2. Ferrara N, *et al.* Neurotoxicity induced by cefepime in a very old hemodialysis patient. *Clin Nephrol* 2003; **59:** 388–90.
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10. Garces EO, *et al.* Renal failure is a risk factor for cefepime-induced encephalopathy. *J Nephrol* 2008; **21:** 526–34.

Antimicrobial Action

Cefepime is a fourth-generation cephalosporin and is active against a wide range of Gram-positive and Gram-negative aerobic organisms. Against Gram-positive cocci, its activity is similar to that of cefotaxime (p.228) and includes staphylococci (but not meticillin-resistant *Staphylococcus aureus*) and streptococci. Against Enterobacteriaceae, it has a broader spectrum of activity than other cephalosporins, including activity against organisms producing chromosomally mediated beta-lactamases such as *Enterobacter* spp. and *Proteus vulgaris*. Against *Pseudomonas aeruginosa*, it has similar or slightly less activity than ceftazidime (p.234), although it may be active against some strains resistant to ceftazidime.

Pharmacokinetics

Cefepime is given by injection as the hydrochloride. It is rapidly and almost completely absorbed on intramuscular injection and mean peak plasma concentrations of about 14 and 30 micrograms/mL have been reported about 1.5 hours after doses of 500 mg and 1 g respectively. Within 30 minutes of similar intravenous doses, peak plasma concentrations of about 40 and 80 micrograms/mL are achieved. The plasma half-life of cefepime is about 2 hours and is prolonged in patients with renal impairment. About 20% of cefepime is bound to plasma proteins.

Cefepime is widely distributed in body tissues and fluids. High concentrations are achieved in bile. Low concentrations have been detected in breast milk.

Cefepime is eliminated principally by the kidneys and about 85% of a dose is recovered unchanged in the urine. Cefepime is substantially removed by haemodialysis.

◊ References.

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2. Rybak M. The pharmacokinetic profile of a new generation of parenteral cephalosporin. *Am J Med* 1996; **100** (suppl 6A): 39S–44S.
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Uses and Administration

Cefepime is a fourth-generation cephalosporin antibacterial used in the treatment of infections due to susceptible organisms. They include infections of the urinary tract, respiratory tract, and skin. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Cefepime is given as the hydrochloride by deep intramuscular injection, or intravenously by infusion over at least 30 minutes. Doses are expressed in terms of the equivalent amount of cefepime; 1.19 g of cefepime hydrochloride is equivalent to about 1 g of cefepime. The usual adult dose is 1 to 2 g daily in 2 divided doses for mild to moderate infections, increased to 4 g daily in 2 divided doses in severe infections, although up to 6 g daily in 3 divided doses has been given for febrile neutropenia. Children aged over 2 months and weighing up to 40 kg may be given 50 mg/kg twice daily; this dose may be given 3 times daily for febrile neutropenia.

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

◊ Reviews.

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2. Barradell LB, Bryson HM. Cefepime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1994; **47:** 471–505.
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4. Wynd MA, Paladino JA. Cefepime: a fourth-generation parenteral cephalosporin. *Ann Pharmacother* 1996; **30:** 1414–24.
5. Wong-Beringer A. Treating serious infections: focus on cefepime. *Pharmacotherapy* 2004; **24:** 216S–23S.
6. Roberts JA, *et al.* Cefepime versus ceftazidime: considerations for empirical use in critically ill patients. *Int J Antimicrob Agents* 2007; **29:** 117–28.

Administration in renal impairment. Dosage of cefepime should be modified in renal impairment. After a normal first dose the maintenance dosage should be adjusted according to the patient's creatinine clearance (CC) and the severity of the infection:

- CC 30 to 60 mL/minute: 0.5 to 2 g every 24 hours (2 g every 12 hours for febrile neutropenia)
- CC 11 to 29 mL/minute: 0.5 to 1 g every 24 hours (2 g every 24 hours for febrile neutropenia)
- CC 10 mL/minute or less: 250 to 500 mg every 24 hours (1 g every 24 hours for febrile neutropenia)

Patients undergoing haemodialysis should be given a dose of 1 g on the first day of treatment, followed by 500 mg daily; the dose should be given after haemodialysis on those days. A dose of 1 g daily should be used for febrile neutropenia. Patients undergoing continuous ambulatory peritoneal dialysis should receive normal recommended doses at intervals of 48 hours. A dose of 2 g every 48 hours is used for febrile neutropenia.

Preparations

USP 31: Cefepime for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Cefimen-K; Maxcef; Rivepime; ***Austral.:*** Maxipime; ***Austria:*** Maxipime; ***Belg.:*** Maxipime; ***Braz.:*** Cefepen†; Cemax†; Clocef; Maxcef; Maxil†; ***Canad.:*** Maxipime; ***Chile:*** Maxipime; ***Cz.:*** Maxipime; ***Denm.:*** Maxipime†; ***Fin.:*** Maxipime; ***Fr.:*** Axepim; ***Ger.:*** Maxipime; ***Gr.:*** Anticepim; Gencef; Maxinject; Maxipime; Verapime; Zefipime; ***Hong Kong:*** Maxipime; ***Hung.:*** Maxipime; ***India:*** Biopime; Cefica; Forpar; ***Indon.:*** Exepime; Maxicef; Maxipime; Procepim; Sandocef; ***Irl.:*** Maxipime†; ***Israel:*** Maxcef†; ***Ital.:*** Cepim; Cepimex; Maxipime; ***Malaysia:*** Maxipime; ***Mex.:*** Maxipime; ***NZ:*** Maxipime; ***Philipp.:*** Cepimax; ***Pol.:*** Maxipime; ***Port.:*** Maxipime; ***Rus.:*** Maxipime (Максипим); ***S.Afr.:*** Maxipime; ***Singapore:*** Maxipime; ***Spain:*** Maxipime; ***Swed.:*** Maxipime; ***Switz.:*** Maxipime; ***Thai.:*** Maxipime; ***Turk.:*** Maxipime; ***USA:*** Maxipime; ***Venez.:*** Maxipime.

