Adverse Effects
As for Rifampicin, p.325.

A higher incidence of hyperuricaemia has been reported with rifapentine than with rifampicin.

Precautions
As for Rifampicin, p.326.

Rifapentine is only licensed for use in once- or twice-weekly regimens, and should not be given to HIV-infected patients because of potential interactions with HIV-protease inhibitors; an increased risk of developing resistance to rifamycins with highly intermittent (once- or twice-weekly) dosing regimens may occur in these patients.

Rifapentine is teratogenic in *animals*.

Interactions
As for Rifampicin, p.327.

Enzyme induction studies have suggested that rifapentine is a more potent inducer of cytochrome P450 isoenzymes than rifabutin, but less potent then rifampicin. It should not be used with HIV-protease inhibitors because of the risk of developing resistance, see Precautions, above.

Antimicrobial Action
As for Rifampicin, p.327.

Cross-resistance is common between rifapentine and rifampicin in *Mycobacterium tuberculosis*.

Antimycobacterial action. References.

1. Mor N, *et al.* Comparison of activities of rifapentine and rifampin against Mycobacterium tuberculosis residing in human macrophages. *Antimicrob Agents Chemother* 1995; **39:** 2073–7.
2. Vernon A, *et al.* Acquired rifamycin monoresistance in patients with HIV-related tuberculosis treated with once-weekly rifapentine and isoniazid. *Lancet* 1999; **353:** 1843–7.

Pharmacokinetics
Rifapentine is absorbed after oral doses. Absorption is enhanced by about 50% when rifapentine is taken with food. Peak plasma concentrations are achieved 5 to 6 hours after a single dose of 600 mg and steady-state concentrations are achieved by day 10 during daily use. A half-life of about 13 hours has been reported. Rifapentine undergoes nonoxidative metabolism and does not induce its own metabolism. Rifapentine and its active metabolite 25-deacetylrifapentine are 98% and 93% bound to plasma proteins, respectively.

Rifapentine and 25-deacetylrifapentine are excreted mainly in the faeces with a small amount appearing in the urine.

◊ References.

1. Keung ACF, *et al.* Pharmacokinetics of rifapentine in patients with varying degrees of hepatic dysfunction. *J Clin Pharmacol* 1998; **38:** 517–24.
2. Keung AC-F, *et al.* Pharmacokinetics of rifapentine in subjects seropositive for the human immunodeficiency virus: a phase I study. *Antimicrob Agents Chemother* 1999; **43:** 1230–3.
3. Conte JE, *et al.* Single-dose intrapulmonary pharmacokinetics of rifapentine in normal subjects. *Antimicrob Agents Chemother* 2000; **44:** 985–90.
4. Weiner M, *et al.* Pharmacokinetics of rifapentine at 600, 900, and 1,200 mg during once-weekly tuberculosis therapy. *Am J Respir Crit Care Med* 2004; **169:** 1191–7.
5. Langdon G, *et al.* Population pharmacokinetics of rifapentine and its primary desacetyl metabolite in South African tuberculosis patients. *Antimicrob Agents Chemother* 2005; **49:** 4429–36.

Uses and Administration
Rifapentine is a rifamycin antibacterial (see Rifampicin, p.325) that is used, with other antimycobacterials, for the treatment of tuberculosis (p.196).

For drug-susceptible organisms rifapentine is given orally in a dose of 600 mg twice weekly during the initial intensive phase of short-course tuberculosis regimens, then once weekly during the continuation phase.

◊ Reviews.

1. Jarvis B, Lamb HM. Rifapentine. *Drugs* 1998; **56:** 607–16.
2. Munsiff SS, *et al.* Rifapentine for the treatment of pulmonary tuberculosis. *Clin Infect Dis* 2006; **43:** 1468–75.

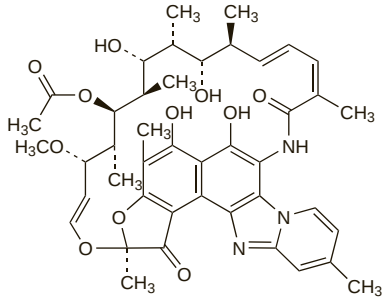
Preparations
Proprietary Preparations (details are given in Part 3)
USA: Priftin.

