Daptomycin *(BAN, USAN, rINN)*

Daptomicina; Daptomycine; Daptomycinum; LY-146032. *N*-Decanoyl-L-tryptophyl-L-asparaginyl-L-aspartyl-L-threonylglycyl-L-ornithyl-L-aspartyl-D-alanyl-L-aspartylglycyl-D-seryl-*threo*-3-methyl-L-glutamyl-3-anthraniloyl-L-alanine 1.13-3.4-lactone.

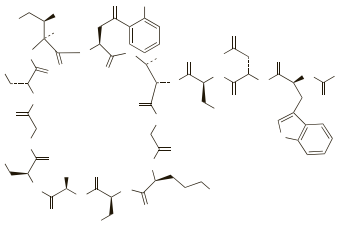
Даптомицин

$C_{72}H_{101}N_{17}O_{26}$ = 1620.7.

CAS — 103060-53-3.

ATC — J01XX09.

ATC Vet — QJ01XX09.



Adverse Effects and Precautions

The most common adverse effects associated with daptomycin are gastrointestinal effects including nausea and vomiting, constipation, diarrhoea, and dyspepsia. Headache, insomnia, dizziness, and fever may occur. Injection site reactions have occurred. Effects on the skin have included rash and pruritus. Abnormal liver function tests and jaundice have been reported. Other reported adverse effects include hypertension or hypotension, renal failure, dyspnoea, and anaemia. There have been rare cases of hypersensitivity, anaphylaxis, and infusion reactions.

Elevated plasma creatine phosphokinase (CPK) concentrations during daptomycin therapy may be associated with muscle pain and/or weakness, myositis, myopathy, and rarely rhabdomyolysis; patients with renal impairment or taking other drugs known to cause myopathy (see Interactions, below) may be at increased risk. All patients should be monitored for the development of muscle pain or weakness, and plasma CPK concentrations measured once weekly. More frequent measurements should be performed in those with an increased risk of myopathy, or with a baseline CPK concentration greater than 5 times the upper limit of normal (ULN), or who develop signs of myopathy. Daptomycin should be stopped in patients with signs of myopathy and CPK concentrations greater than 5 times the ULN, or in those without reported signs of myopathy but with CPK concentrations greater than 10 times the ULN.

Daptomycin should be given with caution and in reduced dosage to patients with renal impairment; clinical response and renal function should be monitored closely.

Consideration should be given to stopping daptomycin therapy in patients who develop signs or symptoms of peripheral neuropathy.

Effects on the lungs. Bronchiolitis obliterans organising pneumonia with eosinophilic infiltration has been reported in an 84-year-old man after 4 weeks of daptomycin therapy;[1] clinical improvement occurred after the drug was stopped. The mechanism of toxicity was unknown and the authors suggested that it might be associated with epithelial injury caused by daptomycin accumulating in the alveolar spaces.

A 60-year-old man receiving daptomycin developed eosinophilic pneumonia resulting in respiratory failure that required mechanical ventilation;[2] he improved after stopping the drug and starting corticosteroid therapy.

1. Cobb E, *et al.* Organizing pneumonia and pulmonary eosinophilic infiltration associated with daptomycin. *Ann Pharmacother* 2007; **41:** 696–701.
2. Hayes D, *et al.* Eosinophilic pneumonia induced by daptomycin. *J Infect* 2007; **54:** e211–e213.

Pregnancy. Intravenous daptomycin, 4 mg/kg daily for 14 days, was successfully used to treat pyelonephritis associated with vancomycin-resistant enterococci (VRE) in a 27-week pregnant woman; no neonatal abnormalities were reported.[1]

1. Shea K, *et al.* Successful treatment of vancomycin-resistant Enterococcus faecium pyelonephritis with daptomycin during pregnancy. *Ann Pharmacother* 2008; **42:** 722–5.

Interactions

There may be an increased risk of myopathy if daptomycin is given with other drugs also known to have this adverse effect, such as statins, fibrates, and ciclosporin. Licensed product information recommends stopping the latter if possible; otherwise, plasma creatine phosphokinase concentrations should be measured more than once weekly in addition to the usual precautions (see Adverse Effects and Precautions, above).

Daptomycin is mainly excreted by renal filtration and caution is advised if given with drugs that reduce renal filtration, such as NSAIDs and selective inhibitors of cyclo-oxygenase-2, since plasma concentrations of daptomycin may be increased.

Daptomycin has been reported to interact with a particular reagent used in some assays of PT-INR resulting in apparent prolongation of PT and elevation of INR.

