Sodium content. Each g of mezlocillin sodium contains about 1.7 mmol of sodium. As mezlocillin sodium has a lower sodium content than carbenicillin sodium, hypernatraemia and hypokalaemia are less likely to occur.

Interactions
As for Benzylpenicillin, p.214.

Cefotaxime. For the effect of mezlocillin on the clearance of cefotaxime, see p.228.

Antimicrobial Action
Mezlocillin has a similar antimicrobial action to piperacillin (p.315). Its activity against *Pseudomonas aeruginosa* is less than that of azlocillin or piperacillin.

Pharmacokinetics
Mezlocillin is not absorbed from the gastrointestinal tract to any significant extent. It is well absorbed after intramuscular injection, with peak plasma concentrations of 15 to 25 micrograms/mL 45 to 90 minutes after a single dose of 1 g. It is reported to have nonlinear dose-dependent pharmacokinetics. Between 16 and 42% of mezlocillin in the circulation is bound to plasma proteins. Mezlocillin is reported to have a plasma half-life of about 1 hour; this is slightly prolonged in neonates, and in patients with renal impairment half-lives of up to about 6 hours have been reported.

Mezlocillin is widely distributed in body tissues and fluids. It crosses the placenta into the fetal circulation and small amounts are distributed into breast milk. There is little diffusion into CSF except when the meninges are inflamed.

Mezlocillin is reported to be metabolised to a limited extent. About 55% of a dose is excreted unchanged in the urine by glomerular filtration and tubular secretion within 6 hours of a dose, hence achieving high urinary concentrations. High concentrations are also found in the bile; up to 30% of a dose has been reported to be excreted by this route.

Plasma concentrations are enhanced by probenecid.

Mezlocillin is removed by haemodialysis, and to some extent by peritoneal dialysis.

Uses and Administration
Mezlocillin is a ureidopenicillin with uses similar to those of piperacillin (p.316). It is commonly used with an aminoglycoside; however they should be given separately as they have been shown to be incompatible.

Administration and dosage. Mezlocillin is given by injection as the sodium salt. Doses are expressed in terms of the equivalent amount of mezlocillin; 1.07 g of mezlocillin sodium is equivalent to about 1 g of mezlocillin. Dosage may need to be reduced in renal impairment. It may be given by slow intravenous injection over 3 to 5 minutes, by intravenous infusion over 30 minutes, or by deep intramuscular injection. Single intramuscular doses should not exceed 2 g.

For the treatment of serious infections, 200 to 300 mg/kg daily in divided doses may be given intravenously. For life-threatening infections, up to 350 mg/kg daily may be used, but the total daily dose should not normally exceed 24 g. For uncomplicated urinary-tract infections, a dose of 1.5 to 2 g may be given intramuscularly or intravenously every 6 hours.

Uncomplicated gonorrhoea may be treated by a single intramuscular or intravenous dose of mezlocillin 1 to 2 g. Probenecid 1 g orally may be given at the same time or up to 30 minutes before the injection.

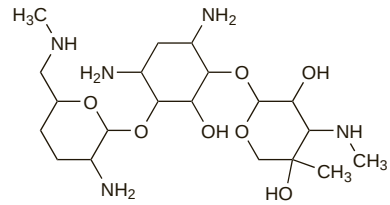
For the prophylaxis of infection during surgery, an intravenous pre-operative dose of mezlocillin 4 g, repeated at 6-hourly intervals for 2 further doses, may be given.

Preparations
USP 31: Mezlocillin for Injection.

Proprietary Preparations (details are given in Part 3)
Austria: Baypen; ***Fr.:*** Baypen; ***Ger.:*** Baypen; ***Israel:*** Baypen†; ***Ital.:*** Baypen.
Multi-ingredient: ***Ger.:*** Optocillin†.

Micronomicin Sulfate *(pINNM)*
Gentamicin C_{2B} Sulphate; KW-1062 (micronomicin); 6′*N*-Methylgentamicin C_{1A} Sulphate; Micronomicin Sulphate; Micronomicine, Sulfate de; Micronomicini Sulfas; Sagamicin Sulphate; Sulfato de micronomicina. *O*-2-Amino-2,3,4,6-tetradeoxy-6-(methylamino)-*α*-D-*erythro*-hexopyranosyl-(1→4)-*O*-[3-deoxy-4-*C*-methyl-3-(methylamino)-β-L-arabinopyranosyl-(1→6)]-2-deoxy-D-streptamine hemipentasulphate.

Микрономицина Сульфат
$(C_{20}H_{41}N_5O_7)_2,5H_2SO_4$ = 1417.5.
CAS — 52093-21-7 (micronomicin).
ATC — S01AA22.
ATC Vet — QS01AA22.



