ble in alcohol; sparingly soluble or slightly soluble in dichloromethane. Protect from light.

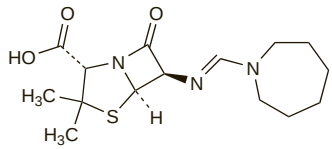
Profile
Marbofloxacin is a fluoroquinolone antibacterial used in veterinary medicine.

Mecillinam *(BAN, rINN)*

Amdinocillin *(USAN)*; FL-1060; Mecilinam; Mécillinam; Mecillinamum; Mesillinaami; Ro-10-9070. (6*R*)-6-(Perhydroazepin-1-ylmethyleneamino)penicillanic acid.

Мециллинам

$C_{15}H_{23}N_3O_3S$ = 325.4.
CAS — 32887-01-7.
ATC — J01CA11.
ATC Vet — QJ01CA11.



Adverse Effects and Precautions
As for Benzylpenicillin, p.213.

Porphyria. Mecillinam has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions
As for Benzylpenicillin, p.214.

Antimicrobial Action
Mecillinam is a derivative of amidinopenicillanic acid. Unlike benzylpenicillin and related antibiotics, it is active against many Gram-negative bacteria, in particular Enterobacteriaceae including *Escherichia coli*, *Enterobacter*, *Klebsiella*, *Salmonella*, and *Shigella* spp. The susceptibility of *Proteus* spp. varies; *Serratia marcescens* is generally resistant. It is less active against *Neisseria* spp. and *Haemophilus influenzae*. *Pseudomonas aeruginosa* and *Bacteroides* spp. are considered to be resistant. It is much less active against Gram-positive bacteria; enterococci including *Enterococcus faecalis* are resistant.

Mecillinam interferes with the synthesis of the bacterial cell wall by binding with a different penicillin-binding protein from benzylpenicillin. This difference in mode of action may explain the synergism against many Gram-negative organisms that has been reported *in vitro* between mecillinam and various penicillins or cephalosporins.

Mecillinam is inactivated by beta-lactamases, but is more stable than ampicillin.

Pharmacokinetics
Mecillinam is poorly absorbed from the gastrointestinal tract. Peak plasma concentrations of about 6 and 12 micrograms/mL have been achieved half an hour after intramuscular doses of 200 and 400 mg, respectively. The usual plasma half-life of about 1 hour has been reported to be prolonged to 3 to 5 hours or more in severe renal impairment. Between 5 and 10% of mecillinam is bound to plasma proteins. Mecillinam is widely distributed into body tissues and fluids; little passes into the CSF unless the meninges are inflamed. It crosses the placenta into the fetal circulation; little appears to be distributed into breast milk.

Mecillinam is metabolised to only a limited extent. From 50 to 70% of a parenteral dose may be excreted in the urine within 6 hours by glomerular filtration and tubular secretion. Renal tubular secretion can be reduced by probenecid. Some mecillinam is excreted in bile where high concentrations are achieved.

Mecillinam is removed by haemodialysis.

Uses and Administration
Mecillinam is a semisynthetic penicillin with a substituted amidino group at the 6-position of the penicillanic acid nucleus. It is given by slow intravenous injection, by intravenous infusion, or intramuscularly, in the treatment of susceptible Gram-negative infections (see under Antimicrobial Action, above).

For urinary-tract infections a dose of 800 mg is given every 6 to 8 hours. A total dose of up to 60 mg/kg daily may be used in very severe infections.

Mecillinam has been used with other beta lactams to extend the spectrum of antimicrobial activity to Gram-positive organisms and because of reported synergism against Gram-negative bacteria *in vitro*.

The pivaloyloxymethyl ester of mecillinam, pivmecillinam, is used orally (see p.317).

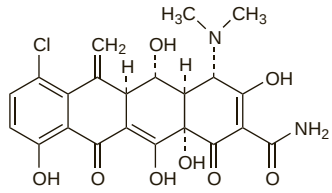
Preparations
Proprietary Preparations (details are given in Part 3)
Denm.: Selexid; ***Gr.:*** Selexid; ***Norw.:*** Selexid; ***Swed.:*** Selexid.

