Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Veramina; ***Austria:*** Monuril; ***Belg.:*** Monuril; ***Braz.:*** Monuril; ***Canad.:*** Monurol; ***Chile:*** Monurol; ***Fin.:*** Monurol†; ***Fr.:*** Fosfocine; Monuril; Uridoz; ***Ger.:*** InfectoFos; Monuril; ***Gr.:*** Monurol†; ***Hong Kong:*** Monurol; ***Hung.:*** Monural; ***Indon.:*** Fosmicin; Fosmidex; Monuril; ***Israel:*** Monurol; ***Ital.:*** Afos†; Faremicin†; Fosfocin; Francital†; Ipamicina†; Monuril; Ultramicina†; ***Jpn:*** Fosmicin-S; ***Malaysia:*** Monurol; ***Mex.:*** Fosfocil; Monurol; ***Neth.:*** Monuril; ***Philipp.:*** Monurol; ***Pol.:*** Monural; ***Port.:*** Monuril; ***Rus.:*** Monural (Монурал); ***S.Afr.:*** Urizone; ***Spain:*** Fosfocina; Monurol; Solufos; ***Swed.:*** Monurol†; ***Switz.:*** Monuril; ***Thai.:*** Fosmicin; ***Turk.:*** Monurol; ***USA:*** Monurol.

Framycetin Sulfate *(rINNM)*

Framicetino sulfatas; Framicetin-szulfát; Framycetin Sulphate *(BANM)*; Framycétine, sulfate de; Framycetini sulfas; Framycetinsulfat; Framycetin-sulfát; Framysetiinisulfaatti; Neomycin B Sulphate; Sulfato de framicetina. 2-Deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-5-*O*-[3-*O*-(2,6-diamino-2,6-dideoxy-β-L-idopyranosyl)-β-D-ribofuranosyl]streptamine sulphate.

Фрамицетина Сульфат

$C_{23}H_{46}N_6O_{13},xH_2SO_4$.

CAS — 119-04-0 (framycetin); 4146-30-9 (framycetin sulfate).

ATC — D09AA01; R01AX08; S01AA07.

ATC Vet — QD09AA01; QR01AX08; QS01AA07.

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

Ph. Eur. 6.2 (Framycetin Sulphate). A substance produced by growth of selected strains of *Streptomyces fradiae* or *S. decaris* or obtained by any other means. It contains not more than 3% of neomycin C (p.305) and loses not more than 8% of its weight on drying. A white or yellowish-white, hygroscopic powder. The potency is not less than 630 units of neomycin B per mg, calculated with reference to the dried substance. Freely soluble in water; very slightly soluble in alcohol; practically insoluble in acetone. A 1% solution in water has a pH of 6.0 to 7.0. Store in airtight containers. Protect from light.

Profile

Framycetin is an aminoglycoside antibiotic which forms the major component of neomycin (p.305) and has similar actions and uses. Framycetin sulfate is used topically in usual concentrations of 1% for the treatment of infections of the skin, and in concentrations of 0.5% for infections of the eye and ear. It is often used with other antibacterials and corticosteroids in topical preparations.

Framycetin sulfate is poorly absorbed from the gastrointestinal tract and has been given orally for the treatment of gastrointestinal infections and pre-operatively for bowel preparation. It has sometimes been given prophylactically as part of regimens for the selective decontamination of the digestive tract in patients in intensive care.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Sofra-Tulle; Soframycin; ***Austria:*** Sofra-Tull; ***Belg.:*** Soframycine; ***Canad.:*** Sofra-Tulle; Soframycin; ***Fin.:*** Sofra-Tulle†; ***Ger.:*** Leukase N; Sofra-Tull†; ***Hong Kong:*** Sofra-Tulle†; ***India:*** Sofra-Tulle; Soframycin; ***Indon.:*** Daryant-Tulle; Sofra-Tulle; ***Irl.:*** Soframycin; ***Israel:*** Sofra-Tulle†; ***Malaysia:*** Sofra-Tulle†; ***Norw.:*** Sofra-Tulle†; ***NZ:*** Soframycin; ***Rus.:*** Isofra (Изофра); ***S.Afr.:*** Sofra-Tulle; Soframycin; ***Singapore:*** Sofra-Tulle†; ***Switz.:*** Frakitacine†; Sofra-Tulle†; Soframycin; ***Thai.:*** Sofra-Tulle; ***UK:*** Sofra-Tulle; Soframycin†.