(micronomicin)

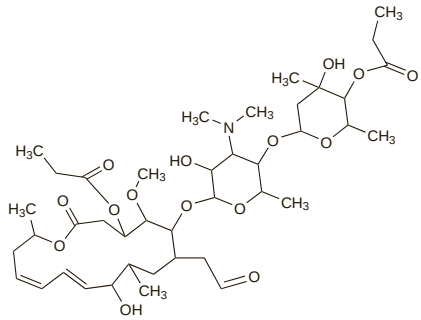
Pharmacopoeias. In *Chin.* and *Jpn*.

Profile
Micronomicin is an aminoglycoside with general properties similar to those of gentamicin (p.282). It is given as the sulfate and doses are expressed in terms of micronomicin; 183 mg of micronomicin sulfate is equivalent to about 120 mg of micronomicin. It is given by intramuscular injection or by intravenous infusion over 30 minutes to 1 hour in doses of 120 to 240 mg daily in 2 or 3 divided doses. Dosage should be adjusted based on serum-micronomicin concentration monitoring. It is also used topically as eye drops or ointment in a concentration of 0.3% for infections of the eye.

Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Luxomicina; ***Jpn:*** Sagamicin; ***Singapore:*** Sagamicin†.

Midecamycin *(rINN)*
Midecamicina; Midecamycin A_1; Midécamycine; Midecamycinum; Mydecamycin. 7-(Formylmethyl)-4,10-dihydroxy-5-methoxy-9,16-dimethyl-2-oxo-oxacyclohexadeca-11,13-dien-6-yl 3,6-dideoxy-4-*O*-(2,6-dideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranosyl)-3-(dimethylamino)-β-D-glucopyranoside 4′,4″-dipropionate.

Мидекамицин
$C_{41}H_{67}NO_{15}$ = 814.0.
CAS — 35457-80-8.
ATC — J01FA03.
ATC Vet — QJ01FA03.



Pharmacopoeias. In *Jpn*.

Midecamycin Acetate *(rINNM)*
Acecamycin; Acetato de midecamicina; Midecamycin Diacetate; Midécamycine, Acétate de; Midecamycini Acetas; Miocamycin; Miokamycin; MOM; Ponsinomycin; 1532-RB. 9,3″-Diacetylmidecamycin; Leucomycin V 3^B, 9-diacetate $3,4^B$-dipropanoate.

Мидекамицина Ацетат
$C_{45}H_{71}NO_{17}$ = 898.0.
CAS — 55881-07-7.
ATC — J01FA11.
ATC Vet — QJ01FA11.

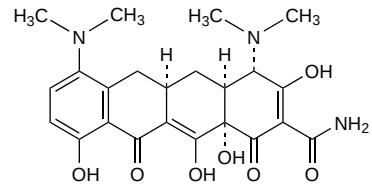
Pharmacopoeias. In *Jpn*.

Profile
Midecamycin is a macrolide antibacterial produced by the growth of *Streptomyces mycarofaciens* with actions and uses similar to those of erythromycin (p.269) but it is somewhat less active. It is given orally for the treatment of susceptible infections as the acetate in usual doses of 0.9 to 1.8 g daily in 2 or 3 divided doses. It has also been given as the base.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Myoxam†; ***Belg.:*** Merced; ***Fr.:*** Mosil; ***Gr.:*** Miocacin; Miocamen; ***Hong Kong:*** Medemycin; ***Ital.:*** Macroral; Midecin; Miocamen; Miokacin; ***Jpn:*** Medemycin; Miocamycin; ***Mex.:*** Midecamin†; ***Port.:*** Miocacin; ***Rus.:*** Macropen (Макропен); ***Spain:*** Momicine; Myoxam; Normicina†; ***Thai.:*** Miotin.

Minocycline *(BAN, USAN, rINN)*
Minociclina; Minocyclinum; Minocyklin; Minosiklin; Minosykliini. (4*S*,4a*S*,5a*R*,12a*S*)4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxonaphthacene-2-carboxamide; 6-Demethyl-6-deoxy-7-dimethylaminotetracycline.

Миноциклин
$C_{23}H_{27}N_3O_7$ = 457.5.
CAS — 10118-90-8;.
ATC — A01AB23; J01AA08.
ATC Vet — QA01AB23; QJ01AA08.



Minocycline Hydrochloride *(BANM, rINNM)*
Hidrocloruro de minociclina; Minociklin-hidroklorid; Minociklino hidrochloridas; Minocycline, chlorhydrate de; Minocyclini hydrochloridum; Minocyklin-hydrochlorid; Minocyklinhydroklorid; Minocykliny chlorowodorek; Minosykliinihydrokloridi.

Миноциклина Гидрохлорид
$C_{23}H_{27}N_3O_7,HCl$ = 493.9.
CAS — 13614-98-7.
ATC — A01AB23; J01AA08.
ATC Vet — QA01AB23; QJ01AA08.