Antimicrobial Action

Daptomycin is a lipopeptide antibacterial that is reported to have a spectrum of antibacterial activity similar to that of vancomycin (p.359) and greater potency against most Gram-positive bacterial strains *in vitro*; it is inactive against Gram-negative bacteria. Daptomycin disrupts the bacterial cell membrane potential by binding to the cell membranes in a calcium-dependent process, but without entering the cytoplasm, thus inhibiting the synthesis of protein, DNA, and RNA.

Daptomycin has shown activity both *in vitro* and in clinical infection with both meticillin-susceptible and meticillin-resistant *Staphylococcus aureus*, vancomycin-susceptible *Enterococcus faecalis*, and some streptococci.

It is reported to show antimicrobial synergy *in vitro* with aminoglycosides, beta lactams, and rifampicin against *Staph. aureus* (including meticillin-resistant strains) and enterococci (including vancomycin-resistant strains).

Resistance to daptomycin has been shown in clinical studies but only rarely; the mechanism of resistance has not been identified.

◊ Reviews.

1. Boucher HW, Sakoulas G. Perspectives on daptomycin resistance, with emphasis on resistance in Staphylococcus aureus. *Clin Infect Dis* 2007; **45:** 601–8.

Pharmacokinetics

Daptomycin is not absorbed to any significant extent after oral doses. The pharmacokinetics of daptomycin are generally linear at intravenous doses ranging from 4 to 12 mg/kg once daily. Peak plasma concentrations are achieved within 0.5 to 0.8 hours. It is distributed mainly into the extracellular space with a volume of distribution of about 0.1 litres/kg. Daptomycin crosses the blood-brain barrier and the placenta. It is about 90% bound to plasma proteins, mainly serum albumin.

In-vitro studies indicate that daptomycin is not metabolised by, and does not affect, the cytochrome P450 isoenzyme system. Little or no metabolism is thought to take place although 4 minor metabolites have been detected in the urine.

Daptomycin is excreted mainly via renal filtration with about 78% and 6% of a dose recovered in the urine and faeces, respectively. It has an elimination half-life of about 8 hours after an intravenous dose of 4 mg/kg once daily for 7 days and is prolonged in patients with renal impairment; a two- to threefold increase has been reported in those with severe impairment or end-stage renal disease.

Daptomycin is removed by haemodialysis or peritoneal dialysis.

◊ References.

1. Dvorchik B, *et al.* Population pharmacokinetics of daptomycin. *Antimicrob Agents Chemother* 2004; **48:** 2799–2807.

Uses and Administration

Daptomycin is given by intravenous infusion over 30 minutes for the treatment of complicated Gram-positive infections of the skin and soft tissues, and *Staphylococcus aureus* bacteraemia, including right-sided endocarditis, caused by meticillin-susceptible and meticillin-resistant strains.

For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

For the treatment of skin and soft-tissue infections, daptomycin is given in a dose of 4 mg/kg once daily for 7 to 14 days. A higher dose of 6 mg/kg once daily is given for 2 to 6 weeks in the treatment of bacteraemia.

For details of dosage modification in patients with renal impairment, see below.

Daptomycin has also been investigated for the treatment of vancomycin-resistant enterococcal infections, complicated urinary-tract infections, and community-acquired pneumonia.

◊ References.

1. Fenton C, *et al.* Daptomycin. *Drugs* 2004; **64:** 445–55.
2. Steenbergen JN, *et al.* Daptomycin: a lipopeptide antibiotic for the treatment of serious Gram-positive infections. *J Antimicrob Chemother* 2005; **55:** 283–8.
3. Schriever CA, *et al.* Daptomycin: a novel cyclic lipopeptide antimicrobial. *Am J Health-Syst Pharm* 2005; **62:** 1145–58.
4. French GL. Bactericidal agents in the treatment of MRSA infections—the potential role of daptomycin. *J Antimicrob Chemother* 2006; **58:** 1107–17.
5. Hair PI, Keam SJ. Daptomycin: a review of its use in the management of complicated skin and soft-tissue infections and *Staphylococcus aureus* bacteraemia. *Drugs* 2007; **67:** 1483–1512.
6. Enoch DA, *et al.* Daptomycin. *J Infect* 2007; **55:** 205–13.
7. Weis F, *et al.* Daptomycin, a lipopeptide antibiotic in clinical practice. *Curr Opin Investig Drugs* 2008; **9:** 879–84.
8. Forrest GN, *et al.* Clinical experience with daptomycin for the treatment of patients with documented gram-positive septic arthritis. *Ann Pharmacother* 2008; **42:** 213–17.

Administration in renal impairment. In patients with a creatinine clearance of less than 30 mL/minute, including those receiving dialysis, the intravenous dosage of daptomycin should be modified to 4 mg/kg once every 48 hours in the treatment of skin and soft-tissue infections, and to 6 mg/kg once every 48 hours in the treatment of bacteraemia.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Cubicin; ***Gr.:*** Cubicin; ***Israel:*** Cubicin; ***Port.:*** Cubicin; ***UK:*** Cubicin; ***USA:*** Cubicin.

