* 1996; **53:** 2320–3.

Adverse Effects and Precautions

As for Cefotaxime Sodium, p.228.

Changes in bowel flora may be more marked than with cefotaxime because of the greater biliary excretion of ceftriaxone; diarrhoea may occur more often, especially in children. Biliary sludge or pseudolithiasis due to a precipitate of calcium ceftriaxone has been seen occasionally in patients given ceftriaxone. Similarly, deposition of the calcium salt has occurred rarely in the urine. Isolated cases of death in term or premature neonates have been associated with precipitation of calcium ceftriaxone in lungs and kidneys, and in some of these cases a calcium-containing product has been given by a different route or line, or at a different time. US licensed product information therefore contra-indicates the use of ceftriaxone within 48 hours of products or solutions containing calcium, particularly in neonates. Ceftriaxone is highly protein bound and is able to displace bilirubin from albumin binding sites, causing hyperbilirubinaemia; its use should be avoided in jaundiced neonates.

Neutropenia has been reported with most cephalosporins; a complex mechanism has been attributed to that associated with ceftriaxone. There have been rare reports of fatal haemolysis associated with ceftriaxone.

Although ceftriaxone has an *N*-methylthiotriazine ring rather than an *N*-methylthiotetrazole side-chain, it might still have the potential to cause hypoprothrombinaemia.

Breast feeding. A study of drug distribution and protein binding between maternal blood and breast milk post partum in a 26-year-old woman given ceftriaxone 2 g daily by intravenous infusion for 10 days found that penetration of ceftriaxone into breast milk increased at these doses as protein binding capacity was saturated, although no adverse effects occurred in the infant.[1] The authors advised caution in breast-feeding mothers given acidic drugs which also have high protein binding such as ceftriaxone[1] although, on the basis that no adverse effects have been observed in breast-fed infants whose mothers were receiving ceftriaxone, the American Academy of Pediatrics considers[2] that it is therefore usually compatible with breast feeding.

1. Bourget P, *et al.* Ceftriaxone distribution and protein binding between maternal blood and milk postpartum. *Ann Pharmacother* 1993; **27:** 294–7.
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 biliary tract. Using abdominal ultrasonography, biliary sludge or pseudolithiasis was found in about 40% of severely ill children being treated with high doses of ceftriaxone[1] and was later reported in adults.[2-4] The sludge has been identified as a calcium salt of ceftriaxone.[5] Patients are often asymptomatic and the sludge usually dissolves once ceftriaxone is stopped. Gallstones with ceftriaxone as a major component have been identified in a patient given long-term high-dose treatment.[6] Similarly, a bile-duct stone composed of ceftriaxone occurred with high-dose ceftriaxone in a child.[7] In another report, intractable hiccups were associated with ceftriaxone-related pseudolithiasis in a 10-year-old boy.[8]

1. Schaad UB, *et al.* Reversible ceftriaxone-associated biliary pseudolithiasis in children. *Lancet* 1988; **ii:** 1411–13.
2. Pigrau C, *et al.* Ceftriaxone-associated biliary pseudolithiasis in adults. *Lancet* 1989; **ii:** 165.
3. Heim-Duthoy KL, *et al.* Apparent biliary pseudolithiasis during ceftriaxone therapy. *Antimicrob Agents Chemother* 1990; **34:** 1146–9.
4. Bickford CL, Spencer AP. Biliary sludge and hyperbilirubinemia associated with ceftriaxone in an adult: case report and review of the literature. *Pharmacotherapy* 2005; **25:** 1389–95.
5. Park HZ, *et al.* Ceftriaxone-associated gallbladder sludge: identification of calcium-ceftriaxone salt as a major component of gallbladder precipitate. *Gastroenterology* 1991; **100:** 1665–70.
6. Lopez AJ, *et al.* Ceftriaxone-induced cholelithiasis. *Ann Intern Med* 1991; **115:** 712–14.
7. Robertson FM, *et al.* Ceftriaxone choledocholithiasis. *Pediatrics* 1996; **98:** 133–5.
8. Bonioli E, *et al.* Pseudolithiasis and intractable hiccups in a boy receiving ceftriaxone. *N Engl J Med* 1994; **331:** 1532.

Effects on the blood. References.