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Minocycline Hydrochloride Dihydrate). A yellow, hygroscopic, crystalline powder. Sparingly soluble in water; slightly soluble in alcohol. It dissolves in solutions of alkali hydroxides and carbonates. A 1% solution in water has a pH of 3.5 to 4.5. Store in airtight containers. Protect from light.
USP 31 (Minocycline Hydrochloride). A yellow crystalline powder. Sparingly soluble in water; slightly soluble in alcohol; practically insoluble in chloroform and in ether; soluble in solutions of alkali hydroxides and carbonates. pH of a solution in water containing the equivalent of minocycline 1% is between 3.5 and 4.5. Store in airtight containers. Protect from light.

Incompatibility. Preparations of minocycline hydrochloride have an acid pH and incompatibility may reasonably be expected with alkaline preparations or with drugs unstable at low pH.

Adverse Effects and Precautions
As for Tetracycline, p.347.

Gastrointestinal disturbances with minocycline are reported to be less frequent than with the less well absorbed tetracyclines.

Oesophageal ulceration has occurred and may be a particular problem if capsules or tablets are taken with insufficient fluid or in a recumbent posture: minocycline should be taken with at least half a glass of water, in an upright position, and well before going to bed.

Vestibular adverse effects including dizziness or vertigo may occur with minocycline, particularly in women. Patients should be advised not to drive or operate machinery if affected. Tinnitus and decreased hearing have been reported rarely.

There have also been reports, some fatal, of a hypersensitivity syndrome (comprising eosinophilia, fever, rash, and varying additional symptoms), a lupus-like syndrome, and a serum-sickness-like syndrome (both comprising arthralgia, fever, and joint stiffness or swelling, amongst other symptoms).

Minocycline may also cause hyperpigmentation of the skin (see below).

Although minocycline, unlike many tetracyclines, does not appear to accumulate in patients with renal impairment, usual doses can lead to higher serum concentrations resulting in possible liver toxicity; reduced doses and monitoring of renal function may be necessary, particularly in those with severe impairment.

The *BNF* recommends that if treatment continues for longer than 6 months patients should be monitored every 3 months for hepatotoxicity, pigmentation, and SLE.

Incidence of adverse effects. Severe complications have been reported in patients given minocycline for acne, including serum-sickness-like disease,[1,2] lupus erythematosus,[3] and hepatitis.[3,4] The number of cases reported probably reflects the widespread use of this drug and the true incidence of such adverse effects is difficult to assess.[5] A study of 700 patients receiving minocycline for acne revealed adverse effects in 13.6%, mostly benign.[6] Gastrointestinal disturbances and vestibular disturbances were the most common, each occurring in about 2% of patients, and pigmentation in up to 4% of patients.

Another problem is that of assessing the efficacy of minocycline and the incidence of severe adverse effects relative to other antibacterials commonly used in acne such as tetracycline and erythromycin. A systematic review[7] suggested that the incidence of adverse effects might be greater with minocycline than with doxycycline. A retrospective analysis[8] of a UK population database found that minocycline was associated with an increased risk for drug-induced lupus erythematosus; no increased risk was reported for the other tetracyclines. Other systematic reviews[9,10] concluded that minocycline should not be used as a first-line oral tetracycline in patients with acne since there is no compelling evidence that it is more effective than some other tetracyclines or commonly used treatments; the risk of rare but serious adverse effects also makes it less suitable.[10]

1. Knowles SR, *et al.* Serious adverse reactions induced by minocycline: report of 13 patients and review of the literature. *Arch Dermatol* 1996; **132:** 934–9.
2. Harel L, *et al.* Serum-sickness-like reaction associated with minocycline therapy in adolescents. *Ann Pharmacother* 1996; **30:** 481–3.
3. Gough A, *et al.* Minocycline induced autoimmune hepatitis and systemic lupus erythematosus-like syndrome. *BMJ* 1996; **312:** 169–72.
4. Australian Adverse Drug Reactions Advisory Committee (ADRAC). Minocycline and the liver, the CNS, the skin. *Aust Adverse Drug React Bull* 1996; **15:** 14. Also available at: http://www.tga.gov.au/adr/aadrb/aadr9611.htm (accessed 11/08/08)
5. Seukeran DC, *et al.* Benefit-risk assessment of acne therapies. *Lancet* 1997; **349:** 1251–2.
6. Goulden V, *et al.* Safety of long-term high-dose minocycline in the treatment of acne. *Br J Dermatol* 1996; **134:** 693–5.
7. Smith K, Leyden JJ. Safety of doxycycline and minocycline: a systematic review. *Clin Ther* 2005; **27:** 1329–42.
8. Margolis DJ, *et al.* Association or lack of association between tetracycline class antibiotics used for acne vulgaris and lupus erythematosus. *Br J Dermatol* 2007; **157:** 540–6.
9. Garner SE, *et al.* Minocycline for acne vulgaris: efficacy and safety. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 16/05/05).
10. McManus P, Iheanacho I. Don't use minocycline as first line oral antibiotic in acne. *BMJ* 2007; **334:** 154.