Multi-ingredient: ***Arg.:*** Biotaer Nasal; ***Austral.:*** Otodex; Sofradex; Soframycin; ***Austria:*** Leukase; Leukase-Kegel; ***Belg.:*** Frakidex; Sofraline; Sofrasolone; ***Braz.:*** Fonergin; ***Canad.:*** Opticort; Proctol; Proctomyxin HC; Proctosedyl; ratio-Proctosone; Sofracort; Soframycin; ***Cz.:*** Pulpomixine; Septomixine; Sofradex†; ***Denm.:*** Proctosedyl; Sofradex; ***Fin.:*** Proctosedyl; Sofradex; ***Fr.:*** Corticetine; Frakidex; Framyxone; Novomyxine†; Polyfra; ***Ger.:*** Leukase N; ***Hong Kong:*** Frakidex; Frazoline; Proctosedyl†; Sofradex; ***India:*** Proctosedyl; Sofracort; Sofradex; Sofradex-F; ***Indon.:*** Sofradex; ***Irl.:*** Proctosedyl; Sofradex; Soframycin†; ***Malaysia:*** Proctosedyl; Sofradex; ***Neth.:*** Proctosedyl; Sofradex; ***Norw.:*** Proctosedyl; Sofradex; ***NZ:*** Sofradex; Soframycin; ***Philipp.:*** Proctosedyl; ***Pol.:*** Caridент; Dexadent; ***Port.:*** Frakidex; ***S.Afr.:*** Proctosedyl; Sofradex; ***Singapore:*** Frakidex†; Proctosedyl; Sofradex; ***Spain:*** Abrasone; Aldo Otico†; Aldoderma; Nesfare; Otomidrin; ***Swed.:*** Proctosedyl†; ***Switz.:*** Corticetine†; Dexalocal-F; Frakidex; Septomixine; Sofradex; ***Thai.:*** Proctosedyl; Sofradex; Topifram; ***UK:*** Sofradex.

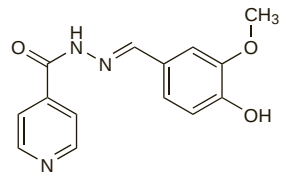
Ftivazide *(rINN)*

Ftivazida; Ftivazidum; Phthivazid; Phthivazidum. 2′-Vanillylideneisonicotinohydrazide monohydrate.

Фтивазид

$C_{14}H_{13}N_3O_3,H_2O$ = 289.3.

CAS — 149-17-7 (anhydrous ftivazide).



(anhydrous ftivazide)

Pharmacopoeias. In *Chin.* and *Int.*

Profile

Ftivazide is an antimycobacterial given orally in the treatment of tuberculosis. It is a derivative of isoniazid.

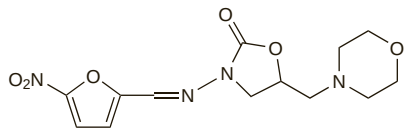
Furaltadone Hydrochloride *(BANM, rINNM)*

Furaltadone, Chlorhydrate de; Furaltadoni Hydrochloridum; Hidrocloruro de furaltadona. (±)-5-Morpholinomethyl-3-(5-nitrofurfurylideneamino)oxazolidin-2-one hydrochloride.

Фуральтадона Гидрохлорид

$C_{13}H_{16}N_4O_6$,HCl = 360.8.

CAS — 139-91-3 (furaltadone); 59302-14-6 (±-furaltadone).



(furaltadone)

Pharmacopoeias. *Fr.* includes Furaltadone for veterinary use.

Profile

Furaltadone was formerly given orally as an antibacterial but was later withdrawn owing to its toxic effects. Furaltadone hydrochloride is still used topically in preparations for ear disorders. Furaltadone has been used in veterinary medicine.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Indon.:*** Otozambon; ***Thai.:*** Otosamthong.

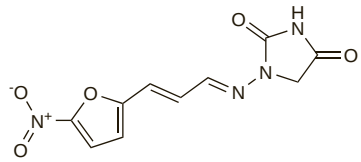
Furazidin

Akritoin; Furagin; Furazidine. 1-{[3-(5-Nitro-2-furyl)allylidene]amino}hydantoin.

Фуразидин

$C_{10}H_8N_4O_5$ = 264.2.

CAS — 1672-88-4.



Profile

Furazidin is a nitrofuran antibacterial with properties similar to those of nitrofurantoin. It is used in the treatment of urinary-tract infections. A usual oral dose is 100 mg given four times daily for one day followed by 100 mg given three times daily for 7 to 8 days.

Preparations

Proprietary Preparations (details are given in Part 3)

Pol.: Furaginum.

Fusafungine *(BAN, rINN)*

Fusafungin; Fusafungina; Fusafunginum.

Фузафунгин

CAS — 1393-87-9.

ATC — R02AB03.

ATC Vet — QR02AB03.

Profile

Fusafungine is a depsipeptide antibacterial produced by *Fusarium lateritium* strain 437. It is active against some Gram-positive and Gram-negative organisms, *Candida albicans*, and *Mycoplasma pneumoniae*. It has also been stated to possess anti-inflammatory activity.

It is used in the form of an aerosol spray in the treatment of infections of the upper respiratory tract, inhaled in usual doses of 500 micrograms every 4 hours into each nostril or via the mouth. These routes may be used simultaneously if necessary.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Locabiosol; ***Belg.:*** Locabiotal; ***Braz.:*** Locabiotal; ***Chile:*** Locabiosol†; ***Cz.:*** Bioparox; ***Ger.:*** Locabiosol; ***Gr.:*** Locabiotal; ***Hong Kong:*** Locabiotal†; ***Hung.:*** Bioparox; ***Irl.:*** Locabiotal; ***Ital.:*** Locabiotal; ***Malaysia:*** Locabiotal; ***Philipp.:*** Locabiotal; ***Pol.:*** Bioparox; ***Port.:*** Locabiosol; ***Rus.:*** Bioparox (Биопарокс); ***S.Afr.:*** Locabiotal; ***Spain:*** Fusaloyos; ***Switz.:*** Locabiotal; ***Turk.:*** Locabiotal; ***UK:*** Locabiotal†.