Meclocycline *(BAN, USAN, rINN)*

GS-2989; Meclociclina; Méclocycline; Meclocyclinum; Meklocyklin; Meklosykliini; NSC-78502. (4*S*,4a*R*,5*S*,5a*R*,6*S*,12a*S*)-7-Chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxonaphthacene-2-carboxamide; 7-Chloro-6-demethyl-6-deoxy-5β-hydroxy-6-methylenetetracycline.

Меклоциклин

$C_{22}H_{21}ClN_2O_8$ = 476.9.
CAS — 2013-58-3.
ATC — D10AF04.
ATC Vet — QD10AF04.



Meclocycline Sulfosalicylate *(USAN)*

Meclociclina, sulfosalicilato de; Meclocycline Sulphosalicylate. Meclocycline 5-sulphosalicylate.

$C_{22}H_{21}ClN_2O_8,C_7H_6O_6S$ = 695.0.
CAS — 73816-42-9.
ATC — D10AF04.
ATC Vet — QD10AF04.

Pharmacopoeias. In *US*.
USP 31 (Meclocycline Sulfosalicylate). pH of a 1% solution in water is between 2.5 and 3.5. Store in airtight containers. Protect from light.

Profile
Meclocycline is a tetracycline antibacterial derived from oxytetracycline (p.312). It is applied topically as the sulfosalicylate for the treatment of acne vulgaris and superficial skin infections. Potency is expressed in terms of meclocycline. Preparations containing the equivalent of 1 or 2% are available. Meclocycline sulfosalicylate has also been given as a pessary in the treatment of vulvovaginal infections.

Preparations
USP 31: Meclocycline Sulfosalicylate Cream.

Proprietary Preparations (details are given in Part 3)
Ger.: Meclosorb; ***Ital.:*** Mecloderm; Mecloderm Antiacne; Mecloderm Ovuli; Mecloderm Polvere Aspersoria†; Meclutin Semplice†.

Multi-ingredient: ***Ital.:*** Anti-Acne; Mecloderm F; Meclutin†.

Meleumycin

Pharmacopoeias. In *Chin.*

Profile
Meleumycin, a macrolide antibacterial produced by the growth of *Streptomyces mycarofaciens*, consists of a mixture of midecamycin A_1 and kitasamycin A_6. It has actions and uses similar to those of erythromycin (p.269) and is given orally in the treatment of susceptible infections.

Meropenem *(BAN, USAN, rINN)*

ICI-194660; Meropeneemi; Méropénem; Meropenemum; SM-7338. (4*R*,5*S*,6*S*)-3-[(3*S*,5*S*)-5-Dimethylcarbamoylpyrrolidin-3-ylthio]-6-[(*R*)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid trihydrate.

Меропенем

$C_{17}H_{25}N_3O_5S,3H_2O$ = 437.5.
CAS — 96036-03-2 (meropenem); 119478-56-7 (meropenem trihydrate).
ATC — J01DH02.
ATC Vet — QJ01DH02.

Pharmacopoeias. In *Chin.*, *Jpn*, and *US*.
USP 31 (Meropenem). Colourless to white crystals. Sparingly soluble in water; very slightly soluble in alcohol; practically insoluble in acetone and in ether; soluble in dimethylformamide and in 5% monobasic potassium phosphate solution. pH of a 1% solution in water is between 4.0 and 6.0. Store in airtight containers.

Adverse Effects and Precautions
As for Imipenem, p.286.

Meropenem is more stable to renal dehydropeptidase I than imipenem and use with cilastatin, which inhibits this enzyme, is not required. Meropenem may have less potential to induce seizures than imipenem (see also below).