Effects on intracranial pressure. Minocycline has been associated with benign intracranial hypertension; for further details, see under Tetracycline, p.348.

Effects on the liver. A systematic review[1] considered 65 published case reports of hepatitis or liver damage associated with the use of minocycline for acne, including 4 fatalities, and also data held by WHO concerning 493 reactions involving the liver in 393 patients in whom the indication for the use of minocycline was largely unspecified.

Of the 65 published cases, 38 occurred in females and 61 in patients under 40 years of age. These cases appeared to be of the following types:

- 16 cases appeared to be attributable to a hypersensitivity reaction, with a rapid onset usually within 1 month of starting treatment and sometimes associated with eosinophilia and exfoliative dermatitis
- 29 cases of hepatitis (of which 20 were in females) appeared to be of an auto-immune nature, occurring after 1 year or more of therapy and sometimes associated with lupus-like symptoms
- 20 cases could not be definitively classified into either group

The 393 patients described by the WHO data had 22 different types of hepatic reaction which could be broadly grouped into 4 categories:

- hepatic dysfunction (32% of patients)
- hepatitis (26%)
- abnormal liver function tests (24%)
- hyperbilirubinaemia or jaundice (14%)

There were, in addition, several other reactions, including hepatic damage or necrosis in 11 patients and fatty liver in 7. Gender distribution was almost even. Of the 393 patients, 14 also experienced lupus-like symptoms. The outcome of the hepatic reactions was reported in less than half of the patients, although it was apparent that there had been at least 3 fatalities.

Despite these findings, the reviewers concluded[1] that there was no clear information regarding the absolute or relative risks of hepatitis in patients given minocycline, and that it was inappropriate to comment as to whether monitoring would be worthwhile. A study of the comparative rates of hepatitis in people exposed to minocycline compared with those who were not was required.

1. Lawrenson RA, *et al.* Liver damage associated with minocycline use in acne: a systematic review of the published literature and pharmacovigilance data. *Drug Safety* 2000; **23:** 333–49.

Effects on the lungs. Hypersensitivity pneumonitis, characterised by pulmonary infiltrates and eosinophilia, has been reported[1-6] with minocycline. In most cases, the pneumonitis resolved after stopping minocycline but some required corticosteroid therapy; however, residual lung damage can occur. In one case[6] relapsing acute respiratory failure that required mechanical ventilation was reported.

1. Guillon J-M, *et al.* Minocycline-induced cell-mediated hypersensitivity pneumonitis. *Ann Intern Med* 1992; **117:** 476–81.
2. Bridges AJ. Minocycline-induced pneumonia. *Ann Intern Med* 1993; **118:** 749–50.
3. Sigmann P. Minocycline-induced pneumonia. *Ann Intern Med* 1993; **118:** 750.
4. Sitbon O, *et al.* Minocycline pneumonitis and eosinophilia: a report on 8 patients. *Arch Intern Med* 1994; **154:** 1633–40.
5. Dykhuizen RS, *et al.* Minocycline and pulmonary eosinophilia. *BMJ* 1995; **310:** 1520–1.
6. Oddo M, *et al.* Relapsing acute respiratory failure induced by minocycline. *Chest* 2003; **123:** 2146–8.

Hyperpigmentation. Minocycline has been associated with pigmentation of the skin and other tissues.[1-3] Three patterns of skin pigmentation have been described:[1] blue-black macules occurring in areas of inflammation and scarring and possibly due to an iron chelate of minocycline within macrophages; blue-grey macules or hyperpigmentation affecting normal skin and which may be due to a breakdown product of minocycline; or a greyish-brown discoloration occurring particularly in sun-exposed areas of skin ('muddy skin syndrome'), apparently due to melanin deposition. In general, pigmentation results from long-term use of minocycline at cumulative doses greater than 100 g; however, skin or oral mucosal pigmentation may occur regardless of dose or duration of therapy.[2] Indeed, there have been reports[3] of skin pigmentation developing after short-term use ranging from 3 to 28 days. Pigmentation of the skin and oral mucosa usually appears to resolve slowly on stopping the drug although recovery may be incomplete; pigmentation is often permanent when other sites are involved.[2]

1. Basler RSW. Minocycline-related hyperpigmentation. *Arch Dermatol* 1985; **121:** 606–8.
2. Eisen D, Hakim MD. Minocycline-induced pigmentation: incidence, prevention and management. *Drug Safety* 1998; **18:** 431–40.
3. Nakamura S, *et al.* Acute pigmentation due to minocycline therapy in atopic dermatitis. *Br J Dermatol* 2003; **148:** 1073–4.