Fusidic Acid *(BAN, USAN, rINN)*

Acide fusidique; Ácido fusídico; Acidum fusidicum; Acidum Fusidicum Hemihydricum; Fucidinsyra; Fusidiinihappo; Fusidik Asit; Fusidinsyra; Fuzidinsav; Fuzido rūgštis; Kyselina fusidová hemihydrát; SQ-16603. *ent*-16α-Acetoxy-3β-dihydroxy-4β,8β,14α-trimethyl-18-nor-5β,10α-cholesta-(17*Z*)-17(20),24-dien-21-oic acid hemihydrate.

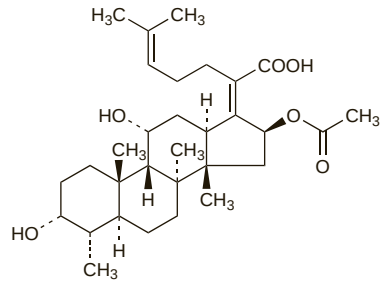
Фэузидовая Кислота

$C_{31}H_{48}O_6$, / H_2O = 525.7.

CAS — 6990-06-3 (anhydrous fusidic acid).

ATC — D06AX01; D09AA02; J01XC01; S01AA13.

ATC Vet — QD06AX01; QD09AA02; QJ01XC01; QS01AA13.



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

Ph. Eur. 6.2 (Fusidic Acid). An antimicrobial substance produced by the growth of certain strains of *Fusidium coccineum* or by any other means. A white or almost white crystalline powder. Practically insoluble in water; freely soluble in alcohol. Store at a temperature of 2° to 8°. Protect from light.

Sodium Fusidate *(BANM, rINNM)*

Fusidate de Sodium; Fusidate Sodium *(USAN)*; Fusidato sódico; Natrii fusidas; Natrio fuzidatas; Natriumfusidaatti; Natriumfusidat; Natrium-fusidát; Nátrium-fuzidát; Sodium, fusidate de; Sodyum Fusidat; SQ-16360.

Натрий Фэузидат

$C_{31}H_{47}NaO_6$ = 538.7.

CAS — 751-94-0.

ATC — D06AX01; D09AA02; J01XC01; S01AA13.

ATC Vet — QD06AX01; QD09AA02; QJ01XC01; QS01AA13.

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

Ph. Eur. 6.2 (Sodium Fusidate). A white or almost white, slightly hygroscopic, crystalline powder. Freely soluble in water and in alcohol. A 1.25% solution in water has a pH of 7.5 to 9.0. Store in airtight containers at a temperature of 2° to 8°. Protect from light.

Incompatibility. UK licensed product information states that reconstituted sodium fusidate injection is incompatible with infusion solutions containing glucose 20% or more, lipid infusions, and peritoneal dialysis fluids; precipitation may occur in solutions with a pH of less than 7.4.

Adverse Effects and Precautions

Apart from mild gastrointestinal upsets, fusidic acid or sodium fusidate appear to be well tolerated when given orally. Treatment with fusidates, orally or especially by the intravenous route, has been associated with jaundice and changes in liver function; normal liver function is usually restored when treatment is stopped. Therefore, fusidates should be given with caution to patients with hepatic impairment, and periodic monitoring of hepatic function is recommended in these patients and in those receiving high or prolonged oral doses. Caution is also required in biliary disease or biliary obstruction.

Venospasm, thrombophlebitis, and haemolysis have occurred in patients given fusidates intravenously. To reduce this it is recommended that solutions be buffered and that the solution should be given as a slow infusion into a large vein where there is a good blood flow. Hypocalcaemia has occurred after use of intravenous doses above those recommended, and has been attributed to the phosphate-citrate buffer in the preparation. Intramuscular or subcutaneous use may lead to tissue necrosis and is contra-indicated.

Hypersensitivity reactions in the form of rashes and irritation may occur with topical fusidates; rash is rare after systemic use.

Fusidic acid competes with bilirubin for binding to albumin *in vitro* and caution has been advised if it is given to premature, jaundiced, acidotic, or seriously-ill neonates because of the risk of kernicterus.

Effects on the blood. There have been occasional reports of granulocytopenia[1-3] and thrombocytopenia[3] after the use of fusidic acid systemically. Sideroblastic anaemia has also been reported.[4] UK licensed product information also states that there have been isolated cases of neutropenia, agranulocytosis, and pancytopenia.

1. Revell P, *et al.* Granulocytopenia due to fusidic acid. *Lancet* 1988; **ii:** 454–5.
2. Evans DIK. Granulocytopenia due to fusidic acid. *Lancet* 1988; **ii:** 851.
3. Leibowitz G, *et al.* Leukopenia and thrombocytopenia due to fusidic acid. *Postgrad Med J* 1991; **67:** 591–2.
4. Vial T, *et al.* Sideroblastic anaemia during fusidic acid treatment. *Eur J Haematol* 2004; **72:** 358–60.