1. Haubenstock A, *et al.* Hypoprothrombinaemic bleeding associated with ceftriaxone. *Lancet* 1983; **i:** 1215–16.
2. Rey D, *et al.* Ceftriaxone-induced granulopenia related to a peculiar mechanism of granulopoiesis inhibition. *Am J Med* 1989; **87:** 591–2.
3. Bernini JC, *et al.* Fatal hemolysis induced by ceftriaxone in a child with sickle cell anemia. *J Pediatr* 1995; **126:** 813–15.
4. Lascari AD, Amyot K. Fatal hemolysis caused by ceftriaxone. *J Pediatr* 1995; **126:** 816–17.
5. Scimeca PG, *et al.* Hemolysis after treatment with ceftriaxone. *J Pediatr* 1996; **128:** 163.
6. Moallem HJ, *et al.* Ceftriaxone-related fatal hemolysis in an adolescent with perinatally acquired human immunodeficiency virus infection. *J Pediatr* 1998; **133:** 279–81.
7. Meyer O, *et al.* Fatal immune haemolysis due to a degradation product of ceftriaxone. *Br J Haematol* 1999; **105:** 1084–5.
8. Viner Y, *et al.* Severe hemolysis induced by ceftriaxone in a child with sickle-cell anemia. *Pediatr Infect Dis J* 2000; **19:** 83–5.
9. Seltsam A, Salama A. Ceftriaxone-induced immune haemolysis: two case reports and a concise review of the literature. *Intensive Care Med* 2000; **26:** 1390–4.
10. Citak A, *et al.* Ceftriaxone-induced haemolytic anaemia in a child with no immune deficiency or haematological disease. *J Paediatr Child Health* 2002; **38:** 209–10.

Effects on the pancreas. References.

1. Zimmermann AE, *et al.* Ceftriaxone-induced acute pancreatitis. *Ann Pharmacother* 1993; **27:** 36–7.
2. Maranan MC, *et al.* Gallstone pancreatitis caused by ceftriaxone. *Pediatr Infect Dis J* 1998; **17:** 662–3.

Neonates. References to the displacement of bilirubin by ceftriaxone in neonates.

1. Gulian J-M, *et al.* Bilirubin displacement by ceftriaxone in neonates: evaluation by determination of 'free' bilirubin and erythrocyte-bound bilirubin. *J Antimicrob Chemother* 1987; **19:** 823–9.
2. Fink S, *et al.* Ceftriaxone effect on bilirubin-albumin binding. *Pediatrics* 1987; **80:** 873–5.

Sodium content. Each g of ceftriaxone sodium contains about 3.0 mmol of sodium.

Interactions

Ceftriaxone has an *N*-methylthiotriazine side-chain and may have the potential to increase the effects of anticoagulants and to cause a disulfiram-like reaction with alcohol.

Unlike many cephalosporins, probenecid does not affect the renal excretion of ceftriaxone.

Antimicrobial Action

As for Cefotaxime Sodium, p.228, although ceftriaxone has no active metabolite.

◊ References.

1. Goldstein FW, *et al.* Resistance to ceftriaxone and other β-lactams in bacteria isolated in the community. *Antimicrob Agents Chemother* 1995; **39:** 2516–19.

Pharmacokinetics

Ceftriaxone demonstrates nonlinear dose-dependent pharmacokinetics because of its protein binding; about 85 to 95% is bound to plasma proteins depending on the concentration of ceftriaxone.

Mean peak plasma concentrations of about 40 and 80 micrograms/mL have been reported 2 hours after intramuscular injection of 0.5 and 1 g of ceftriaxone respectively. The plasma half-life of ceftriaxone is not dependent on the dose and varies between 6 and 9 hours; it may be prolonged in neonates. The half-life does not change appreciably in patients with moderate renal impairment, but it may be prolonged in severe impairment especially when there is also hepatic impairment.

Ceftriaxone is widely distributed in body tissues and fluids. It crosses both inflamed and non-inflamed meninges, generally achieving therapeutic concentrations in the CSF. It crosses the placenta and low concentrations have been detected in breast milk. High concentrations are achieved in bile.

About 40 to 65% of a dose of ceftriaxone is excreted unchanged in the urine, principally by glomerular filtration; the remainder is excreted in the bile and is ultimately found in the faeces as unchanged drug and microbiologically inactive compounds.

◊ Reviews.