Interactions

As for Tetracycline, p.348.

Minocycline has a lower affinity for binding with calcium than tetracycline. Consequently its absorption is less likely to be affected by milk or food, although it is still affected by calcium-containing antacids and other divalent and trivalent cations such as aluminium, bismuth, iron, magnesium, and zinc.

Antimicrobial Action

Minocycline has a spectrum of activity and mode of action similar to that of tetracycline (p.348) but it is more active against many species including *Staphylococcus aureus*, streptococci, *Neisseria meningitidis*, various enterobacteria, *Acinetobacter*, *Bacteroides*, *Haemophilus*, *Nocardia*, and some mycobacteria, including *M. leprae*.

Partial cross-resistance exists between minocycline and other tetracyclines but some strains resistant to other drugs of the group remain sensitive to minocycline, perhaps because of better cell-wall penetration.

Pharmacokinetics

For the general pharmacokinetics of the tetracyclines, see Tetracycline, p.349.

Minocycline is readily absorbed from the gastrointestinal tract and absorption is not significantly affected by the presence of food or moderate amounts of milk. Oral doses of 200 mg followed by 100 mg every 12 hours are reported to produce plasma concentrations of about 2 to 4 micrograms/mL. It is more lipid-soluble than doxycycline and the other tetracyclines and is widely distributed in body tissues and fluids with high concentrations being achieved in the hepatobiliary tract, lungs, sinuses and tonsils, as well as in tears, saliva, and sputum. Penetration into the CSF is relatively poor, although a higher ratio of CSF to blood concentrations has been reported with minocycline than with doxycycline. It crosses the placenta and is distributed into breast milk. About 75% of minocycline in the circulation is bound to plasma proteins. It has a low renal clearance: only about 5 to 10% of a dose is excreted in the urine and up to about 34% is excreted in the faeces. However, in contrast to most tetracyclines it appears to undergo some metabolism in the liver, mainly to 9-hydroxyminocycline. Sources differ as to whether the normal plasma half-life of 11 to 26 hours is prolonged in patients with renal impairment, with a consequent risk of accumulation; hepatic impairment does not appear to lead to accumulation. Little minocycline is removed by haemodialysis and peritoneal dialysis.

◊ Reviews.

1. Saivin S, Houin G. Clinical pharmacokinetics of doxycycline and minocycline. *Clin Pharmacokinet* 1988; **15:** 355–66.

Uses and Administration

Minocycline is a tetracycline derivative with uses similar to those of tetracycline (p.349). It is also a component of multidrug regimens for the treatment of leprosy (p.176) and has been used in the prophylaxis of meningococcal infection to eliminate the carrier state, but the high incidence of vestibular disturbances means that it is not the drug of choice for the latter.

Minocycline is usually given orally as the hydrochloride; doses are expressed in terms of the base. Minocycline hydrochloride 108 mg is equivalent to about 100 mg of minocycline. Minocycline capsules and tablets should be taken with plenty of fluid, with the patient in an upright position, and well before going to bed.

In patients in whom oral therapy is not feasible, minocycline hydrochloride has been given by slow intravenous infusion in doses equivalent to those given orally. In some countries it has also been given by intramuscular injection.

The usual adult oral dose is 200 mg daily in divided doses, usually every 12 hours; an initial loading dose of 200 mg may be given.

An oral dose of 50 mg twice daily or 100 mg once daily is used for the treatment of acne; alternatively, a dose of about 1 mg/kg once daily is also given as a modified-release preparation to patients weighing 45 kg and over. In asymptomatic meningococcal carriers, 100 mg has been given orally twice daily for 5 days, usually followed by a course of rifampicin.

For multibacillary leprosy an oral dose of minocycline 100 mg daily with clofazimine and ofloxacin *or* 100 mg monthly with rifampicin and ofloxacin have been recommended by WHO as alternative multidrug therapy regimens. As an alternative regimen for patients with single-lesion paucibacillary leprosy WHO suggests a single dose of minocycline 100 mg with rifampicin and ofloxacin.

For details of doses in children and adolescents, see below.

For dosage recommendations in patients with renal impairment, see below.

In adults with periodontitis, a modified-release subgingival gel containing minocycline hydrochloride has been inserted into the periodontal pocket as an adjunct to scaling and root planing; each cartridge contains the equivalent of 1 mg of minocycline and the total used depends on the size, shape, and number of pockets being treated. Minocycline has also been applied as a 2% gel for periodontal infections.

Administration in children. In children, the effects on teeth should be considered and tetracyclines only used when absolutely essential. In the UK, minocycline is licensed for use in children aged 12 years and over; the usual adult dose (see above) may be given orally. However, in the USA, it may be given to those over 8 years old in usual oral doses of 4 mg/kg initially followed by 2 mg/kg every 12 hours.

