Interactions
As for Tetracycline, p.348.

Antimicrobial Action
As for Tetracycline, p.348.

Demeclocycline is stated to be somewhat more active against certain strains of some organisms including *Neisseria gonorrhoeae* and *Haemophilus influenzae*, as well as to being the most active of the tetracyclines *in vitro* against *Brucella* spp.

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

About 60 to 80% of a dose of demeclocycline is absorbed from the gastrointestinal tract. Peak plasma concentrations of about 1.5 to 1.7 micrograms/mL have been reported 3 to 4 hours after a single oral dose of 300 mg, but higher plasma concentrations may be achieved with repeated dosage. Its plasma elimination half-life is about 12 hours, although this may be prolonged in patients with renal impairment; values of 42 to 68 hours have been reported in severe impairment. The renal clearance of demeclocycline is about half that of tetracycline.

Uses and Administration
Demeclocycline is a tetracycline derivative with uses similar to those of tetracycline (p.349). It is excreted more slowly and effective blood concentrations are maintained for a longer period.

Demeclocycline is given orally as the hydrochloride; the usual adult dose is 600 mg daily in 2 or 4 divided doses, preferably 1 hour before or 2 hours after meals. For atypical pneumonia, 900 mg daily in 3 divided doses may be given. It is also sometimes given orally with other tetracycline derivatives.

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

Demeclocycline may also be given to adults in the treatment of chronic hyponatraemia associated with the syndrome of inappropriate antidiuretic hormone secretion, when water restriction has proved ineffective. Initially 900 to 1200 mg is given daily in divided doses, reducing to maintenance doses of 600 to 900 mg daily.

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

The calcium and magnesium salts of demeclocycline have also been used.

Administration in children. In children, the effects on teeth should be considered and tetracyclines only used when absolutely essential; demeclocycline may be used for the treatment of susceptible infections. In the UK, it 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 doses of 7 to 13 mg/kg daily by mouth in 2 or 4 divided doses.

Administration in hepatic impairment. UK licensed product information states that the dosage of demeclocycline should not exceed 1 g daily in patients with known liver disease.

Syndrome of inappropriate ADH secretion. Demeclocycline may be given in the treatment of the syndrome of inappropriate ADH (antidiuretic hormone) secretion (SIADH—p.2182) to antagonise the effect of ADH on the renal tubules; lithium has been given as an alternative. Both lithium and demeclocycline act by interfering with the cellular action of ADH to produce nephrogenic diabetes insipidus. Demeclocycline was reported to be superior to lithium[1] and became the preferred treatment for chronic SIADH if water restriction was unsuccessful,[2] although fluid restriction is probably still the treatment of choice. However, since nephrotoxicity has been reported in patients with cardiac or hepatic disease, the usefulness of demeclocycline in the treatment of hyponatraemic states might be limited; this view was supported by studies in patients with heart failure[3] and cirrhosis.[4]

1. Forrest JN, *et al.* Superiority of demeclocycline over lithium in the treatment of chronic syndrome of inappropriate secretion of antidiuretic hormone. *N Engl J Med* 1978; **298:** 173–7.
2. Schrier RW. Treatment of hyponatremia. *N Engl J Med* 1985; **312:** 1121–2.
3. Zegers de Beyl D, *et al.* Demeclocycline treatment of water retention in congestive heart failure. *BMJ* 1978; **1:** 760.
4. Miller PD, *et al.* Plasma demeclocycline levels and nephrotoxicity: correlation in hyponatremic cirrhotic patients. *JAMA* 1980; **243:** 2513–15.

Preparations
BP 2008: Demeclocycline Capsules;
USP 31: Demeclocycline Hydrochloride Capsules; Demeclocycline Hydrochloride Tablets; Demeclocycline Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Austral.: Ledermycin†; ***Canad.:*** Declomycin; ***Fr.:*** Ledermycine; ***India:*** Ledermycin; ***Neth.:*** Ledermycin; ***UK:*** Ledermycin; ***USA:*** Declomycin.