1. Hayton WL, Stoeckel K. Age-associated changes in ceftriaxone pharmacokinetics. *Clin Pharmacokinet* 1986; **11:** 76–86.
2. Yuk JH, *et al.* Clinical pharmacokinetics of ceftriaxone. *Clin Pharmacokinet* 1989; **17:** 223–35.
3. Perry TR, Schentag JJ. Clinical use of ceftriaxone: a pharmacokinetic-pharmacodynamic perspective on the impact of minimum inhibitory concentration and serum protein binding. *Clin Pharmacokinet* 2001; **40:** 685–94.

Hepatic impairment. References.

1. Stoeckel K, *et al.* Single-dose ceftriaxone kinetics in liver insufficiency. *Clin Pharmacol Ther* 1984; **36:** 500–9.
2. Hary L, *et al.* The pharmacokinetics of ceftriaxone and cefotaxime in cirrhotic patients with ascites. *Eur J Clin Pharmacol* 1989; **36:** 613–16.
3. Toth A, *et al.* Pharmacokinetics of ceftriaxone in liver-transplant recipients. *J Clin Pharmacol* 1991; **31:** 722–8.

Pregnancy. References.

1. Bourget P, *et al.* Pharmacokinetics and protein binding of ceftriaxone during pregnancy. *Antimicrob Agents Chemother* 1993; **37:** 54–9.

Renal impairment. The pharmacokinetics of ceftriaxone are not markedly altered in mild to moderate renal impairment,[1] but the half-life can be prolonged in severe or end-stage renal disease.[1-4] Ceftriaxone is generally not removed by peritoneal dialysis[4] or by haemodialysis[1-3] although a decrease in half-life has been reported during haemodialysis.[5] In many patients no alteration in dosage is necessary, but some individuals have reduced non-renal clearance despite apparently normal hepatic function.[2,3] It is advisable to monitor plasma ceftriaxone in

patients with severe renal impairment and unknown non-renal clearance.

1. Patel IH, *et al.* Ceftriaxone pharmacokinetics in patients with various degrees of renal impairment. *Antimicrob Agents Chemother* 1984; **25:** 438–42.
2. Stoeckel K, *et al.* Single-dose ceftriaxone kinetics in functionally anephric patients. *Clin Pharmacol Ther* 1983; **33:** 633–41.
3. Cohen D, *et al.* Pharmacokinetics of ceftriaxone in patients with renal failure and in those undergoing hemodialysis. *Antimicrob Agents Chemother* 1983; **24:** 529–32.
4. Ti T-Y, *et al.* Kinetic disposition of intravenous ceftriaxone in normal subjects and patients with renal failure on hemodialysis or peritoneal dialysis. *Antimicrob Agents Chemother* 1984; **25:** 83–7.
5. Garcia RL, *et al.* Single-dose pharmacokinetics of ceftriaxone in patients with end-stage renal disease and hemodialysis. *Chemotherapy* 1988; **34:** 261–6.

Uses and Administration

Ceftriaxone is a third-generation cephalosporin antibacterial used similarly to cefotaxime for the treatment of susceptible infections. They include chancroid, endocarditis, gastro-enteritis (invasive salmonellosis; shigellosis), gonorrhoea, Lyme disease, meningitis (including meningococcal meningitis prophylaxis), pneumonia, septicaemia, syphilis, typhoid fever, and Whipple's disease. 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. Ceftriaxone is given as the sodium salt by slow intravenous injection over at least 2 to 4 minutes, by intermittent intravenous infusion over at least 30 minutes, or by deep intramuscular injection. If more than 1 g is to be injected intramuscularly then the dose should be divided between more than one site. Doses are expressed in terms of the equivalent amount of ceftriaxone; 1.19 g of ceftriaxone sodium is equivalent to about 1 g of ceftriaxone. The usual adult dose is 1 to 2 g daily as a single dose or in two divided doses; in severe infections up to 4 g daily may be given. Doses for infants and children (under 50 kg) are 20 to 50 mg/kg once daily; for severe infections up to 80 mg/kg daily may be given. In neonates, the maximum dose should not exceed 50 mg/kg daily; intravenous doses in neonates should be given over 60 minutes. Doses above 50 mg/kg should be given by intravenous infusion only.

A single intramuscular dose of 250 mg is recommended for the treatment of uncomplicated gonorrhoea.