Administration in renal impairment. US licensed product information states that pharmacokinetics in patients with renal

impairment have not been fully characterised and therefore recommends that no more than 200 mg in any 24-hour period should be given to these patients.

Motor neurone disease. Minocycline is being investigated as a potential treatment for amyotrophic lateral sclerosis, a form of motor neurone disease (p.2380), on the basis of its neuroprotective properties.

Movement disorders. Minocycline is under investigation[1,2] for the management of Huntington's chorea (p.953).

1. Huntington Study Group. Minocycline safety and tolerability in Huntington disease. *Neurology* 2004; **63:** 547–9.
2. Bonelli RM, *et al.* Neuroprotection in Huntington's disease: a 2-year study on minocycline. *Int Clin Psychopharmacol* 2004; **19:** 337–42.

Musculoskeletal and joint disorders. For reference to the use of minocycline in the treatment of rheumatoid arthritis, see under Tetracycline, p.350.

Skin disorders. For reference to the use of minocycline in the treatment of various skin disorders, see under Tetracycline, p.350.

Preparations

BP 2008: Minocycline Tablets; Prolonged-release Minocycline Capsules; ***USP 31:*** Minocycline for Injection; Minocycline Hydrochloride Capsules; Minocycline Hydrochloride Oral Suspension; Minocycline Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Acneclin; Asolmicina†; Clinax; Meibi; Minocin; Pimple; Seboclear; ***Austral.:*** Akamin; Minomycin; ***Austria:*** Auramin; Klinoc†; Minocin†; Minostad; Minotyrol†; Udima; ***Belg.:*** Klinotab; Mino-50; Minocin; Minotab; ***Braz.:*** Minoderm; Minomax†; ***Canad.:*** Enca; Minocin; ***Chile:*** Bagomicina; Minocin†; Pracne; ***Cz.:*** Skid†; ***Fr.:*** Mestacine; Minolis; Mynocine; Parocline; Yelnac†; Zacnar; ***Ger.:*** Akne-Puren†; Aknefug Mino; Aknin-Mino†; Aknosan; Klinomycin; Lederderm†; Minakne; Mino-Wolff†; Minoclir; Minoplus; Skid; Skinocyclin; Udima; ***Gr.:*** Cycline; Minocin; ***Hong Kong:*** Minaxen; Minocin; ***India:*** CNN†; Cynomycin; ***Indon.:*** Minocin; ***Irl.:*** Minocin; Minox; ***Israel:*** Minocin†; Minoclin; ***Ital.:*** Minocin; ***Jpn:*** Periocline; ***Malaysia:*** Borymycin; Minocin†; Minoclin; ***Mex.:*** Banimed; Micromycin; Minocin; Ranmino; ***Neth.:*** Aknemin; Minocin; Minotab; Peritrol; ***NZ:*** Minomycin; Minotabs; ***Philipp.:*** Minocin; ***Port.:*** Arestin; Cipancin; Minocin; Minotrex; ***S.Afr.:*** Cyclimycin; Minotabs; Triomin; ***Singapore:*** Borymycin; Minocin†; ***Spain:*** Minocin; ***Switz.:*** Aknin-N; Aknoral; Minac 50; Minocin; ***Thai.:*** Minocin†; ***UK:*** Aknemin; Blemix†; Dentomycin; Minocin; Sebomin; Sebren; ***USA:*** Arestin; Cleeravue-M; Dynacin; Minocin; Myrac; Solodyn; ***Venez.:*** Minocin†.

Morinamide *(pINN)*

Morinamida; Morinamidum; Morphazinamide. *N*-Morpholinomethylpyrazine-2-carboxamide.

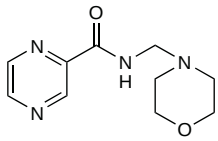
Моринамид

$C_{10}H_{14}N_4O_2$ = 222.2.

CAS — 952-54-5.

ATC — J04AK04.

ATC Vet — QJ04AK04.



Profile

Morinamide is an antimycobacterial that has been given orally as the hydrochloride in the treatment of tuberculosis.

Preparations

Proprietary Preparations (details are given in Part 3)

Turk.: Morfozid.

Moxifloxacin Hydrochloride *(BANM, USAN, rINNM)*

Bay-12-8039; Hidrocloruro de moxifloxacino; Moxifloxacine, chlorhydrate de; Moxifloxacini hydrochloridum. 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid hydrochloride.

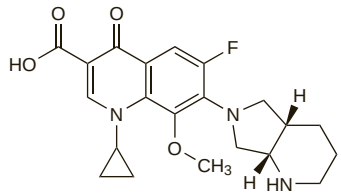
Моксифлоксацина Гидрохлорид

$C_{21}H_{24}FN_3O_4$,HCl = 437.9.