Interactions

Although the exact metabolic pathways of fusidic acid are not known, an interaction has been suspected with drugs metabolised by the hepatic cytochrome P450 isoenzyme CYP3A4, and UK licensed product information suggests avoiding their use with fusidic acid.

Antivirals. An HIV-infected patient had fusidic acid toxicity after taking fusidic acid orally for one week with his usual antiretroviral treatment of *ritonavir*, *saquinavir*, and stavudine.[1] The plasma-fusidic acid concentration was about twice that expected and the ritonavir and saquinavir concentrations were also elevated. Fusidic acid was stopped and the patient initially improved. However, 4 days later he presented with jaundice, nausea, weakness, and further increases in liver function tests and hence all medications were stopped. The fusidic acid concentration, as well as those of ritonavir and saquinavir, were found to be still significantly elevated 6 days after fusidic acid had been stopped. The patient was able to restart his antiretroviral therapy later with no problems. The authors suggested that this interaction may be due to mutual inhibition of metabolism between the HIV-protease inhibitors and fusidic acid, and recommended that use of fusidic acid with either saquinavir or ritonavir should be avoided.

1. Khaliq Y, *et al.* A drug interaction between fusidic acid and a combination of ritonavir and saquinavir. *Br J Clin Pharmacol* 2000; **50:** 82–3.

Statins. For reference to the effect of fusidic acid in patients receiving statins, see p.1392.

Antimicrobial Action

Fusidic acid is a steroidal antibacterial with a bacteriostatic or bactericidal activity, mainly against Gram-positive bacteria.

Fusidic acid inhibits bacterial protein synthesis although, in contrast to drugs such as the macrolides or tetracyclines, it does not bind to the bacterial ribosome, but inhibits a factor necessary for translocation of peptide subunits and elongation of the peptide chain. It is capable of inhibiting protein synthesis in mammalian cells but exerts a selective action against susceptible infecting organisms because of poor penetration into the host cell.

Fusidic acid is very active against staphylococci, notably *Staph. aureus* and *Staph. epidermidis* (including meticillin-resistant strains). *Nocardia asteroides* and many clostridial strains are also highly susceptible. The streptococci and enterococci are less susceptible.

Most Gram-negative bacteria are intrinsically resistant but fusidic acid is active against *Neisseria* spp. and *Bacteroides fragilis*. It has some activity against strains of *Mycobacterium tuberculosis* and is highly active against *M. leprae*.

Fungi are resistant, but fusidic acid has some activity against a range of protozoa including *Giardia lamblia* and *Plasmodium falciparum*. High concentrations of fusidate are reported to inhibit viral growth *in vitro*, including that of HIV, although it is unclear whether this represents a surfactant effect, a general cytotoxic effect, or a genuine antiviral action.

No synergy has been shown *in vitro* in most studies between fusidic acid and rifampicin or vancomycin, and antagonism of the effects of ciprofloxacin has been reported. Interactions with the penicillins are complex, with either antagonism of the effect of one or both drugs, or no interaction. However, use of an antistaphylococcal penicillin with fusidic acid may prevent the emergence of fusidic acid-resistant staphylococcal mutants, and such combinations may be clinically effective.

Resistance. Resistance may be chromosomally mediated, representing altered protein synthesis, or plasmid-mediated, which appears to be due to reduced penetration of active drug into the cell. For further details on the increase of resistance to fusidic acid, see below.

Resistance. There has been an increase in the number of reports of fusidic acid resistance in *Staphylococcus aureus* particularly in dermatological isolates. The number of clinical isolates of initially resistant staphylococci has historically been low at about 1 to 2% overall.[1-3] However, in the UK the rate of fusidic acid resistance in staphylococcal isolates increased by up to 200% during the 1990s, and over half of all isolates are resistant in some samples.[3] This has been attributed to the widespread topical use of fusidic acid.[1-3]

The rate of resistance to short courses of fusidic acid used in systemic monotherapy is reported to be about 5%. In contrast, when given systemically with other antibacterials, the rate of resistance remains low at 0.8%.[4] Therefore, it has been suggested that systemic fusidic acid should be restricted to use with other antibacterial agents where clinically indicated in order to reduce the rate of resistance.[3,4]

1. Livermore D, *et al.* Fusidic-acid use and resistance. *Lancet* 2002; **360:** 806.
2. Mason BW, *et al.* Fusidic acid resistance in community isolates of methicillin-susceptible Staphylococcus aureus and fusidic acid prescribing. *J Antimicrob Chemother* 2003; **51:** 1033–6.
3. Dobie D, Gray J. Fusidic acid resistance in Staphylococcus aureus. *Arch Dis Child* 2004; **89:** 74–7.
4. Howden BP, Grayson ML. Dumb and dumber—the potential waste of a useful antistaphylococcal agent: emerging fusidic acid resistance in Staphylococcus aureus. *Clin Infect Dis* 2006; **42:** 394–400.