Rifaximin *(USAN, rINN)*

L-105; Rifaxidin; Rifaximina; Rifaximine; Rifaximinum. (2*S*,16*Z*,18*E*,20*S*,21*S*,22*R*,23*R*,24*R*,25*S*,26*S*,27*S*,28*E*)-5,6,21,23,25-Pentahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-2,7-(epoxypentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-*a*]benzimidazole-1,15(2*H*)-dione 25-acetate.

Рифаксимин

$C_{43}H_{51}N_3O_{11}$ = 785.9.
CAS — 80621-81-4.
ATC — A07AA11; D06AX11.
ATC Vet — QA07AA11; QD06AX11; QG51AA06; QJ51XX01.



NOTE. The code L-105 has also been applied to the cephalosporin cefuzonam.

Profile
Rifaximin is a rifamycin antibacterial with antimicrobial actions similar to those of rifampicin *in-vitro* (p.327), but which is poorly absorbed from the gastrointestinal tract, having a bioavailability of about only 0.4%. Therefore, it does not have the usual adverse effects or interactions of rifampicin. Hypersensitivity reactions, including exfoliative dermatitis and angioneurotic oedema have been reported. Rifaximin should not be given to patients with travellers' diarrhoea complicated by fever or blood in the stool.

It has been licensed in the USA and some other countries for the treatment of travellers' diarrhoea caused by noninvasive strains of *Escherichia coli*. It has also been tried for other gastrointestinal disorders, including infectious diarrhoea in nontravellers, inflammatory bowel disease, abdominal distension, bloating, and flatulence, small bowel bacterial overgrowth, diverticulitis, Crohn's disease, for surgical infection prophylaxis, and hepatic encephalopathy (p.1697).

For the treatment of travellers' diarrhoea in those 12 years of age and older, the recommended oral dose is 200 mg three times daily for 3 days. Doses given for other indications range from 600 to 1200 mg daily, in 2 to 4 divided doses.

Rifaximin has also been used topically as a 5% ointment.

◊ References.

1. Gillis JC, Brogden RN. Rifaximin: a review of its antibacterial activity, pharmacokinetic properties and therapeutic potential in conditions mediated by gastrointestinal bacteria. *Drugs* 1995; **49:** 467–84.
2. DuPont HL, *et al.* Rifaximin versus ciprofloxacin for the treatment of traveler's diarrhea: a randomized, double-blind clinical trial. *Clin Infect Dis* 2001; **33:** 1807–15.
3. Pakyz AL. Rifaximin: a new treatment for travelers' diarrhea. *Ann Pharmacother* 2005; **39:** 284–9.
4. Robins GW, Wellington K. Rifaximin: a review of its use in the management of traveller's diarrhoea. *Drugs* 2005; **65:** 1697–1713.
5. Ericsson CD. Safety and tolerability of the antibacterial rifaximin in the treatment of travellers' diarrhoea. *Drug Safety* 2006; **29:** 201–7.
6. Adachi JA, DuPont HL. Rifaximin: a novel nonabsorbed rifamycin for gastrointestinal disorders. *Clin Infect Dis* 2006; **42:** 541–7. Correction. *ibid.*; 896. [dose frequency]
7. Pimentel M, *et al.* The effect of a nonabsorbed oral antibiotic (rifaximin) on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med* 2006; **145:** 557–63.
8. Fumi AL, Trexler K. Rifaximin treatment for symptoms of irritable bowel syndrome. *Ann Pharmacother* 2008; **42:** 408–12.

Diverticular disease. Rifaximin may be used in the management of diverticular disease (p.1695); for reference to its use in combination with mesalazine see p.1747.

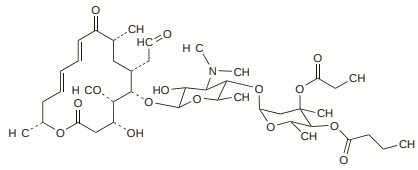
Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Normix; ***Gr.:*** Lormyx; Rifacol; ***Hung.:*** Normix; ***Ital.:*** Normix; Rifacol; ***Mex.:*** Flonorm; Redactiv†; ***Pol.:*** Xifaxan; ***Port.:*** Flonorm; ***Spain:*** Spiraxin; Zaxine; ***USA:*** Xifaxan.