For surgical infection prophylaxis, a single dose of 1 g may be given 0.5 to 2 hours before surgery; a 2-g dose is suggested before colorectal surgery.

For the prevention of secondary cases of meningococcal meningitis, a single intramuscular dose of 250 mg may be used for adults and 125 mg for children.

◊ References.

1. Brogden RN, Ward A. Ceftriaxone: a reappraisal of its antibacterial activity and pharmacokinetic properties, and an update on its therapeutic use with particular reference to once-daily administration. *Drugs* 1988; **35:** 604–45.
2. Lamb HM, *et al.* Ceftriaxone: an update of its use in the management of community-acquired and nosocomial infections. *Drugs* 2002; **62:** 1041–89.
3. Bijie H, *et al.* In vitro activity, pharmacokinetics, clinical efficacy, safety and pharmacoeconomics of ceftriaxone compared with third and fourth generation cephalosporins: review. *J Chemother* 2005; **17:** 3–24.

Administration in hepatic and renal impairment. A reduction in dosage of ceftriaxone may be necessary in patients with severe renal impairment (creatinine clearance below 10 mL/minute), in whom the daily dose should not exceed 2 g. In patients undergoing dialysis, and in those with both renal and hepatic impairment, plasma concentrations of ceftriaxone should be monitored to determine whether dose adjustment is needed.

Preparations

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

Proprietary Preparations (details are given in Part 3)
Arg.: Acantex; Bioteral; Cefomax; Ceftriaz†; Exempla; Rivacefin; Soltrimox; ***Austral.:*** Rocephin; ***Austria:*** Exogran; Rocephin; ***Belg.:*** Rocephine; ***Braz.:*** Amplospec†; Bioteral†; Ceft†; Ceftriax; Glicocef; Mesporan; Neoceftriona; Prodoxin; Rocefin; Rofoxin†; Triaxon; Triaxton; Trioxina; ***Canad.:*** Rocephin; ***Chile:*** Acantex; Grifotriaxona; ***Cz.:*** Cefaxone†; Lendacin; Longaceph†; Megion; Novosef†; Oframax†; Rocephin†; Samixon; ***Denm.:*** Cefotrix; Rocephalin; ***Fin.:*** Rocephalin; ***Fr.:*** Rocephine; ***Ger.:*** Cefotrix; Rocephin; ***Gr.:*** Antibacin; Azatyl; Bresec; Ceftrixon; Farcef; Gladius; Glorixone; Labilex; Medaxone; Rocephin; Rolisporin; Travilan; Ugotrex; Veracol; ***Hong Kong:*** Medaxonum; Mesporin; Rocephin; ***Hung.:*** Cefotrix; Lendacin; Megion; Rocephin; ***India:*** Cefocef; Ciplacef; Lyceft; Monocef; Monotax; Oframax; Powercef; Stericef†; ***Indon.:*** Biotriax; Bioxon; Broadced; Brospec; Cefaxon; Cefriex; Ceftrox; Cefxon; Cephaflox; Criax; Ecotrixon; Elpicef; Erocef; Foricef; Intrix; Rocephin; Socef; Starxon; Terfacef; Termicef; Tricefin; Trijec; Tyason; Zeftrix; ***Irl.:*** Rocephin; ***Israel:*** Keftriaxon; Rocephin; Triax; ***Ital.:*** Axobat; Bixon; Davixon; Daytrix; Deixim; Eftry; Fidato; Frineg; Iliaxone; Kappacef; Kocefan; Monoxar; Nilson; Panatrix; Pantoxon; Ragex; Rocefin; Setriox; Sirtap; Valexime; ***Jpn:*** Rocephin; ***Malaysia:*** Cefaxone; Ceftrex; Eftriax; Mesporin; Rocephin; Trixone; ***Mex.:*** Amcef; Aurofox; Axtar; Benaxona; Cefaxona; Cefraden; Ceftrex; Ceftrilem; Centrifal; Limiprol; Megion; Primotox; Rocephin; Tacex; Terbac; Triaken; Triox; Xonatil; ***Neth.:*** Elfaxone; Exogran; Lopratin; Rocephin; ***Norw.:*** Rocephalin; ***NZ:*** Rocephin; ***Philipp.:*** Acrexon; CEF-3; Cikedrix; Cryaxon; Eurosef; Fenadef; Forgram; Keptrix; Megion; Monocrin; Noxoram; Pantrixon; Retrokor; Rocephin; Roxon; Samjizon; Sergimax; Trixophin; Xtenda; ***Pol.:*** Biotrakson; Lendacin; Rocephin; Tartriakson; ***Port.:*** Betasporina; Ceriax; Kemudin; Mesporin; Rocephin; ***Rus.:*** Azaran (Азаран); Ceftrifin (Цефтрифин); Ificef (Ифицеф); Lendacin (Лендацин); Loraxone (Лораксон); Medaxone (Медаксон); Novosef (Новосеф); Oframax (Офрамакс); Stericef (Стерицеф); Tercef (Терцеф); Torocef (Торацеф); ***S.Afr.:*** Fraxone†; Oframax; Rocephin; Rociject; ***Singapore:*** Antibacin; Cefaxone; Cefin†; Oframax; Rocephin; Trexofin; Tricefin; ***Spain:*** Rocefalin; ***Swed.:*** Rocephalin; ***Switz.:*** Rocephine; ***Thai.:*** CEF-3; Cef-Zone; Cefine†; Ceftrex; Ceftriphin; Lephin†; Oframax; Rinxofay; Rocephin; Sedalin†; Triacef; Tricephin; Trixone; Zefaxone; ***Turk.:*** Baktisef; Cefaday; Cephaxon; Desefin; Equiceft; Forsef; Iesef; Nevakson; Novosef; Rocephin; Unacefin; ***UAE:*** Triaxone; ***UK:*** Rocephin; ***USA:*** Rocephin; ***Venez.:*** Bioceftrax; Cefin; Cefix; Ceftrialin; Ciplacef; Eftrival; Felident†; Megion; Rocephin; Strixone; Tricefi.