Pharmacokinetics

Sodium fusidate is well absorbed from the gastrointestinal tract, and a single oral 500-mg dose is reported to produce mean plasma concentrations of about 30 micrograms/mL within 2 to 4 hours, although there is considerable interindividual variation. Oral suspensions of fusidic acid are less well absorbed, with a bioavailability reported to be about 70% of that for sodium fusidate. Absorption may be delayed by food and may be more rapid in children than adults. Some accumulation occurs with repeated dosage and plasma concentrations of 100 micrograms/mL or more have been reported after 500 mg of sodium fusidate given three times daily for 4 days.

Fusidate is widely distributed into tissues and body fluids, including bone, pus, and synovial fluid; it penetrates cerebral abscesses but does not enter CSF in appreciable amounts. It has been found in the fetal circulation and in breast milk. About 95% or more of fusidate in the circulation is bound to plasma proteins.

Fusidate has a plasma half-life of about 10 to 15 hours. It is excreted in the bile, almost entirely as metabolites, some of which have weak antimicrobial activity. About 2% appears unchanged in the faeces. Little is excreted in the urine or removed by haemodialysis.

◊ References.

1. Reeves DS. The pharmacokinetics of fusidic acid. *J Antimicrob Chemother* 1987; **20:** 467–76.
2. Peter J-D, *et al.* Pharmacokinetics of intravenous fusidic acid in patients with cholestasis. *Antimicrob Agents Chemother* 1993; **37:** 501–6.
3. Brown NM, *et al.* The pharmacokinetics and protein-binding of fusidic acid in patients with severe renal failure requiring either haemodialysis or continuous ambulatory peritoneal dialysis. *J Antimicrob Chemother* 1997; **39:** 803–9.
4. Turnidge J. Fusidic acid pharmacology, pharmacokinetics and pharmacodynamics. *Int J Antimicrob Agents* 1999; **12** (suppl 2): S23–S34.

Uses and Administration

Fusidic acid and its salts are antibacterials used mainly in the treatment of staphylococcal infections, often with other drugs. They have been used in the treatment of abscess, including brain abscess, in bone and joint infections, in staphylococcal infections in patients with cystic fibrosis, in the treatment of staphylococcal endocarditis, and topically in eye infections and infections of the skin. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

The fusidates are given orally or topically as fusidic acid or sodium fusidate, or intravenously as sodium fusidate. Sodium fusidate 1 g is equivalent to about 0.98 g of fusidic acid. Because of differences in absorption (see Pharmacokinetics, above) 250 mg of fusidic acid is therapeutically equivalent to only 175 mg of the sodium salt, so doses of fusidic acid suspension (commonly used in children) appear relatively higher (see below). The diolamine salt was formerly used intravenously in humans but is still used in topical preparations in veterinary medicine.

Sodium fusidate is given as tablets in a usual oral adult dose of 500 mg every 8 hours, although this dose may be doubled in severe infection. For cutaneous staphylococcal infections, a dose of 250 mg twice daily is suitable. When given orally as the suspension the usual adult dose is 750 mg of fusidic acid three times daily.

In severe infections in adults weighing over 50 kg, sodium fusidate 500 mg is given three times daily by slow intravenous infusion. Each 500-mg dose is usually given as a buffered solution (pH 7.4 to 7.6) diluted to 500 mL with sodium chloride or other suitable intravenous solution. For those weighing less than 50 kg, a dose of 6 to 7 mg/kg three times daily is used. For details of doses in children, see below.

Sodium fusidate as a 2% ointment or medicated dressing, or fusidic acid as a 2% cream or gel, are used in the local treatment of skin infections. Eye drops containing fusidic acid 1% are used in eye infections. Topical use may lead to problems of resistance (see Antimicrobial Action, above).

Administration in children. In the UK, the licensed *oral* doses of **fusidic acid suspension**, given three times daily, are:

- up to 1 year old: about 15 mg/kg
- 1 to 5 years: 250 mg
- 5 to 12 years: 500 mg
- over 12 years: usual adult doses (see above)

Suggested doses of **sodium fusidate** by *intravenous* infusion are:

- 1 month and above: if weighing less than 50 kg, 6 to 7 mg/kg three times daily; heavier children may be given usual adult doses (see above)

The *BNFC* suggests that neonates up to 1 month of age may be given an intravenous dose of 10 mg/kg every 12 hours.

Preparations

BP 2008: Fusidic Acid Cream; Fusidic Acid Eye Drops; Fusidic Acid Oral Suspension; Sodium Fusidate Ointment.