Rokitamycin *(rINN)*

M-19-Q; 3″-Propionyl-leucomycin A_5; Rikamycin; Rokitamicina; Rokitamycine; Rokitamycinum; TMS-19Q. [(4*R*,5*S*,6*S*,7*R*,9*R*,10*R*,11*E*,13*E*,16*R*)-7-(Formylmethyl)-4,10-dihydroxy-5-methoxy-9,16-dimethyl-2-oxooxacyclohexadeca-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″-butyrate 3″-propionate.

Рокитамицин

$C_{42}H_{69}NO_{15}$ = 828.0.
CAS — 74014-51-0.
ATC — J01FA12.
ATC Vet — QJ01FA12.



Pharmacopoeias. In *Jpn*.

Profile
Rokitamycin is a macrolide antibacterial with actions and uses similar to those of erythromycin (p.269). It has been given orally in usual doses of 400 mg twice daily in the treatment of susceptible infections.

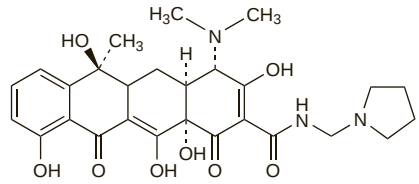
Preparations
Proprietary Preparations (details are given in Part 3)
Ital.: Paidocin; Rokital.

Rolitetracycline *(BAN, USAN, rINN)*

PMT; Pyrrolidinomethyltetracycline; Rolitetraciclina; Rolitétracycline; Rolitetracyclinum; Rolitetracyklin; Rolitetrasykliini; SQ-15659. N^2-(Pyrrolidin-1-ylmethyl)tetracycline.

Ролитетрациклин

$C_{27}H_{33}N_3O_8$ = 527.6.
CAS — 751-97-3.
ATC — J01AA09.
ATC Vet — QJ01AA09.



Profile
Rolitetracycline is a tetracycline derivative with general properties similar to those of tetracycline (p.347). It is included in some topical eye preparations used for the treatment of susceptible infections. It has also been given by injection, when it has been associated with shivering and, more rarely, rigor, due to a Jarisch-Herxheimer reaction. Injection has also been followed by a peculiar taste sensation, often similar to ether.

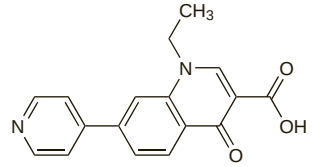
Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Eubetal Biotic†; ***Ital.:*** Colbiocin; Eubetal Antibiotico; Vitecaf; ***Rus.:*** Colbiocin (Колбиоцин).

Rosoxacin *(BAN, USAN, rINN)*

Acrosoxacin; Rosoksasiini; Rosoxacine; Rosoxacino; Rosoxacinum; Win-35213. 1-Ethyl-1,4-dihydro-4-oxo-7-(4-pyridyl)quinoline-3-carboxylic acid.

Розоксацин

$C_{17}H_{14}N_2O_3$ = 294.3.
CAS — 40034-42-2.
ATC — J01MB01.
ATC Vet — QJ01MB01.



Adverse Effects and Precautions
As for Nalidixic Acid, p.304.

Dizziness, drowsiness, and visual disturbances occur relatively frequently, and patients should be advised not to drive or operate machinery if affected.

Uses and Administration
Rosoxacin is a 4-quinolone antibacterial with actions similar to those of nalidixic acid (p.304). It is active against *Neisseria gonorrhoeae* and has been given as single-dose oral treatment for gonorrhoea. It has also been used in the treatment of urinary-tract infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Eradacil; ***Mex.:*** Eradacil; ***Port.:*** Eradacil†.

Roxithromycin *(USAN, rINN)*

Roksitromicinas; Roksitromisin; Roksitromysiini; Roxithromycine; Roxithromycinum; Roxitromicin; Roxitromicina; Roxitromycin; RU-965; RU-28965. Erythromycin 9-{*O*-[(2-methoxyethoxy)-methyl]oxime}.

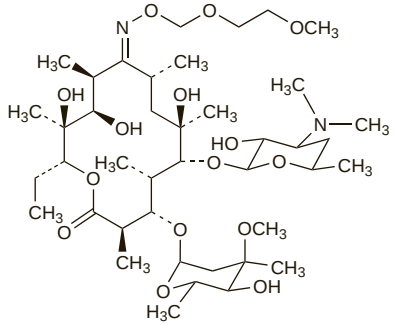
Рокситромицин

$C_{41}H_{76}N_2O_{15}$ = 837.0.

