Adverse Effects and Precautions
As for Cefalotin Sodium, p.219.

The most frequently reported adverse effects of ceftibuten are gastrointestinal disturbances, especially diarrhoea, and headache.

Antimicrobial Action
As for Cefixime, p.224. It is less active *in vitro* against *Streptococcus pneumoniae*.

◊ References.

1. Shawar R, *et al.* Comparative in vitro activity of ceftibuten (Sch-39720) against bacterial enteropathogens. *Antimicrob Agents Chemother* 1989; **33:** 781–4.
2. Bragman SGL, Casewell MW. The in-vitro activity of ceftibuten against 475 clinical isolates of Gram-negative bacilli, compared with cefuroxime and cefadroxil. *J Antimicrob Chemother* 1990; **25:** 221–6.
3. Wise R, *et al.* Ceftibuten—in-vitro activity against respiratory pathogens, β-lactamase stability and mechanism of action. *J Antimicrob Chemother* 1990; **26:** 209–13.
4. Maioli E, *et al.* In vitro activity of ceftibuten at sub-inhibitory concentrations in comparison with other antibiotics against respiratory and urinary tract pathogens. *J Chemother* 2007; **19:** 152–60.

Pharmacokinetics
Ceftibuten is rapidly absorbed from the gastrointestinal tract, although the rate and extent of absorption are somewhat decreased by the presence of food. Peak plasma concentrations of about 17 micrograms/mL are attained about 2 hours after a 400-mg dose. The plasma half-life of ceftibuten is about 2.0 to 2.3 hours and is prolonged in patients with renal impairment. Ceftibuten is 65 to 77% bound to plasma proteins.

Ceftibuten distributes into middle-ear fluid and bronchial secretions. About 10% of a dose is converted to the *trans*-isomer, which has about one-eighth of the activity of the *cis*-isomer. Ceftibuten is excreted mainly in the urine and also in the faeces. Significant amounts are removed by haemodialysis.

Uses and Administration
Ceftibuten is a third-generation cephalosporin antibacterial used similarly to cefixime (p.225) in the treatment of urinary-tract and respiratory-tract infections. It is given orally as the dihydrate, but doses are expressed in terms of anhydrous ceftibuten; 435 mg of ceftibuten dihydrate is equivalent to about 400 mg of anhydrous ceftibuten. The usual adult dose is 400 mg once daily on an empty stomach. Children over 6 months of age and weighing 45 kg or less may be given 9 mg/kg daily as a single dose. For reduced doses in patients with moderate to severe renal impairment, see below.

◊ Reviews.

1. Wiseman LR, Balfour JA. Ceftibuten: review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. *Drugs* 1994; **47:** 784–808.
2. Nelson JD, McCracken GH (eds). Ceftibuten: a new orally active cephalosporin for pediatric infections. *Pediatr Infect Dis J* 1995; **14** (suppl): S76–S133.
3. Guay DRP. Ceftibuten: a new expanded-spectrum oral cephalosporin. *Ann Pharmacother* 1997; **31:** 1022–33.
4. Owens RC, *et al.* Ceftibuten: an overview. *Pharmacotherapy* 1997; **17:** 707–20.

Administration in renal impairment. Doses of ceftibuten should be reduced in patients with moderate to severe renal impairment. The following doses based on creatinine clearance (CC) may be used:

- CC 30 to 49 mL/minute: 200 mg once daily
- CC 5 to 29 mL/minute: 100 mg once daily

Patients undergoing haemodialysis 2 or 3 times weekly may be given a dose of 400 mg after each dialysis session.