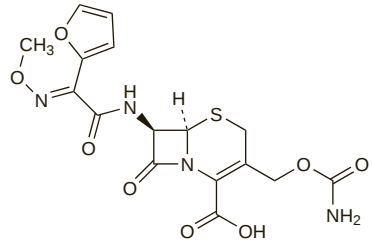
Multi-ingredient: ***India:*** Axone; Dibact†; Keftragard.

Cefuroxime *(BAN, USAN, rINN)*

640/359; Cefuroxim; Cefuroxima; Céfuroxime; Cefuroximum; Kefuroksiimi; Sefuroksim. (*Z*)-3-Carbamoyloxymethyl-7-[2-(2-furyl)-2-methoxyiminoacetamido]-3-cephem-4-carboxylic acid.

Цефуроксим

$C_{16}H_{16}N_4O_8S$ = 424.4.
CAS — 55268-75-2.
ATC — J01DC02.
ATC Vet — QJ01DC02; QJ51DA06.



Cefuroxime Axetil *(BANM, USAN, rINNM)*

CCI-15641; Cefuroksimas aksetilas; Cefuroksymu aksetyl; Cefuroxima axetilo; Cefuroximaxetil; Cefuroxim-axetil; Céfuroxime axétil; Céfuroxime, Axétil de; Cefuroximi Axetilum; Cefuroximum axetili; Cefuroximum Axetilum; Kefuroksiimiaksetiili; Sefuroksim Aksetil.

Цефуроксима Аксетил

$C_{20}H_{22}N_4O_{10}S$ = 510.5.
CAS — 64544-07-6.
ATC — J01DC02.
ATC Vet — QJ01DC02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefuroxime Axetil). A white or almost white powder. Slightly soluble in water and in alcohol; soluble in acetone, in ethyl acetate, and in methyl alcohol. Store in airtight containers. Protect from light.
USP 31 (Cefuroxime Axetil). A mixture of the diastereoisomers of cefuroxime axetil. A white or almost white powder. The amorphous form is insoluble in water and in ether; slightly soluble in dehydrated alcohol; freely soluble in acetone; soluble in chloroform, in ethyl acetate, and in methyl alcohol. The crystalline form is insoluble in water and in ether; slightly soluble in dehydrated alcohol; freely soluble in acetone; sparingly soluble in chloroform, in ethyl acetate, and in methyl alcohol. Store in airtight containers.

Cefuroxime Sodium *(BANM, rINNM)*

Cefuroksimo natrio druska; Cefuroksym sodowy; Cefuroxim sodná sůl; Cefuroxima sódica; Céfuroxime sodique; Cefuroximnatrium; Cefuroxim-nátrium; Cefuroximum natricum; Kefuroksiiminatrium; Natrii Cefuroximum; Sefuroksim Sodyum.