CAS — 151096-09-2 (moxifloxacin); 186826-86-8 (moxifloxacin hydrochloride).

ATC — J01MA14; S01AX22.

ATC Vet — QJ01MA14; QS01AX22.



(moxifloxacin)

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Moxifloxacin Hydrochloride). Produced using a method validated to demonstrate the satisfactory enantiomeric purity of the final product. A light yellow or yellow powder or crystals, slightly hygroscopic. Sparingly soluble in water; slightly soluble in alcohol; practically insoluble in acetone. A 0.2% solution in water has a pH of 3.9 to 4.6. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

◊ References.

1. Faich GA, *et al.* Clinical experience with moxifloxacin in patients with respiratory tract infections. *Ann Pharmacother* 2004; **38:** 749–54.
2. Ball P, *et al.* Safety profile of oral and intravenous moxifloxacin: cumulative data from clinical trials and postmarketing studies. *Clin Ther* 2004; **26:** 940–50.
3. Andriole VT, *et al.* Retrospective analysis of the safety profile of oral moxifloxacin in elderly patients enrolled in clinical trials. *Drug Safety* 2005; **28:** 443–52.

Interactions

As for Ciprofloxacin, p.246.

Moxifloxacin does not appear to interact significantly with theophylline or probenecid.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Moxifloxacin is reported to have greater activity against Gram-positive bacteria, including pneumococci, than ciprofloxacin.

◊ References.

1. Stein GE, *et al.* Bactericidal activities of methoxyfluoroquinolones gatifloxacin and moxifloxacin against aerobic and anaerobic respiratory pathogens in serum. *Antimicrob Agents Chemother* 2003; **47:** 1308–12.
2. Pletz MWR, *et al.* Early bactericidal activity of moxifloxacin in treatment of pulmonary tuberculosis: a prospective, randomized study. *Antimicrob Agents Chemother* 2004; **48:** 780–2.

Pharmacokinetics

Moxifloxacin is readily absorbed from the gastrointestinal tract after oral doses with an absolute bioavailability of about 90%. It is widely distributed throughout the body tissues and is about 30 to 50% bound to plasma proteins. Moxifloxacin has an elimination half-life of about 12 hours, allowing once-daily dosing. It is metabolised mainly via sulfate and glucuronide conjugation, and is excreted in the urine and the faeces as unchanged drug and as metabolites, the sulfate conjugate primarily in the faeces and the glucuronide exclusively in the urine. Distribution into milk has been found in *animals*.

Uses and Administration

Moxifloxacin is a fluoroquinolone antibacterial with actions and uses similar to those of ciprofloxacin (p.247).

It is given orally, or by intravenous infusion over 60 minutes, for the treatment of susceptible infections including respiratory, skin and skin structure, and intra-abdominal infections. Moxifloxacin is given as the hydrochloride but doses are expressed in terms of the base; moxifloxacin hydrochloride 436.3 mg is equivalent to about 400 mg of moxifloxacin. The usual dose is 400 mg once daily.

Moxifloxacin is also used topically as the hydrochloride in eye drops containing the equivalent of 0.5% of moxifloxacin for the treatment of bacterial conjunctivitis.

◊ Reviews.

1. Keating GM, Scott LJ. Moxifloxacin: a review of its use in the management of bacterial infections. *Drugs* 2004; **64:** 2347–77.
2. Miravitlles M, *et al.* Eficacia clínica del moxifloxacino en el tratamiento de las agudizaciones de la bronquitis crónica: revisión sistemática y metaanálisis. *Arch Bronconeumol* 2007; **43:** 22–8.
3. Miravitlles M. Moxifloxacin in the management of exacerbations of chronic bronchitis and COPD. *Int J Chron Obstruct Pulmon Dis* 2007; **2:** 191–204.
4. O'Brien TP. Evidence-based review of moxifloxacin. *Int Ophthalmol Clin* 2006; **46:** 61–72.

Eye infections. In order to attain therapeutic concentrations most antibacterials used in the treatment of bacterial endophthalmitis need to be given by the intravitreal route but moxifloxacin given systemically may produce adequate concentrations. An oral dose of moxifloxacin 400 mg daily may be given for 10 days.[1]