Proprietary Preparations (details are given in Part 3)
Arg.: Drum; Fucidin; Fucithalmic; Fusimed; Fusitop; Gelbiotic; ***Austral.:*** Fucidin; ***Austria:*** Fucidin; Fucithalmic; ***Belg.:*** Fucidin; Fucithalmic; ***Braz.:*** Verutex; ***Canad.:*** Fucidin; Fucithalmic; ***Chile:*** Fucidin; Fucithalmic; ***Cz.:*** Fucidin; Fucithalmic; ***Denm.:*** Fucidin; Fucithalmic; ***Fin.:*** Fucidin; Fucithalmic; ***Fr.:*** Fucidine; Fucithalmic; ***Ger.:*** Fucidine; Fucithalmic; ***Gr.:*** Flusterix; Fucidin; ***Hong Kong:*** Fucidin; Fucithalmic; Fusidate; Qualifutin; ***Hung.:*** Fucidin; Fucithalmic; ***India:*** Fusibact; Fusiwal; ***Indon.:*** Fucidin; Fucilex; Fucithalmic; Fuladic; Fuson; Fusycom; Futaderm; ***Irl.:*** Fucidin; Fucithalmic; ***Israel:*** Fucidin; Fucithalmic; ***Ital.:*** Dermomycin; Fucidin; Fucithalmic; ***Malaysia:*** Foban; Fucidin; Fucithalmic; Germacid†; ***Mex.:*** Fucidin; Uniderm; ***Neth.:*** Fucidin; Fucithalmic; ***Norw.:*** Fucidin; Fucithalmic; ***NZ:*** Foban; Fucidin; Fucithalmic; ***Philipp.:*** Flexid; Fucidin; Fucithalmic; Hopaq; ***Pol.:*** Fucidin; ***Port.:*** Desdek; Fucidine; Fucithalmic; Fusextrine; Infloc; Nadiclox; ***Rus.:*** Fucidin (Фуцидин); Fucithalmic (Фуциталмик); ***S.Afr.:*** Fucidin; Fucithalmic; ***Singapore:*** Balad†; Duzen; Foban; Forsuderm; Fucidin; Fucithalmic; Fudikin; ***Spain:*** Fucidine; Fucithalmic; ***Swed.:*** Fucidin; Fucithalmic; ***Switz.:*** Fucidin; Fucithalmic; ***Thai.:*** Foban; Fucidin; Fucithalmic; Fusid; ***Turk.:*** Fucidin; Fucithalmic; Stafine; ***UAE:*** Futasole; ***UK:*** Fucidin; Fucithalmic.

Multi-ingredient: ***Arg.:*** Drum B; Fucicort; Fusimed B; Gelbiotic Plus; ***Austria:*** Fucicort; ***Belg.:*** Fucicort; Fucidin Hydrocortisone; ***Braz.:*** Verutex

B; ***Canad.:*** Fucidin H; ***Chile:*** Fucicort; Fucidin H; ***Cz.:*** Fucicort; Fucidin H; ***Denm.:*** Fucicort; Fucidin-Hydrocortison; ***Fin.:*** Fucicort; Fucidin-Hydrocortison; ***Ger.:*** Fucicort; Fucidine plus†; ***Gr.:*** Alpider; Befucil; Betacort; Betafusin; Betasid; Betfu; Fubecot; Fucicort; Fucicream; Fucidin H; Fusibet; Hydrofusin; Roseti; Sensibio; Staficort; ***Hong Kong:*** Fucicort; Fucidin H; ***Hung.:*** Fucicort; Fucidin H; ***Indon.:*** Fucicort; ***Irl.:*** Fucibet; Fucidin H; ***Israel:*** Fucicort; Fucidin H†; ***Ital.:*** Fucicort; Fucidin H; Piodermina; ***Malaysia:*** Axcel Fusi-Corte; Foban-Hydro; Fobancort; Fucicort; Fucidin H; Fusidic B; ***Mex.:*** Fucicort; ***Norw.:*** Fucidin-Hydrocortison; ***NZ:*** Fucicort; ***Philipp.:*** Fucicort; Fucidin H; Hoebedic; ***Port.:*** Fucicort; Fucidine H; ***Rus.:*** Fucicort (Фуцикорт); Fucidin H (Фуцидин Г); ***S.Afr.:*** Fucidin H; ***Singapore:*** Fobancort; Fucicort; Fucidin H; ***Spain:*** Fucibet; Fucidine H; ***Swed.:*** Fucidin-Hydrocortison; ***Switz.:*** Fucicort; Fucidin H; ***Thai.:*** Fucicort; Fucidin H; ***UAE:*** Futasone; ***UK:*** Fucibet; Fucidin H.

Garenoxacin Mesilate *(BANM, rINNM)*

BMS-284756-01; Garenoxacin Mesylate *(USAN)*; Garénoxacine, Mésilate de; Garenoxacini Mesilas; Mesilato de garenoxacino; T-3811ME. 1-Cyclopropyl-8-(difluoromethoxy)-7-[(1*R*)-1-methyl-2,3-dihydro-1*H*-isoindol-5-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid methanesulfonate monohydrate.

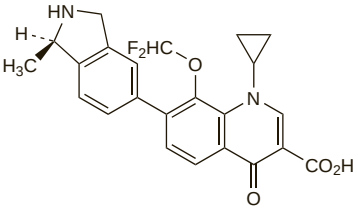
Гареноксацина Мезилат

$C_{23}H_{20}F_2N_2O_4,CH_4O_3S,H_2O$ = 540.5.

CAS — 194804-75-6 (garenoxacin); 223652-82-2 (garenoxacin mesilate); 223652-90-2 (garenoxacin mesilate monohydrate).

ATC — J01MA19.

ATC Vet — QJ01MA19.