Preparations
Proprietary Preparations (details are given in Part 3)

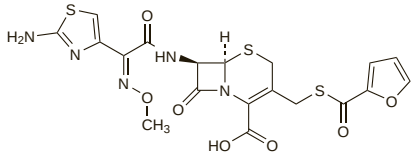
Arg.: Cedax†; Sepex†; ***Austria:*** Caedax†; ***Cz.:*** Cedax†; ***Ger.:*** Keimax; ***Gr.:*** Caedax†; ***Hong Kong:*** Cedax; ***Hung.:*** Cedax; ***India:*** Procadax; ***Israel:*** Cedax; ***Ital.:*** Cedax; Isocef; ***Jpn:*** Seftem; ***Malaysia:*** Cedax; ***Mex.:*** Cedax; ***Neth.:*** Cedax; ***Philipp.:*** Cedax; ***Pol.:*** Cedax; ***Port.:*** Caedax; ***Rus.:*** Cedax (Цедекс); ***S.Afr.:*** Cedax†; Sepexin†; ***Singapore:*** Cedax; ***Spain:*** Biocef; Cedax; Cepifran†; ***Swed.:*** Cedax; ***Switz.:*** Cedax; ***Thai.:*** Cedax; ***USA:*** Cedax; ***Venez.:*** Cedax; Sepexin†.

Ceftiofur Hydrochloride *(BANM, USAN, rINNM)*
Ceftiofur, Chlorhydrate de; Ceftiofuri Hydrochloridum; Hidrocloruro de ceftiofur; U-64279A. (6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)-glyoxylamido]-3-mercaptomethyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7²-(*Z*)-(*O*-methyloxime), 2-furoate (ester), monohydrochloride.

Цефтиофура Гидрохлорид

$C_{19}H_{17}N_5O_7S_3.HCl$ = 560.0.

CAS — 80370-57-6 (ceftiofur); 103980-44-5 (ceftiofur hydrochloride).



(ceftiofur)

Ceftiofur Sodium *(BANM, USAN, rINNM)*
Ceftiofur sódico; Ceftiofur sodique; Ceftiofurum natricum; CM-31-916; Natrii Ceftiofurum; U-64279E.

Натрий Цефтиофур

$C_{19}H_{16}N_5NaO_7S_3$ = 545.5.

CAS — 104010-37-9.

Profile
Ceftiofur is a cephalosporin antibacterial used as the hydrochloride and sodium salts in veterinary practice.

Ceftizoxime Sodium *(BANM, USAN, rINNM)*
Ceftizoxima sódica; Ceftizoxime Sodique; Ceftizoximnatrium; Ceftizoximum Natricum; FK-749; FR-13749; Keftitsoksiiminatrium; Natrii Ceftizoximum; Seftizoksim Sodyum; SKF-88373-Z. Sodium (*Z*)-7-[2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-cephem-4-carboxylate.

Натрий Цефтизоксим

$C_{13}H_{12}N_5NaO_5S_2$ = 405.4.

CAS — 68401-81-0 (ceftizoxime); 68401-82-1 (ceftizoxime sodium).

ATC — J01DD07.

ATC Vet — QJ01DD07.

Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Ceftizoxime Sodium). A white to pale yellow crystalline powder. Freely soluble in water. pH of a 10% solution in water is between 6.0 and 8.0. Store in airtight containers.

Stability. References.

1. Lesko AB, *et al.* Ceftizoxime stability in iv solutions. *DICP Ann Pharmacother* 1989; **23**: 615–18.

Adverse Effects and Precautions
As for Cefotaxime Sodium, p.228.

Sodium content. Each g of ceftizoxime sodium contains about 2.5 mmol of sodium.

Interactions
Probenecid reduces the renal clearance of ceftizoxime.

Antimicrobial Action
As for Cefotaxime Sodium, p.228, although ceftizoxime has no active metabolite.

Pharmacokinetics
After intramuscular injection of 0.5 and 1 g of ceftizoxime, mean peak plasma concentrations of about 14 and 39 micrograms/mL respectively have been reported after 1 hour. The plasma half-life of ceftizoxime is about 1.7 hours and is prolonged in neonates and in renal impairment. Ceftizoxime is 30% bound to plasma proteins.

Ceftizoxime is widely distributed in body tissues and fluids; therapeutic concentrations are achieved in the CSF when the meninges are inflamed. It crosses the placenta and low concentrations have been detected in breast milk.

Nearly all of a dose is excreted unchanged in the urine within 24 hours of dosage, thus achieving high urinary concentrations. Ceftizoxime is excreted by tubular secretion as well as glomerular filtration and giving it with probenecid results in higher and more prolonged plasma concentrations. Some ceftizoxime is removed by haemodialysis.