CAS — 80214-83-1.

ATC — J01FA06.

ATC Vet — QJ01FA06.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn*.
Ph. Eur. 6.2 (Roxithromycin). A white or almost white, crystalline powder. It exhibits polymorphism. Very slightly soluble in water; freely soluble in alcohol, in acetone, and in dichloromethane; slightly soluble in dilute hydrochloric acid. Store in airtight containers.

Adverse Effects and Precautions

As for Erythromycin, p.270.

Gastrointestinal disturbances are the most frequent adverse effect, but are less frequent than with erythromycin.

The dose of roxithromycin may need to be reduced in patients with hepatic or renal impairment.

Effects on the kidneys. Acute interstitial nephritis has been reported[1] in a patient given roxithromycin; renal function improved over several days after the drug was stopped.

1. Akcay A, *et al.* Acute renal failure and hepatotoxicity associated with roxithromycin. *Ann Pharmacother* 2004; **38:** 721–2.

Effects on the lungs. Acute eosinophilic pneumonia was attributed in a patient to the use of roxithromycin.[1] The condition resolved after treatment with methylprednisolone.

1. Pérez-Castrillón JL, *et al.* Roxithromycin-induced eosinophilic pneumonia. *Ann Pharmacother* 2002; **36:** 1808–9.

Effects on the pancreas. Acute pancreatitis, with duodenal inflammation, pain, pancreatic enlargement, and raised serum-amylase developed in a patient within 24 hours of substituting roxithromycin for erythromycin ethyl succinate.[1] Symptoms resolved rapidly once roxithromycin was stopped.

1. Souweine B, *et al.* Acute pancreatitis associated with roxithromycin therapy. *DICP Ann Pharmacother* 1991; **25:** 1137.

Eosinophilia. For a report of an eosinophilic syndrome in a patient after treatment with azithromycin or roxithromycin, see Azithromycin, p.207. See also under Effects on the Lungs, above.

Interactions

For a discussion of drug interactions of macrolide antibacterials, see Erythromycin, p.271.

Roxithromycin has a much lower affinity for cytochrome P450 isoenzymes than erythromycin and therefore has fewer interactions. It does not appear to interact with antacids, carbamazepine, oral contraceptives, prednisolone, or ranitidine.

Antimicrobial Action

As for Erythromycin, p.271. It is reported to be as active or slightly less active than erythromycin.

Pharmacokinetics

Roxithromycin is absorbed after oral doses with a bioavailability of about 50%. Peak plasma concentrations of about 6 to 8 micrograms/mL occur around 2 hours after a single dose of 150 mg. The mean peak plasma concentration at steady state after a dose of 150 mg twice daily is 9.3 micrograms/mL. Absorption is reduced when taken after a meal. It is widely distributed into tissues and body fluids; high concentrations are taken up into white blood cells. Small amounts of roxithromycin are distributed into breast milk. It is about 96% bound to plasma proteins (mainly α_1-acid glycoprotein) at trough concentrations, but binding is saturable, and only about 87% is bound at usual peak concentrations. Small amounts of roxithromycin are metabolised in the liver, and the majority of a dose is excreted in the faeces as unchanged drug and metabolites; about 7 to 10% is excreted in urine, and up to 15% via the lungs. The elimination half-life is reported to range from about 8 to 13 hours, but may be more prolonged in patients with hepatic or renal impairment and in children. It has been reported that roxithromycin is not substantially removed by peritoneal dialysis.

◊ References.

1. Puri SK, Lassman HB. Roxithromycin: a pharmacokinetic review of a macrolide. *J Antimicrob Chemother* 1987; **20** (suppl B): 89–100.

Uses and Administration

Roxithromycin is a macrolide antibacterial with actions and uses similar to those of erythromycin (p.272). It is given orally to adults in a usual dose of 150 mg twice daily or sometimes 300 mg once daily, at least 15 minutes before meals, for 5 to 10 days in the treatment of susceptible infections.

Dosage may need to be modified in patients with hepatic or renal impairment (see below).

For doses in infants and children, see below.