(garenoxacin)

Profile

Garenoxacin is a fluoroquinolone antibacterial with properties similar to those of ciprofloxacin (p.247). Garenoxacin is used as the mesilate but doses are given in terms of the base: about 507 mg of the mesilate is equivalent to 400 mg of garenoxacin. It is given orally in the treatment of susceptible infections in usual doses equivalent to 400 mg of garenoxacin daily.

Gatifloxacin *(USAN, rINN)*

AM-1155; BMS-206584-01; CG-5501; Gatifloxacine; Gatifloxacino; Gatifloxacinum. (±)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid sesquihydrate.

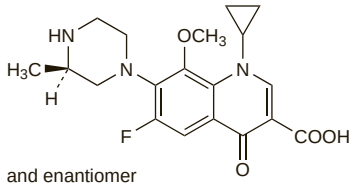
Гатифлоксацин

$C_{19}H_{22}FN_3O_4,1/_2H_2O$ = 402.4.

CAS — 160738-57-8 (anhydrous gatifloxacin); 180200-66-2 (gatifloxacin sesquihydrate).

ATC — J01MA16; S01AX21.

ATC Vet — QJ01MA16; QS01AX21.



and enantiomer

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Symptomatic hyperglycaemia and/or hypoglycaemia have been reported in patients (usually diabetics) taking gatifloxacin. However, hypoglycaemia, and particularly hyperglycaemia, have occurred in non-diabetic patients. Severe life-threatening events, including hyperosmolar nonketotic hyperglycaemic coma, diabetic ketoacidosis, hypoglycaemic coma, convulsions, and mental status changes have been reported very rarely. Although in most cases the blood-glucose disturbance was reversible, fatalities have been reported. Gatifloxacin should not be given to diabetic patients. Other risk factors for developing blood-glucose disturbances include older age (patients 65 years of age or over), renal impairment, or use of other drugs that alter blood-glucose concentrations, particularly hypoglycaemics. Patients with risk factors should have their blood-glucose concentrations closely monitored and if signs or symptoms of glucose disturbances develop, gatifloxacin should be stopped.

Effects on glucose metabolism. Hypoglycaemia and hyperglycaemia have been associated with gatifloxacin in both diabetic and non-diabetic patients.[1-6] A review[7] of spontaneous adverse effects reported to the FDA in the USA between November 1997 and September 2003 found the rate of blood-glucose disturbances with gatifloxacin to be 10-fold higher when compared with ciprofloxacin, levofloxacin, and moxifloxacin. Subsequent population-based case-control studies[8] in elderly patients given fluoroquinolones (ciprofloxacin, gatifloxacin, levofloxacin, or moxifloxacin), second-generation cephalosporins, or macrolides also found an increased risk of blood-glucose disturbances with gatifloxacin.

While blood-glucose disturbances appear to be mainly associated with gatifloxacin, the possibility that they may also be a class effect of fluoroquinolones cannot be excluded; patients most at risk are the elderly, those with diabetes and/or those taking hypoglycaemic drugs, and patients with impaired renal function.[9] Twenty two case reports of dysglycaemia associated with the use of levofloxacin were received by Health Canada between January 1997 and June 2006; reported cases included 15 diabetic patients.[10] In contrast a review of the effects of moxifloxacin on blood glucose, including data from large postmarketing studies, suggested it had no significant effect.[11]

1. Baker SE, Hangii MC. Possible gatifloxacin-induced hypoglycemia. *Ann Pharmacother* 2002; **36:** 1722–6.
2. Donaldson AR, *et al.* Possible gatifloxacin-induced hyperglycemia. *Ann Pharmacother* 2004; **38:** 602–5.
3. Happe MR, *et al.* Gatifloxacin-induced hyperglycemia. *Ann Intern Med* 2004; **141:** 968–9.
4. Khovidhunkit W, Sunthornyothin S. Hypoglycemia, hyperglycemia, and gatifloxacin. *Ann Intern Med* 2004; **141:** 969.
5. Greenberg AL, *et al.* Gatifloxacin therapy associated with hypoglycemia. *Clin Infect Dis* 2005; **40:** 1210–11.
6. Blommel AL, Lutes RA. Severe hyperglycemia during renally adjusted gatifloxacin therapy. *Ann Pharmacother* 2005; **39:** 1349–52.
7. Frothingham R. Glucose homeostasis abnormalities associated with use of gatifloxacin. *Clin Infect Dis* 2005; **41:** 1269–76.
8. Park-Wyllie LY, *et al.* Outpatient gatifloxacin therapy and dysglycemia in older adults. *N Engl J Med* 2006; **354:** 1352–61.
9. Lewis RJ, Mohr JF. Dysglycaemias and fluoroquinolones. *Drug Safety* 2008; **31:** 283–92.
10. Health Canada. Levofloxacin: dysglycemia and liver disorders. *Can Adverse React News* 2007; **17:** 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/ carn-bcei_v17n1-eng.pdf (accessed 17/06/08)
11. Gavin JR, *et al.* Moxifloxacin and glucose homeostasis: a pooled-analysis of the evidence from clinical and postmarketing studies. *Drug Safety* 2004; **27:** 671–86.

