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.

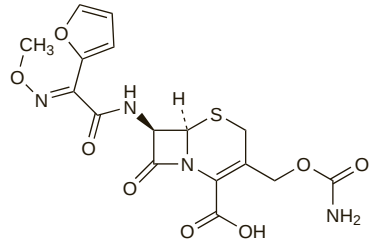
Multi-ingredient: ***India:*** Axone; Dibact†; Keftragard.

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-