Multi-ingredient: ***Austria:*** Ledermix; ***Denm.:*** Ledermix†; ***Ger.:*** Ledermix; ***Israel:*** Ledermix; ***Ital.:*** Rubrociclina†; ***S.Afr.:*** Tritet; ***Switz.:*** Ledermix; ***UK:*** Deteclo†; Ledermix.

Dibekacin Sulfate *(rINNM)*

Dibekacin Sulphate *(BANM)*; Dibékacine, Sulfate de; Dibekacini Sulfas; 3′,4′-Dideoxykanamycin B; Sulfato de dibekacina. 6-*O*-(3-Amino-3-deoxy-α-D-glucopyranosyl)-2-deoxy-4-*O*-(2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranosyl)-streptamine sulphate.

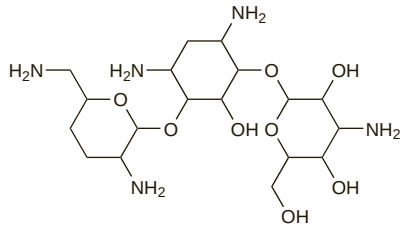
Дибекацина Сульфат

$C_{18}H_{37}N_5O_8.xH_2SO_4$.

CAS — 34493-98-6 (dibekacin); 58580-55-5 (dibekacin sulfate).

ATC — J01GB09.

ATC Vet — QJ01GB09.



(dibekacin)

Pharmacopoeias. In *Jpn.*

Profile
Dibekacin is an aminoglycoside derived from kanamycin with actions and uses similar to those of gentamicin (p.282). It has been given intramuscularly as the sulfate in doses equivalent to dibekacin 1 to 3 mg/kg daily in divided doses. It has also been given in similar doses by slow intravenous infusion. Dosage should be adjusted based on serum-dibekacin concentration monitoring. It has also been used topically for eye infections.

Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Dikacine†; ***Jpn:*** Panimycin; ***Venez.:*** Dibekan.

Dicloxacillin *(BAN, USAN, rINN)*

BRL-1702; Dicloxacilina; Dicloxacilline; Dicloxacillinum; Diklоksasilliini; Dikloxacillin; R-13423. (6*R*)-6-[3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carboxamido]penicillanic acid.

Диклоксациллин

$C_{19}H_{17}Cl_2N_3O_5S$ = 470.3.

CAS — 3116-76-5.

ATC — J01CF01.

ATC Vet — QJ01CF01; QJ51CF01.

Dicloxacillin Sodium *(BANM, USAN, rINNM)*

Dicloxacilina sódica; Dicloxacilline sodique; Dicloxacillinum natricum; Dicloxacillinum Natricum Monohydricum; Diklоksacilino natrio druska; Dikloksasilliininatrium; Dikloxacilin sodná sůl monohydrát; Dikloxacillinnatrium; Dikloxacillin-nátrium; Natrii Dicloxacillinum; P-1011. Sodium dicloxacillin monohydrate.

Натрий Диклоксациллин

$C_{19}H_{16}Cl_2N_3NaO_5S,H_2O$ = 510.3.

CAS — 343-55-5 (anhydrous dicloxacillin sodium); 13412-64-1 (dicloxacillin sodium monohydrate).

ATC — J01CF01.

ATC Vet — QJ01CF01.

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

Ph. Eur. 6.2 (Dicloxacillin Sodium). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; soluble in alcohol and in methyl alcohol. A 10% solution in water has a pH of 5.0 to 7.0. Store at a temperature not exceeding 25° in airtight containers.

USP 31 (Dicloxacillin Sodium). A white to off-white crystalline powder. Freely soluble in water. pH of a 1% solution in water is between 4.5 and 7.5. Store in airtight containers.

Adverse Effects and Precautions
As for Flucloxacillin, p.277.

Effects on the liver. References.

1. Kleinman MS, Presberg JE. Cholestatic hepatitis after dicloxacillin-sodium therapy. *J Clin Gastroenterol* 1986; **8**: 77–8.

Sodium content. Each g of dicloxacillin sodium contains about 2 mmol of sodium.

Interactions
As for Benzylpenicillin, p.214.

Antimicrobial Action
As for Flucloxacillin, p.277.