Demeclocycline *(BAN, rINN)*

Demeclociclina; Déméclocycline; Demeclocyclinum; Demeklocyklin; Demeklosykliini; Demethylchlortetracycline. (4*S*,4a*S*,5a*S*,6*S*,12a*S*)-7-Chloro-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-1,11-dioxonaphthacene-2-carboxamide; 7-Chloro-6-demethyltetracycline.

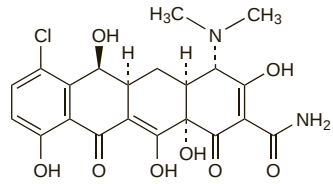
Демеклоциклин

$C_{21}H_{21}ClN_2O_8$ = 464.9.

CAS — 127-33-3 (demeclocycline); 13215-10-6 (demeclocycline sesquihydrate).

ATC — D06AA01; J01AA01.

ATC Vet — QD06AA01; QJ01AA01.



Pharmacopoeias. In *US.*

USP 31 (Demeclocycline). A yellow, odourless crystalline powder. Sparingly soluble in water; soluble 1 in 200 of alcohol and 1 in 40 of methyl alcohol; dissolves readily in 3N hydrochloric acid and in alkaline solutions. pH of a 1% solution in water is between 4.0 and 5.5. Store in airtight containers. Protect from light.

Demeclocycline Hydrochloride *(BANM, rINNM)*

Déméclocycline, chlorhydrate de; Demeclocyclini hydrochloridum; Demeklociklin-hidroklorid; Demeklociklino hidrochloridas; Demeklocyklin-hydrochlorid; Demeklocyklinhydroklorid; Demeklocykliny chlorowodorek; Demeklosiklin Hidroklorür; Demeklosykliinihydrokloridi; Demethylchlortetracycline Hydrochloride; Hidrocloruro de demeclociclina.

Демеклоциклина Гидрохлорид

$C_{21}H_{21}ClN_2O_8$,HCl = 501.3.

CAS — 64-73-3.

ATC — D06AA01; J01AA01.

ATC Vet — QD06AA01; QJ01AA01.

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

Ph. Eur. 6.2 (Demeclocycline Hydrochloride). The hydrochloride of a substance produced by certain strains of *Streptomyces aureofaciens* or by any other means. A yellow powder. Soluble or sparingly soluble in water; slightly soluble in alcohol; very slightly soluble in acetone. It dissolves in solutions of alkali hydroxides and carbonates. A 1% solution in water has a pH of 2.0 to 3.0. Protect from light.

USP 31 (Demeclocycline Hydrochloride). A yellow, odourless, crystalline powder. Soluble 1 in 60 of water and 1 in 50 of methyl alcohol; slightly soluble in alcohol; practically insoluble in acetone and in chloroform; sparingly soluble in solutions of alkali hydroxides and carbonates. pH of a 1% solution in water is between 2.0 and 3.0. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Tetracycline, p.347.

Phototoxic reactions occur more frequently with demeclocycline than with other tetracyclines and patients should avoid direct exposure to sunlight or artificial ultraviolet light.

Reversible nephrogenic diabetes insipidus with polyuria, polydipsia, and weakness may occur in patients treated with demeclocycline, particularly with prolonged treatment and/or high doses. Plasma creatinine should be monitored in patients receiving demeclocycline for long periods for the treatment of inappropriate secretion of antidiuretic hormone, since tetracycline-induced renal impairment may not otherwise be apparent in the absence of oliguria. For a comment that the usefulness of demeclocycline for this indication may be limited by nephrotoxicity in patients with cardiac or hepatic disease, see Syndrome of Inappropriate ADH Secretion under Uses and Administration, below.

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.

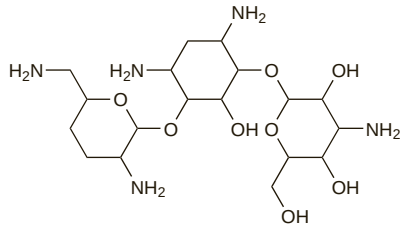
Дибекацина Сульфат

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

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.

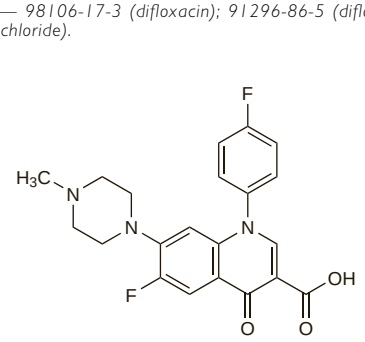
Difloxacin Hydrochloride *(USAN, rINNM)*

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)