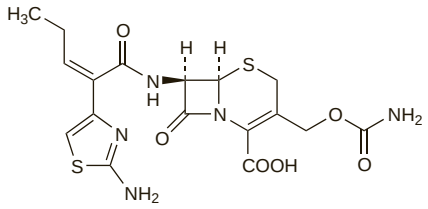
Cefcapene Pivoxil Hydrochloride *(rINNM)*

Cefcapène Pivoxil, Chlorhydrate de; Cefcapeni Pivoxili Hydrochloridum; Hidrocloruro de cefcapeno pivoxilo. Pivaloyloxymethyl (+)-(6*R*,7*R*)-7-[(*Z*)-2-(2-amino-4-thiazolyl)-2-pentenamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid carbamate monohydrochloride monohydrate.

Цефкапена Пивоксила Гидрохлорид

$C_{23}H_{29}N_5O_8S_2,HCl,H_2O$ = 622.1.

CAS — 135889-00-8 (cefcapene); 105889-45-0 (cefcapene pivoxil); 147816-23-7 (anhydrous cefcapene pivoxil hydrochloride); 147816-24-8 (cefcapene pivoxil hydrochloride);.



(cefcapene)

Pharmacopoeias. In *Jpn.*

Profile

Cefcapene is an oral cephalosporin antibacterial given orally as the pivaloyloxymethyl ester, cefcapene pivoxil hydrochloride.

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

Preparations

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

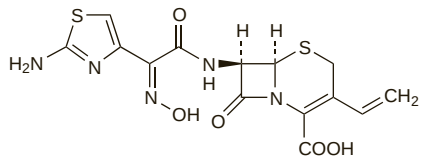
Cefdinir *(BAN, USAN, rINN)*

Cefdinirum; CI-983; FK-482; Kefdiniiri. (–)-(6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7^2-(*Z*)-oxime; 7-{(2-Amino-1,3-thiazol-4-yl)-2-[(*Z*)-hydroxyimino]acetamido}-3-vinylcephem-4-carboxylic acid.

Цефдинир

$C_{14}H_{13}N_5O_5S_2$ = 395.4.

CAS — 91832-40-5.
ATC — J01DD15.
ATC Vet — QJ01DD15.



Pharmacopoeias. In *Chin.* and *Jpn*.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219. There have been reports of reddish stools in patients given cefdinir with iron supplements (see also Interactions, below).

Interactions

Absorption of cefdinir is decreased by antacids or iron supplements and doses should be separated by an interval of at least 2 hours. Probenecid reduces the renal excretion of cefdinir.

Iron. A report[1] of red stools in an infant given cefdinir whilst being fed with an infant formula containing supplemental iron. It was considered important to be aware of the interaction because of the risk that it might be mistaken for a sign of gastrointestinal bleeding.

1. Lancaster J, *et al.* Nonbloody, red stools from coadministration of cefdinir and iron-supplemented infant formulas. *Pharmacotherapy* 2008; **28:** 678–81.

Antimicrobial Action

As for Cefixime, p.224. However, cefdinir is reported to be much more active *in vitro* than cefixime against *Staphylococcus aureus*, but not meticillin-resistant strains, and it is less active against some Enterobacteriaceae.

Pharmacokinetics

Cefdinir is absorbed from the gastrointestinal tract after oral doses, peak plasma concentrations occurring 2 to 4 hours after a dose. Oral bioavailability has been estimated to range from 16 to 25%. It is widely distributed into tissues and is 60 to 70% bound to plasma proteins. Cefdinir is not appreciably metabolised and is excreted in the urine with an elimination half-life of 1.7 hours.

Cefdinir is removed by dialysis.

Uses and Administration

Cefdinir is a third-generation oral cephalosporin antibacterial with actions and uses similar to those of cefixime (p.224). It is given orally in a usual adult dose of 600 mg daily as a single dose or in two divided doses. Children may be given 14 mg/kg daily up to a maximum of 600 mg daily. Doses may need to be reduced in patients with renal impairment (see below).

◊ Reviews.