Pharmacokinetics
Dicloxacillin is better absorbed from the gastrointestinal tract than cloxacillin but absorption is reduced by the presence of food in the stomach. After an oral dose of 500 mg, peak plasma concentrations of 10 to 18 micrograms/mL in about 1 hour have been reported in fasting subjects. Doubling the dose can double the plasma concentration. About 97% of dicloxacillin in the circulation is bound to plasma proteins. Dicloxacillin has been reported to have a plasma half-life of 0.5 to 1 hour. The half-life is prolonged in neonates.

The distribution of dicloxacillin in body tissues and fluids is similar to that of cloxacillin (p.256).

Dicloxacillin is metabolised to a limited extent and the unchanged drug and metabolites are excreted in the urine by glomerular filtration and renal tubular secretion. About 60% of an oral dose is excreted in the urine. Only small amounts are excreted in the bile. Dicloxacillin is not removed by haemodialysis.

Plasma concentrations are enhanced by probenecid. Reduced concentrations have been reported in patients with cystic fibrosis.

Uses and Administration
Dicloxacillin is an isoxazolyl penicillin used similarly to flucloxacillin (p.277) in the treatment of infections due to staphylococci resistant to benzylpenicillin.

Dicloxacillin is given intravenously and orally as the sodium salt. All doses are expressed in terms of the equivalent amount of dicloxacillin; 1.09 g of dicloxacillin sodium is equivalent to about 1 g of dicloxacillin. Oral doses should be taken at least 1 hour before, or 2 hours after, meals since the presence of food in the stomach reduces absorption. The usual adult oral dose is 250 mg every 6 hours. Similar doses may be given by slow intravenous injection or, preferably, by intravenous infusion. Doses may be doubled in severe infections.

Preparations
USP 31: Dicloxacillin Sodium Capsules; Dicloxacillin Sodium for Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Austral.: Diclocil; Dicloxsig; Distaph; ***Denm.:*** Dicillin; Diclocil; ***Fin.:*** Diclocil; ***Ger.:*** InfectoStaph; ***Gr.:*** Diclocil; ***Mex.:*** Amifarin; Antiben; Brispen; Butimaxil; Cilpen; Clobioxal; Dicleophen; Diclo-Tecno; Dicloxaquim; Diluxina; Dipxapen†; Ditterolina; Dixen; Doxil; Pardix; Penclox; Posipen; ***Norw.:*** Diclocil; ***NZ:*** Diclocil; ***Port.:*** Diclocil; ***Swed.:*** Diclocil; ***Thai.:*** Amcidil; Cloxydin; Diclex; Diclocil; Diclocillin; Dicloson; Diclox†; Dicloxia; Dicloxin; Dicloxman†; Dicloxno; Diloxin; Ditum†; Dixocillin; Dorox; Servidiclox†; ***Venez.:*** Diclocil; Diclolak†.

Multi-ingredient: ***Ital.:*** Ampiplus†; Diamplicil†; ***Mex.:*** Ampiclox-D; Anglotex; Brucilina; Diamprex; Doxapen; Panac; Panac K; Pentidix.

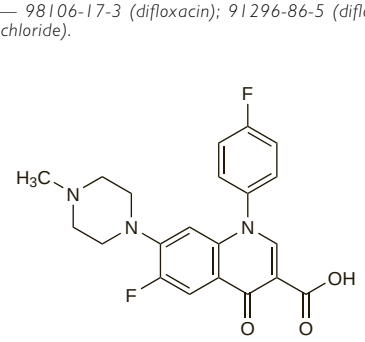
Difloxacin Hydrochloride *(USAN, rINNM)*

A-56619; Abbott-56619; Difloxacine, chlorhydrate de; Difloxacini hydrochloridum; Hidrocloruro de difloxacino. 6-Fluoro-1-(*p*-fluorophenyl)-1,4-dihydro-7-(4-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid hydrochloride.

Дифлоксацина Гидрохлорид

$C_{21}H_{19}F_2N_3O_3$,HCl = 435.9.

CAS — 98106-17-3 (difloxacin); 91296-86-5 (difloxacin hydrochloride).



(difloxacin)