Натрий Цефуроксим

$C_{16}H_{15}N_4NaO_8S$ = 446.4.
CAS — 56238-63-2.
ATC — J01DC02.
ATC Vet — QJ01DC02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefuroxime Sodium). A white or almost white slightly hygroscopic powder. Freely soluble in water; very slightly soluble in alcohol. A 1% solution in water has a pH of 5.5 to 8.5. Store in airtight containers.
USP 31 (Cefuroxime Sodium). A white or faintly yellow powder. Freely soluble in water; very slightly soluble in alcohol, in chloroform, in ether, and in ethyl acetate; soluble in methyl alcohol. pH of a 10% solution in water is between 6.0 and 8.5. Store in airtight containers.

Incompatibility and stability. Cefuroxime sodium may be incompatible with aminoglycosides.

References.
1. Barnes AR. Chemical stabilities of cefuroxime sodium and metronidazole in an admixture for intravenous infusion. *J Clin Pharm Ther* 1990; **15:** 187–96.
2. Stiles ML, *et al.* Stability of ceftazidime (with arginine) and of cefuroxime sodium in infusion-pump reservoirs. *Am J Hosp Pharm* 1992; **49:** 2761–4.
3. Hebron B, Scott H. Shelf life of cefuroxime eye-drops when dispensed in artificial tear preparations. *Int J Pharm Pract* 1993; **2:** 163–7.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Gastrointestinal disturbances, including diarrhoea, nausea, and vomiting, have occurred in some patients receiving cefuroxime axetil. There have been rare reports of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Mild to moderate hearing loss has been reported in some children given cefuroxime for the treatment of meningitis.

Antibiotic-associated colitis. For reports of pseudomembranous colitis associated with cefuroxime axetil, see Cefalotin, p.219.

Hypersensitivity. A report[1] of a serum sickness-like reaction to cefuroxime. Similar reactions have occurred with cefaclor (p.217), although it is unclear whether they represent a class effect.

1. Katta R, Anusuri V. Serum sickness-like reaction to cefuroxime: a case report and review of the literature. *J Drugs Dermatol* 2007; **6:** 747–8.

Porphyria. Cefuroxime is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

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

Interactions

Probenecid reduces the renal clearance of cefuroxime.

Antimicrobial Action

Cefuroxime is bactericidal and has a similar spectrum of antimicrobial action and pattern of resistance to those of cefamandole (p.221). It is more resistant to hydrolysis by beta-lactamases than cefamandole, and therefore may be more active against beta-lactamase-producing strains of, for example, *Haemophilus influenzae* and *Neisseria gonorrhoeae*. However, treatment failures have occurred in patients with *H. influenzae* meningitis given cefuroxime and might be associated with a relatively high minimum bactericidal concentration when compared with the minimum inhibitory concentration or with a significant inoculum effect. Reduced affinity of penicillin-binding proteins for cefuroxime has also been reported to be responsible for resistance in a beta-lactamase-negative strain of *H. influenzae*.

◊ References.

1. Arditi M, *et al.* Cefuroxime treatment failure and Haemophilus influenzae meningitis: case report and review of literature. *Pediatrics* 1989; **84:** 132–5.
2. Mendelman PM, *et al.* Cefuroxime treatment failure of nontypable Haemophilus influenzae meningitis associated with alteration of penicillin-binding proteins. *J Infect Dis* 1990; **162:** 1118–23.
3. Brown NM, *et al.* Cefuroxime resistance in Haemophilus influenzae. *Lancet* 1992; **340:** 552.

Pharmacokinetics

Cefuroxime axetil is absorbed from the gastrointestinal tract and is rapidly hydrolysed in the intestinal mucosa and blood to cefuroxime; absorption is enhanced in the presence of food. Peak plasma concentrations are reported about 2 to 3 hours after an oral dose. The sodium salt is given by intramuscular or intravenous injection. Peak plasma concentrations of about 27 micrograms/mL have been achieved 45 minutes after an intramuscular dose of 750 mg with measurable amounts present 8 hours after a dose. Up to 50% of cefuroxime in the circulation is bound to plasma proteins. The plasma half-life is about 70 minutes and is pro-