1. Moorfields Eye Hospital NHS Foundation Trust. *Pharmacists Handbook 2006*. London: Moorfields Pharmaceuticals, 2006.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Avelox; Octegra†; Vigamox; ***Austral.:*** Avelox; ***Austria:*** Actira; Avelox; Octegra; ***Belg.:*** Avelox; Proflox; ***Braz.:*** Avalox; Vigamox; ***Canad.:*** Avelox; Vigamox; ***Chile:*** Avelox; Flovacil; Octegra†; Vigamox; ***Cz.:*** Avelox; ***Denm.:*** Avelox; ***Fin.:*** Avelox; ***Fr.:*** Izilox; ***Ger.:*** Avalox; ***Gr.:*** Avelox; Octegra; Proflox; ***Hong Kong:*** Avelox; Vigamox; ***Hung.:*** Avelox; Octegra; ***India:*** Moxicip; Moxif; ***Indon.:*** Avelox; ***Irl.:*** Avelox; ***Israel:*** Megaxin; Vigamox; ***Ital.:*** Actira; Avalox; Octegra; ***Jpn:*** Avelox; ***Malaysia:*** Avelox; Vigamox; ***Mex.:*** Avelox; Vigamoxi; ***Neth.:*** Actira†; Avelox; Octegra; ***NZ:*** Avelox; ***Philipp.:*** Avelox; Vigamox; ***Pol.:*** Avelox; ***Port.:*** Avelox; Proflox; ***Rus.:*** Avelox (Авелокс); ***S.Afr.:*** Avelon; ***Singapore:*** Avelox; Vigamox; ***Spain:*** Actira; Octegra; Proflox; ***Swed.:*** Avelox; ***Switz.:*** Avalox; ***Thai.:*** Avelox; Vigamox; ***Turk.:*** Avelox; ***UK:*** Avelox; ***USA:*** Avelox; Vigamox; ***Venez.:*** Avelox; Vigamox.

Mupirocin *(BAN, USAN, rINN)*

BRL-4910A; Mupirocina; Mupirocinas; Mupirocine; Mupirocinum; Mupirosiini; Pseudomonic Acid. 9-[(2*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxypyran-2-yl]-3-methylbut-2-enoyloxy]nonanoic acid; (2*S*-{2α(*E*),3β,4β,5α[2*R**,3*R**(1*R**,2*R**)]})-9-{[3-Methyl-1-oxo-4-(tetrahydro-3,4-dihydroxy-5-{[3-(2-hydroxy-1-methyl-propyl)oxiranyl]methyl}-2*H*-pyran-2-yl)-2-butenyl]oxy}nonanoic acid.

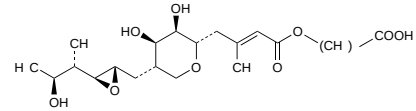
Мупироцин

$C_{26}H_{44}O_9$ = 500.6.

CAS — 12650-69-0.

ATC — D06AX09; R01AX06.

ATC Vet — QD06AX09; QR01AX06.



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

Ph. Eur. 6.2 (Mupirocin). A white or almost white powder. It shows polymorphism. Slightly soluble in water; freely soluble in dehydrated alcohol, in acetone, and in dichloromethane. The pH of a freshly prepared saturated solution in water is 3.5 to 4.0. Protect from light.

USP 31 (Mupirocin). A white to off-white crystalline solid. Very slightly soluble in water; freely soluble in dehydrated alcohol, in acetone, in chloroform, and in methyl alcohol; slightly soluble in ether. pH of a saturated solution in water is between 3.5 and 4.5. Store in airtight containers.

Mupirocin Calcium *(BANM, USAN, rINNM)*

BRL-4910F; Calcii Mupirocinum; Mupirocin vápenatá sůl dihydrát; Mupirocina cálcica; Mupirocine calcique; Mupirocinkalcium; Mupirocin-kalcium; Mupirocino kalcio druska; Mupirocinum calcicum; Mupirocinum Calcicum Dihydricum; Mupirosiinikalsium.

Кальций Мупироцин

$C_{52}H_{86}O_{18}Ca,2H_2O$ = 1075.3.

CAS — 104486-81-9 (anhydrous mupirocin calcium); 115074-43-6 (mupirocin calcium dihydrate).

ATC — D06AX09; R01AX06.

ATC Vet — QD06AX09; QR01AX06.

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

Ph. Eur. 6.2 (Mupirocin Calcium). A white or almost white powder. Very slightly soluble in water; sparingly soluble in dehydrated alcohol and in dichloromethane.

USP 31 (Mupirocin Calcium). Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

Mupirocin is usually well tolerated but local reactions such as burning, stinging, and itching may occur after the application of mupirocin to the skin.

Some mupirocin products are formulated in a macrogol base: such formulations are not suitable for application to mucous membranes and should be used with caution in patients with extensive burns or wounds because of the possibility of macrogol toxicity. Care is also required in patients with renal impairment.

Antimicrobial Action

Mupirocin is an antibacterial that inhibits bacterial protein synthesis by binding to isoleucyl transfer RNA synthetase. It is mainly bacteriostatic at low concentrations, although it is usually bactericidal in the high concentrations achieved by topical application to the skin. At these concentrations it may have some activity against organisms reported to be relatively resistant to mupirocin *in vitro*.