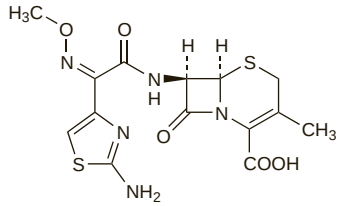
Cefetamet *(USAN, rINN)*

Céfétamet; Cefetametum; LY-097964; Ro-15-8074. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-methyl-3-cephem-4-carboxylic acid.

Цефетамет

$C_{14}H_{15}N_5O_5S_2$ = 397.4.

CAS — 65052-63-3 (cefetamet).
ATC — J01DD10.
ATC Vet — QJ01DD10.



Cefetamet Pivoxil Hydrochloride *(rINNM)*

Céfétamet Pivoxil, Chlorhydrate de; Cefetameti Pivoxili Hydrochloridum; Cefetametpivoxilhydroklorid; Cefetametum Pivoxili Hydrochloridum; Hidrocloruro de cefetamet pivoxilo; Kefetameettipivoksiilihydrokloridi; Ro-15-8075 (cefetamet pivoxil). Cefetamet pivaloyloxymethyl hydrochloride.

Цефетамета Пивоксила Гидрохлорид

$C_{20}H_{25}N_5O_7S_2$,HCl = 548.0.

CAS — 65243-33-6 (cefetamet pivoxil); 111696-23-2 (cefetamet pivoxil hydrochloride).
ATC — J01DD10.
ATC Vet — QJ01DD10.

Profile

Cefetamet is a third-generation cephalosporin antibacterial similar to cefixime (below). It has been given orally as the hydrochloride of the pivaloyloxymethyl ester, cefetamet pivoxil hydrochloride, which is hydrolysed to cefetamet *in vivo*. The usual dose is 500 mg twice daily.

For reference to carnitine deficiency occurring with some pivaloyloxymethyl esters, see Pivampicillin, p.317.

◊ Reviews.

1. Bryson HM, Brogden RN. Cefetamet pivoxil: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1993; **45:** 589–621.
2. Blouin RA, Stoeckel K. Cefetamet pivoxil clinical pharmacokinetics. *Clin Pharmacokinet* 1993; **25:** 172–88.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Globocef†; ***Ger.:*** Globocef†; ***Hong Kong:*** Globocef†; ***Ital.:*** Globocef†; ***Pol.:*** Tarcevis†; ***Port.:*** Cefec†; Globocef†; ***Switz.:*** Globocef†.

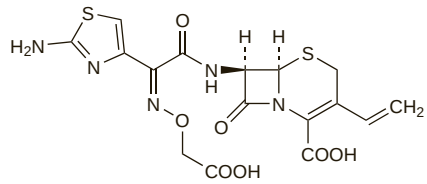
Cefixime *(BAN, USAN, rINN)*

Cefiksimas; Cefixim; Cefixim trihydrát; Cefixima; Céfixime; Cefiximum; Cefiximum Trihydricum; CL-284635; FK-027; FR-17027; Kefiksiimi; Sefiksim. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-(carboxymethoxyimino)acetamido]-3-vinyl-3-cephem-4-carboxylic acid trihydrate.

Цефиксим

$C_{16}H_{15}N_5O_7S_2$,3H_2O = 507.5.

CAS — 79350-37-1.
ATC — J01DD08.
ATC Vet — QJ01DD08.



Pharmacopoeias. In *Eur.* (see p.vii) and *US. Jpn* includes the anhydrous substance.

Ph. Eur. 6.2 (Cefixime). A white or almost white, slightly hygroscopic, powder. Slightly soluble in water; sparingly soluble in dehydrated alcohol; practically insoluble in ethyl acetate; freely soluble in methyl alcohol. A 5% suspension in water has a pH of 2.6 to 4.1. Store in airtight containers. Protect from light.

USP 31 (Cefixime). A white to light yellow crystalline powder. Practically insoluble in water, in ether, in ethyl acetate, and in hexane; slightly soluble in alcohol, in acetone, and in glycerol; soluble in methyl alcohol and in propylene glycol; very slightly soluble in 70% sorbitol and in octanol. pH of a solution in water containing the equivalent of cefixime 0.07% is between 2.6 and 4.1. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

The most frequently reported adverse effects of cefixime are gastrointestinal disturbances, especially diarrhoea. Cefixime should be stopped if diarrhoea is severe.

Although cefixime does not have the *N*-methylthiotetrazole side-chain usually associated with hypoprothrombinaemia increases in prothrombin times have occurred in a few patients.

Antibiotic-associated colitis. For reports of diarrhoea and pseudomembranous colitis associated with cefixime, see Cefalotin, p.219.

Interactions

Care should be exercised in patients receiving anticoagulants and cefixime due to the possibility that cefixime may increase prothrombin times (see above).

Antimicrobial Action

Cefixime is bactericidal and is stable to hydrolysis by many beta-lactamases. It has a mode of action and spectrum of activity similar to those of the third-generation cephalosporin cefotaxime (p.228), but some Enterobacteriaceae are less susceptible to cefixime. *Haemophilus influenzae*, *Moraxella catarrhalis* (*Branhamella catarrhalis*), and *Neisseria gonorrhoeae* are sensitive, including penicillinase-producing strains. Of the Gram-positive bacteria, streptococci are