◊ References.

1. Williams JD, Sefton AM. Comparison of macrolide antibiotics. *J Antimicrob Chemother* 1993; **31** (suppl C): 11–26.
2. Markham A, Faulds D. Roxithromycin: an update of its antimicrobial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1994; **48:** 297–326.
3. Young LS, Lode H, eds. Roxithromycin: first of a new generation of macrolides: update and perspectives. *Infection* 1995; **23** (suppl 1): S1–S52.
4. Lovering AM, *et al.*, eds. Roxithromycin—additional therapeutic potential. *J Antimicrob Chemother* 1998; **41** (suppl B): 1–97.

Administration in children. In children weighing from 6 up to 40 kg a dose of 5 to 8 mg/kg daily of roxithromycin may be used.

Administration in hepatic impairment. The licensed product information for roxithromycin notes that safety in hepatic impairment has not been established and advises halving the usual daily dose (see above) if used.

Administration in renal impairment. The licensed product information for roxithromycin notes that safety in renal impairment has not been established and dosage adjustment details are not specified.

A pharmacokinetic study[1] in 20 subjects (10 with normal renal function and 10 with severely impaired function) suggested that doubling the dosage interval of roxithromycin would be suitable in those with a creatinine clearance of less than 15 mL/minute.

1. Halstenson CE, *et al.* Disposition of roxithromycin in patients with normal and severely impaired renal function. *Antimicrob Agents Chemother* 1990; **34:** 385–9.

Hyperplasia. Gingival hyperplasia is a well recognised adverse effect of ciclosporin treatment; a small study[1] indicated that roxithromycin could reduce overgrowth, possibly by an effect on transforming growth factor-β. For the use of another macrolide, azithromycin, for this indication see Hyperplasia, p.1824.

1. Condé SAP, *et al.* Roxithromycin reduces cyclosporine-induced gingival hyperplasia in renal transplant patients. *Transplant Proc* 2008; **40:** 1435–8.

Ischaemic heart disease. For mention of studies investigating roxithromycin in the prevention of ischaemic heart disease, see under Azithromycin, p.208.

Respiratory disorders. For reference to the use of roxithromycin in the management of respiratory disorders, see under Erythromycin, p.273.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Anuar†; Delos; Klomicina; Rulid; Sinurit†; ***Austral.:*** Biaxsig; Roxar; Roximycin; Rulide; ***Austria:*** Roxithrostad; Rulide; ***Belg.:*** Claramid†; Docroxithro; Rulid; ***Braz.:*** Floxid; Rotram; Roxid†; Roxina; Roxitran; Roxitricina†; Roxitrom; Roxitromin†; Rulid; ***Chile:*** Ramivan; ***Cz.:*** Rovenal†; Rulid†; ***Denm.:*** Forilin†; Forimycin; Roximstad; Surlid; ***Fin.:*** Roxibion; Surlid; ***Fr.:*** Claramid; Rulid; Subroxine; ***Ger.:*** Infectoroxit; Romyk†; Roxi; Roxipaed†; Roxi-Puren; Roxi-Q; Roxi-saar; Roxibeta; Roxidura; Roxigamma; Roxigrun; RoxiHefa; RoxiHexal; Roxiklinge†; Roxithro-Lich; Rulid; ***Gr.:*** Acevor; Anti-Bio; Aristomycin; Asmetic; Azuril; Bazuctril; Bicofen; Delitroxin; Erybros; Macrolid-S; Neo-Suxigal; Nirox; Oxetine; Redotrin; Roxibron; Roxicillin; Roximin; Roxitazon; Roxivinol; Roxy-Due; Roxyspes; Rulid; Seide; Siguon; Thriostaxil; Tirabicin; Toscamycin-R; Uramilon; Vaselpin; Vomitoran; ***Hong Kong:*** Roxicin; Rudin; Rulid; Uonin; ***Hung.:*** Renicin; Rulid; ***India:*** Biorox; Roxee; Roxem; Roxeptin; Roxibid; Roxid; Roxivista; Roxyrol; Unorox†; ***Indon.:*** Anbiolid; Biostatik; Ixor; Rolexit; Rulid; Ruxcine; Simacron; Sitro; Uplores; Xorin; ***Israel:*** Roxo; Rulid; ***Ital.:*** Assoral; Overal; Rossitrol; Rulid; ***Malaysia:*** Roxcin; Roxinox; Rulid; Uonin; ***Mex.:*** Crolix; Kensodic; Rulid; Sertrom; ***Neth.:*** Rulide; ***NZ:*** Romicin; ***Philipp.:*** Macrol; Marulide; Rulid; Ruthison; Thromyn; ***Pol.:*** Renicin; Rolicyn; Roxiratio; Roxitron; Rulid; Xitrocin; ***Port.:*** Inferoxin; Odonticina; Roxitron; Rulide; ***Rus.:*** Elrox (Элрокс); Roxeptin (Роксептин); Roxihexal (Роксигексал); Roxylor (Роксилор); Rulid (Рулид); ***S.Afr.:*** Roxulide; Roxxibid; Rulide; Throsyn; ***Singapore:*** Roxid; Rulid†; ***Spain:*** Macrosil; Rotramin; Rulide; ***Swed.:*** Surlid; ***Switz.:*** Rulid; ***Thai.:*** Ammirox; Eroxade; Poliroxin; Rothricin; Roxcin; Roxicin; Roxilan; Roximin; Roxithro; Roxithroxyl; Roxitin; Roxitop; Roxlecon; Roxomycin; Roxthomed; Roxthrin; Roxto; Roxtrocin; Roxy; Roxydin; Rucin; Rulid; Uonin; Utolid; Vesthromycin; ***Turk.:*** Remora; Ritosin; Roksimin; Roksolit; Rulid; ***Venez.:*** Rancolid†; Roxicure; Roxitrol; Rulid.