Interactions

As for Ciprofloxacin, p.246.

Use of gatifloxacin with drugs that alter blood-glucose concentrations increases the risk of blood-glucose disturbances.

Antidiabetics. Given the adverse effects of gatifloxacin, pharmacodynamic interactions with antidiabetics might reasonably be anticipated. Severe and persistent hypoglycaemia occurred in 3 patients taking oral hypoglycaemics (*repaglinide*, *glibenclamide* and *pioglitazone*, and *glimepiride*) when gatifloxacin was added to their therapy.[1]

1. Menzies DJ, *et al.* Severe and persistent hypoglycemia due to gatifloxacin interaction with oral hypoglycemic agents. *Am J Med* 2002; **113:** 232–4.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Gatifloxacin 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.

Pharmacokinetics

Gatifloxacin is readily absorbed from the gastrointestinal tract with an absolute bioavailability of 96%. Peak plasma concentrations occur within 1 to 2 hours of an oral dose. Gatifloxacin is widely distributed into body tissues and is about 20% bound to plasma proteins. It undergoes limited metabolism and has an elimination half-life of 7 to 14 hours. Gatifloxacin is excreted primarily unchanged in the urine with less than 1% as metabolites. About 5% is also excreted unchanged in the faeces. Distribution into milk occurs in *animals*.

Uses and Administration

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

It is given orally, or by intravenous infusion as a 2 mg/mL solution over 60 minutes, for the treatment of susceptible infections, including respiratory- and urinary-tract infections and skin infections. The usual adult dose is 400 mg once daily. A single dose of 400 mg or a dose of 200 mg daily for 3 days may be adequate for uncomplicated urinary-tract infections.

For details of reduced doses to be used in renal impairment, see below.

A single dose of 400 mg may also be given for the treatment of uncomplicated gonorrhoea.

Gatifloxacin is also used as 0.3% eye drops for the treatment of bacterial conjunctivitis.

◊ Reviews.

1. Keam SJ, *et al.* Gatifloxacin: a review of its use in the treatment of bacterial infections in the US. *Drugs* 2005; **65:** 695–724.

Administration in renal impairment. Doses of gatifloxacin should be reduced in patients with renal impairment; the usual initial dose of 400 mg should be followed by reduced maintenance doses of 200 mg daily in those with a creatinine clearance of less than 40 mL/minute and in those on haemodialysis or continuous peritoneal dialysis.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Gatif; Tequin†; Zymaran; ***Austral.:*** Tequin; ***Braz.:*** Tequin; Zymar; ***Canad.:*** Tequin; Zymar; ***Chile:*** Starox†; Zymar; ***Ger.:*** Bonoq†; ***India:*** Biogat†; Gaticin; Gatiquin; Gatt; Zyquin; ***Indon.:*** Gaticin; Gatimax; ***Jpn:*** Gatiflo; ***Malaysia:*** Tequin†; ***Mex.:*** Tequin; Zymar; ***NZ:*** Tequin; ***Philipp.:*** Tequin; Zymar; ***S.Afr.:*** Tequin; ***Singapore:*** Tequin†; Zymar; ***Thai.:*** Tequin†; Zymar; ***USA:*** Tequin†; Zymar.

Multi-ingredient: ***India:*** Gatiquin Oz Kit.

Gemifloxacin Mesilate *(rINNM)*

Gemifloxacin Mesylate *(USAN)*; Gémifloxacine, Mésilate de; Gemifloxacini Mesilas; LB-20304 (gemifloxacin); LB-20304a; Mesilato de gemifloxacino; SB-265805 (gemifloxacin); SB-265805S. (±)-7-[3-(Aminomethyl)-4-oxo-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 7[4]-(*Z*)-(*O*-methyloxime) methanesulfonate.

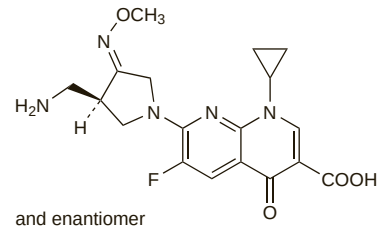
Гемифлоксацина Мезилат

$C_{18}H_{20}FN_5O_4,CH_4O_3S$ = 485.5.

CAS — 204519-64-2 (gemifloxacin); 204519-65-3 (gemifloxacin mesilate).

ATC — J01MA15.

ATC Vet — QJ01MA15.



and enantiomer

(gemifloxacin)

Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Skin rashes may be more common with gemifloxacin and treatment should be stopped if they occur.

Interactions

As for Ciprofloxacin, p.246.

Antimicrobial Action

As for Ciprofloxacin, p.246.

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

◊ References.

1. Morrissey I, Tillotson G. Activity of gemifloxacin against Streptococcus pneumoniae and Haemophilus influenzae. *J Antimicrob Chemother* 2004; **53:** 144–8.

Pharmacokinetics

Gemifloxacin is rapidly absorbed from the gastrointestinal tract with an absolute bioavailability of about 71%. Peak plasma concentrations occur 0.5 to 2 hours after an oral dose. Gemifloxacin is widely distributed into body tissues including the bronchial