1. Guay DRP. Cefdinir: an expanded-spectrum oral cephalosporin. *Ann Pharmacother* 2000; **34:** 1469–77.
2. Guay DR, *et al.* Cefdinir: an advanced-generation, broad-spectrum oral cephalosporin. *Clin Ther* 2002; **24:** 473–89.
3. Perry CM, Scott LJ. Cefdinir: a review of its use in the management of mild-to-moderate bacterial infections. *Drugs* 2004; **64:** 1433–64.
4. Sader HS, Jones RN. Cefdinir: an oral cephalosporin for the treatment of respiratory tract infections and skin and skin structure infections. *Expert Rev Anti Infect Ther* 2007; **5:** 29–43. Correction. *ibid.*; 754. [dose error]

Administration in renal impairment. Doses of cefdinir should be reduced to 300 mg once daily in patients with renal impairment whose creatinine clearance is less than 30 mL/minute.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Kefnir†; Sefdin; ***Jpn:*** Cefzon; ***Mex.:*** Omnicef; ***Thai.:*** Omnicef; ***USA:*** Omnicef.

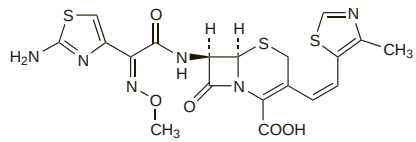
Cefditoren Pivoxil *(rINNM)*

Cefditorène, Pivoxil de; Cefditoreni Pivoxil; Cefditoreno pivoxilo; ME-1207; ME-1206 (cefditoren). Pivaloyloxymethyl (+)-(6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-3-[(*Z*)-2-(4-methyl-5-thiazolyl)vinyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid 7^2-(*Z*)-(*O*-methyloxime).

Цефдиторена Пивоксил

$C_{25}H_{28}N_6O_7S_3$ = 620.7.

CAS — 104145-95-1 (cefditoren); 117467-28-4 (cefditoren pivoxil).
ATC — J01DD16.
ATC Vet — QJ01DD16.



(cefditoren)

Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

As for Cefalotin, p.219.

The most frequently reported adverse effects of cefditoren are gastrointestinal disturbances, especially diarrhoea.

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

Interactions

Absorption of cefditoren after oral doses is decreased by antacids or histamine H_2-receptor antagonists. Probenecid reduces the renal excretion of cefditoren.

Antimicrobial Action

As for Cefixime, p.224. Cefditoren also has activity against *Staphylococcus aureus.*

Pharmacokinetics

Cefditoren pivoxil is absorbed from the gastrointestinal tract and is hydrolysed to cefditoren by esterases to release active cefditoren in the bloodstream. Peak plasma concentrations average 1.8 micrograms/mL in fasting subjects 1.5 to 3 hours after a 200-mg dose. Bioavailability is about 14% in fasting subjects and is increased when cefditoren pivoxil is given with a high-fat meal. Plasma protein binding is reported to be 88%. The plasma half-life is about 1.6 hours and is prolonged in patients with renal impairment.

Cefditoren is not appreciably metabolised and is excreted mainly in the urine by glomerular filtration and tubular secretion. It is removed by haemodialysis.

Uses and Administration

Cefditoren is a cephalosporin antibacterial with a broad spectrum of activity used in the treatment of susceptible infections, particularly of the respiratory tract and skin. It is given orally as the pivaloyloxymethyl ester, cefditoren pivoxil, but doses are expressed in terms of cefditoren; 245 mg of cefditoren pivoxil is equivalent to about 200 mg of cefditoren. A usual dose is 200 to 400 mg given twice daily.

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

◊ Reviews.

1. Wellington K, Curran MP. Cefditoren pivoxil: a review of its use in the treatment of bacterial infections. *Drugs* 2004; **64:** 2597–2618.

Administration in renal impairment. Doses of cefditoren pivoxil should be reduced in patients with moderate to severe renal impairment according to creatinine clearance (CC):

- CC 30 to 49 mL/minute: the dose should not exceed 200 mg twice daily
- CC less than 30 mL/minute: the dose should be 200 mg once daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Gr.: Spectracef; ***India:*** Cefditran; ***Indon.:*** Meiact; ***Jpn:*** Meiact; ***Mex.:*** Spectracef; ***Port.:*** Meiact; Spectracef; ***Spain:*** Meiact; Spectracef; Telo; ***Thai.:*** Meiact; ***Turk.:*** Spektracef; ***USA:*** Spectracef.