Multi-ingredient: ***India:*** Roxeptin-ME.

Rufloxacin Hydrochloride *(BANM, rINNM)*

Hidrocloruro de rufloxacino; MF-934 (rufloxacin); Rufloxacine, Chlorhydrate de; Rufloxacini Hydrochloridum. 9-Fluoro-2,3-dihydro-10-[4-methylpiperazin-1-yl]-7-oxo-7*H*-pyrido[1,2,3-*de*]-1,4-benzothiazine-6-carboxylic acid hydrochloride.

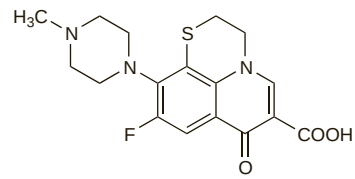
Руфлоксацина Гидрохлорид

$C_{17}H_{18}FN_3O_3S,HCl$ = 399.9.

CAS — 101363-10-4 (rufloxacin); 106017-08-7 (rufloxacin hydrochloride).

ATC — J01MA10.

ATC Vet — QJ01MA10.



(rufloxacin)

Profile

Rufloxacin is a fluoroquinolone antibacterial with properties similar to those of ciprofloxacin (p.243). It is given orally as the hydrochloride in the treatment of susceptible infections in a usual initial dose of 400 mg on the first day followed by 200 mg daily thereafter. A plasma half-life of 30 hours or more has been reported.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Monos; Qari; Tebraxin; ***Mex.:*** Uroflox; ***Philipp.:*** Uroclar; ***Thai.:*** Uroflox.

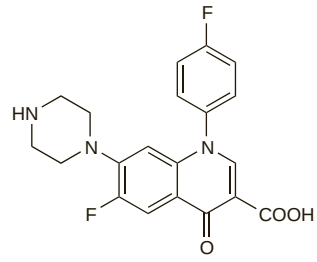
Sarafloxacin Hydrochloride *(BANM, USAN, rINNM)*

A-57135 (sarafloxacin); A-56620 (sarafloxacin or sarafloxacin hydrochloride); Abbott-56620 (sarafloxacin or sarafloxacin hydrochloride); Hidrocloruro de sarafloxacino; Sarafloxacine, Chlorhydrate de; Sarafloxacini Hydrochloridum.

Сарафлоксацина Гидрохлорид

$C_{20}H_{17}F_2N_3O_3,HCl$ = 421.8.

CAS — 98105-99-8 (sarafloxacin); 91296-87-6 (sarafloxacin hydrochloride).



(sarafloxacin)

Profile

Sarafloxacin is a fluoroquinolone antibacterial that has been used as the hydrochloride in veterinary medicine.