Neonates. References.

1. Fujii R. Investigation of half-life and clinical effects of ceftizoxime in premature and newborn infants. *Drug Invest* 1990; **2:** 143–9.
2. Reed MD, *et al.* Ceftizoxime disposition in neonates and infants during the first six months of life. *DICP Ann Pharmacother* 1991; **25:** 344–7.

Uses and Administration
Ceftizoxime is a third-generation cephalosporin antibacterial used similarly to cefotaxime (p.229) for the treatment of susceptible infections.

It is given as the sodium salt by deep intramuscular injection, or intravenously as a slow injection over 3 to 5 minutes or as a continuous or intermittent infusion. If 2 g of ceftizoxime is injected intramuscularly the dose should be divided between sites.

Doses are expressed in terms of the equivalent amount of ceftizoxime; 1.06 g of ceftizoxime sodium is equivalent to about 1 g of ceftizoxime. It is usually given in an adult dose of 1 to 2 g every 8 to 12 hours. In severe infections 2 to 4 g may be given intravenously every 8 hours; doses up to 2 g every 4 hours have been given in life-threatening infections.

Children over 6 months of age may be given 50 mg/kg every 6 to 8 hours.

For the treatment of uncomplicated urinary-tract infections, a dose of 500 mg every 12 hours is used.

For details of reduced doses in patients with renal impairment, see below.

A single intramuscular dose of 1 g has been given in uncomplicated gonorrhoea.

◊ References.

1. Richards DM, Heel RC. Ceftizoxime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1985; **29:** 281–329.

Administration in renal impairment. Doses of ceftizoxime should be modified in renal impairment; after a loading dose of 0.5 to 1 g, the maintenance dosage should be adjusted according to creatinine clearance (CC) and the severity of the infection:

- CC 50 to 79 mL/minute: 0.5 to 1.5 g every 8 hours
- CC 5 to 49 mL/minute: 0.25 to 1 g every 12 hours
- CC less than 5 mL/minute: 250 to 500 mg every 24 hours or 0.5 to 1 g every 48 hours, after dialysis.

Preparations
USP 31: Ceftizoxime for Injection; Ceftizoxime Injection.

Proprietary Preparations (details are given in Part 3)

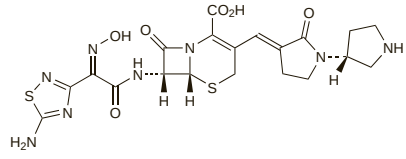
Arg.: Ceftix†; Ceftizon†; ***Canad.:*** Cefizox; ***Cz.:*** Cefizox†; ***Fr.:*** Cefizox†; ***India:*** Cefizox; ***Indon.:*** Cefizox; Tizos; ***Ital.:*** Eposerin; ***Jpn:*** Epocelin†; ***Mex.:*** Cefizox†; ***Neth.:*** Cefizox; ***Philipp.:*** Tergecin; Unizox; ***Port.:*** Cefizox; ***Turk.:*** Cefizox; ***USA:*** Cefizox.

Ceftobiprole Medocaril *(USAN, rINN)*
BAL-5788; BAL-5788-001; BAL-9141 (ceftobiprole); Ceftobiprol Medocarilo; Ceftobiprole Médocaril; Ceftobiprolum Medocarilum; Ro-65-5788; Ro-63-9141 (ceftobiprole). (6*R*,7*R*)-7-[(2*Z*)-2-(5-Amino-1,2,4-thiadiazol-3-yl)-2-(hydroxyimino)acetamido]-3-((*E*){(3′*R*)-1′-[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxycarbonyl]-2-oxo-(1,3′-bipyrrolidin)-3-ylidene}methyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

Цефтобипрол Медокарил

$C_{26}H_{26}N_8O_{11}S_2$ = 690.7.

CAS — 209467-52-7 (ceftobiprole); 376653-43-9 (ceftobiprole medocaril); 252188-71-9 (ceftobiprole medocaril sodium).



(ceftobiprole)

Profile
Ceftobiprole is a broad-spectrum cephalosporin that is being tried in the treatment of susceptible infections, including meticil-