Cefepime Hydrochloride

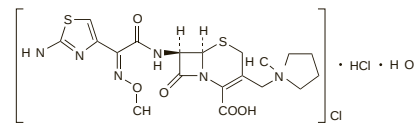
(BANM, USAN, rINNM)

BMY-28142 (cefepime); Céfépime, Chlorhydrate de; Céfépime, dichlorhydrate de; Cefepimi dihydrochloridum; Cefepimi Hydrochloridum; Hidrocloruro de cefepima; Sefepim Hidroklorür. {6*R*-[6α,7β(*Z*)]}-1-[(7-{[(2-Amino-4-thiazolyl)-(methoxyimino)acetyl]amino}-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl)methyl]-1-methylpyrrolidinium chloride monohydrochloride monohydrate; 7-{(2-Amino-1,3-thiazol-4-yl)-2-[(*Z*)-methoxyimino]acetamido}-3-(1-methylpyrrolidiniomethyl)-3-cephem-4-carboxylate hydrochloride.

Цефепима Гидрохлорид

$C_{19}H_{25}ClN_6O_5S_2,HCl,H_2O$ = 571.5.

CAS — 88040-23-7 (cefepime); 123171-59-5 (cefepime hydrochloride monohydrate).
ATC — J01DE01.
ATC Vet — QJ01DE01.



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

Ph. Eur. 6.2 (Cefepime Dihydrochloride Monohydrate). A white or almost white, crystalline powder. Freely soluble in water and in methyl alcohol; practically insoluble in dichloromethane. Protect from light.

USP 31 (Cefepime Hydrochloride). A white to off-white, non-hygroscopic, crystalline powder. Freely soluble in water. Store in airtight containers. Protect from light.

Incompatibility and stability. References.

1. Stewart JT, *et al.* Stability of cefepime hydrochloride injection in polypropylene syringes at –20°C, 4°C, and 22-24°C. *Am J Health-Syst Pharm* 1999; **56:** 457–9.
2. Stewart JT, *et al.* Stability of cefepime hydrochloride in polypropylene syringes. *Am J Health-Syst Pharm* 1999; **56:** 1134.
3. Williamson JC, *et al.* Stability of cefepime in peritoneal dialysis solution. *Ann Pharmacother* 1999; **33:** 906–9.
4. Baririan N, *et al.* Stability and compatibility study of cefepime in comparison with ceftazidime for potential administration by continuous infusion under conditions pertinent to ambulatory treatment of cystic fibrosis patients and to administration in intensive care units. *J Antimicrob Chemother* 2003; **51:** 651–8.
5. Trissel LA, Xu QA. Stability of cefepime hydrochloride in AutoDose infusion system bags. *Ann Pharmacother* 2003; **37:** 804–7.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

◊ The safety of cefepime has been reviewed.[1-3] A meta-analysis[2] of studies involving cefepime suggested that there might be an increased risk of all-cause mortality compared with other beta-lactams. The FDA subsequently announced that it would review safety data to further evaluate the risk of death associated with cefepime use.[4]

1. Neu HC. Safety of cefepime: a new extended-spectrum parenteral cephalosporin. *Am J Med* 1996; **100** (suppl 6A): 68S–75S.
2. Yahav D, *et al.* Efficacy and safety of cefepime: a systematic review and meta-analysis. *Lancet Infect Dis* 2007; **7:** 338–48.
3. Drago L, De Vecchi E. The safety of cefepime in the treatment of infection. *Expert Opin Drug Saf* 2008; **7:** 377–87.
4. FDA. Early communication about an ongoing safety review: cefepime (marketed as Maxipime) (issued 14th November 2007). Available at: http://www.fda.gov/cder/drug/early_comm/cefepime.htm (accessed 04/08/08)

Effects on the nervous system. References to neurotoxicity, sometimes manifesting as nonconvulsive status epilepticus, associated with use of cefepime (particularly but not exclusively in patients with impaired renal function).

1. Chow KM, *et al.* Retrospective review of neurotoxicity induced by cefepime and ceftazidime. *Pharmacotherapy* 2003; **23:** 369–73.