Effects on the nervous system. *Animal* studies have indicated that meropenem induces fewer seizures than imipenem-cilastatin and clinical data from the manufacturer have substantiated this.[1] Comparison of data[2] from 4872 patients with a variety of infections (including meningitis) treated with meropenem with that from 4752 patients who received other antibacterials, principally cephalosporin-based regimens or imipenem-cilastatin, showed that meropenem was not associated with any greater risk of seizures than the other antibacterials and was likely to have less neurotoxic potential than imipenem-cilastatin, making it a suitable drug to use in the treatment of meningitis.

1. Norrby SR, *et al.* Safety profile of meropenem: international clinical experience based on the first 3125 patients treated with meropenem. *J Antimicrob Chemother* 1995; **36** (suppl A): 207–23.
2. Norrby SR, Gildon KM. Safety profile of meropenem: a review of nearly 5,000 patients treated with meropenem. *Scand J Infect Dis* 1999; **31:** 3–10.

Interactions
Probenecid inhibits the renal excretion of meropenem thereby increasing its plasma concentrations and prolonging its elimination half-life.

Antiepileptics. For reports of decreased plasma-*valproate* concentrations (sometimes with loss of seizure control) attributed to meropenem, see p.510.

Antimicrobial Action
As for Imipenem, p.287.

Meropenem is slightly more active than imipenem against Enterobacteriaceae and slightly less active against Gram-positive organisms.

Pharmacokinetics
After intravenous injection of meropenem 0.5 and 1 g over 5 minutes, peak plasma concentrations of about 50 and 112 micrograms/mL respectively are attained. The same doses infused over 30 minutes produce peak plasma concentrations of 23 and 49 micrograms/mL, respectively.

Meropenem has a plasma elimination half-life of about 1 hour; this may be prolonged in patients with renal impairment and is also slightly prolonged in children. Meropenem is widely distributed into body tissues and fluids including the CSF and bile. It is about 2% bound to plasma proteins. It is more stable to renal dehydropeptidase I than imipenem and is mainly excreted in the urine by tubular secretion and glomerular filtration. About 70% of a dose is recovered unchanged in the urine over a 12-hour period and urinary concentrations above 10 micrograms/mL are maintained for up to 5 hours after a 500-mg dose. Meropenem is reported to have one metabolite (ICI-213689), which is inactive and is excreted in the urine.

Meropenem is removed by haemodialysis.

◊ References.

1. Chimata M, *et al.* Pharmacokinetics of meropenem in patients with various degrees of renal function, including patients with end-stage renal disease. *Antimicrob Agents Chemother* 1993; **37:** 229–33.
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3. Mouton JW, Van den Anker JN. Meropenem clinical pharmacokinetics. *Clin Pharmacokinet* 1995; **28:** 275–86.
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5. Novelli A, *et al.* Clinical pharmacokinetics of meropenem after the first and tenth intramuscular administration. *J Antimicrob Chemother* 1996; **37:** 775–81.
6. Thalhammer F, *et al.* Continuous infusion versus intermittent administration of meropenem in critically ill patients. *J Antimicrob Chemother* 1999; **43:** 523–7.
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8. Thalhammer F, Horl WH. Pharmacokinetics of meropenem in patients with renal failure and patients receiving renal replacement therapy. *Clin Pharmacokinet* 2000; **39:** 271–9.
9. Ververs TF, *et al.* Pharmacokinetics and dosing regimen of meropenem in critically ill patients receiving continuous veno-venous hemofiltration. *Crit Care Med* 2000; **28:** 3412–16.
10. van Enk JG, *et al.* Pharmacokinetics of meropenem in preterm neonates. *Ther Drug Monit* 2001; **23:** 198–201.
11. Goldstein SL, *et al.* Meropenem pharmacokinetics in children and adolescents receiving hemodialysis. *Pediatr Nephrol* 2001; **16:** 1015–18.
12. Ariano RE, *et al.* Pharmacokinetics and pharmacodynamics of meropenem in febrile neutropenic patients with bacteremia. *Ann Pharmacother* 2005; **39:** 32–8.