Preparations

USP 31: Kanamycin Injection; Kanamycin Sulfate Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: Cristalomicina; ***Ger.:*** Kan-Ophtal; Kana-Stulln; Kanamytrex; ***India:*** Kancin; Kaycin; ***Indon.:*** Kanabiotic; Kanarco; Kanoxin; ***Ital.:*** Keimicina; ***Malaysia:*** Kancin; ***Mex.:*** Cancina; Kanacil†; Kanadrex†; Kanapat; Kantrex; Randikan†; Solkan; Sulmyn; ***Singapore:*** Kancin-L; Kancin†; ***Spain:*** Kantrex†; ***Thai.:*** Anbikan; Kan-Mycin†; Kancin; Kangen; KMH; ***USA:*** Kantrex; ***Venez.:*** Kanacyl†; Kantrex.

Multi-ingredient: ***Arg.:*** Cristalomicina; ***Fr.:*** Sterimycine†; ***Ital.:*** Dermaflogil; ***S.Afr.:*** Kantrexil; ***Spain:*** Kanafosal; Kanafosal Predni; Kanapomada; Naso Pekamin; ***Thai.:*** KA-Cilone; ***Venez.:*** Kanasone†; Monosulpa; Rinomax.

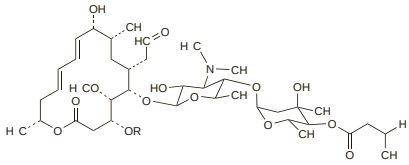
Kitasamycin *(BAN, USAN, rINN)*

Kitasamicina; Kitasamycine; Kitasamycinum; Leucomycin.

Китазамицин

CAS — 1392-21-8 (kitasamycin); 37280-56-1 (kitasamycin tartrate); 178234-32-7 (acetylkitasamycin).

ATC Vet — QJ01FA93.



Kitasamycin A : *R* = H
Kitasamycin A : *R* = COCH

Pharmacopoeias. In *Chin.* and *Jpn.*
Jpn also includes Acetylkitasamycin and Kitasamycin Tartrate.

Profile

Kitasamycin is a macrolide antibacterial produced by *Streptomyces kitasatoensis*, consisting mainly of kitasamycins A_4 and A_5. It has actions and uses similar to those of erythromycin (p.269) and has been given orally as the base or intravenously as the tartrate in the treatment of susceptible infections. Acetylkitasamycin has also been given orally.

Kitasamycin has been added to animal feeding stuffs as growth promotors for pigs.

Latamoxef Disodium *(BANM, rINNM)*

Latamoksefidinatrium; Latamoxef disódico; Latamoxef Disodique; Latamoxefdinatrium; Latamoxefum Dinatricum; LY-127935; Moxalactam Disodium *(USAN)*; 6059-S. (7*R*)-7-[2-Carboxy-2-(4-hydroxyphenyl)acetamido]-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-1-oxa-3-cephem-4-carboxylic acid, disodium salt.

Динатрий Латамоксеф

$C_{20}H_{18}N_6Na_2O_9S$ = 564.4.

CAS — 64952-97-2 (latamoxef); 64953-12-4 (latamoxef disodium).

ATC — J01DD06.

ATC Vet — QJ01DD06.

Pharmacopoeias. In *Jpn*.

Profile

Latamoxef is an oxacephalosporin antibacterial that has been given intramuscularly or intravenously as the disodium salt in the treatment of susceptible infections. It differs from the cephalosporins in that the sulfur atom of the 7-aminocephalosporanic acid nucleus is replaced by oxygen. Like cefamandole (p.220) it has an *N*-methylthiotetrazole side-chain and may cause hypoprothrombinaemia. Serious bleeding episodes have been reported with latamoxef and prophylaxis with vitamin K and monitoring of bleeding time have been recommended during treatment. In addition to hypoprothrombinaemia, inhibition of platelet function and more rarely immune-mediated thrombocytopenia may be responsible for interference with haemostasis. As with the methylthiotetrazole-containing cephalosporins, a disulfiram-like reaction with alcohol may occur.

Latamoxef has antimicrobial activity similar to that of the third-generation cephalosporin cefotaxime (p.228), although it is generally less active against Gram-positive bacteria and more active against *Bacteroides fragilis*.

Breast feeding. The authors of a pharmacokinetic study[1] in 8 lactating women given latamoxef cautioned that there was a possibility of colonisation of the infant's bowel with Gram-positive bacteria and in consequence a risk of enterocolitis. They therefore advised against breast feeding during maternal use of the drug. However, no adverse effects have been seen in breast-fed infants whose mothers were receiving latamoxef, and the American Academy of Pediatrics considers[2] that it is therefore usually compatible with breast feeding.

1. Miller RD, *et al.* Human breast milk concentration of moxalactam. *Am J Obstet Gynecol* 1984; **148:** 348–9.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 27/05/04)

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Shiomarin.

Levofloxacin *(BAN, USAN, rINN)*

DR-3355; HR-355; Levofloksasiini; Levofloksasin; Lévofloxacine; Levofloxacino; Levofloxacinum; *S*-(–)-Ofloxacin; RWJ-25213. (–)-(*S*)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid.

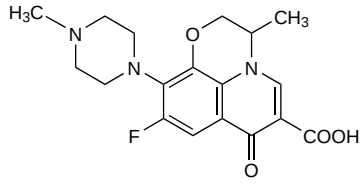
Левофлоксацин

$C_{18}H_{20}FN_3O_4$ = 361.4.

CAS — 100986-85-4 (levofloxacin); 138199-71-0 (levofloxacin hemihydrate).

ATC — J01MA12; S01AX19.

ATC Vet — QJ01MA12; QS01AX19.



Adverse Effects and Precautions

As for Ciprofloxacin, p.244.

Symptomatic hyperglycaemia and/or hypoglycaemia have been reported, usually in diabetics who are also taking hypoglycaemics or insulin. Such patients should have their blood-glucose concentrations closely monitored and if signs or symptoms of glucose disturbances develop, levofloxacin should be stopped.

Effects on glucose metabolism. See also under Gatifloxacin, p.281.

Interactions

As for Ciprofloxacin, p.246.

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

Levofloxacin does not appear to interact significantly with theophylline or ciclosporin.

Antimicrobial Action

As for Ciprofloxacin, p.246.

Levofloxacin is generally considered to be about twice as active as ofloxacin (p.310), the racemic substance. Levofloxacin has a broad spectrum of activity which includes Gram-positive bacteria.

◊ References.

1. Brown DFJ, *et al.*, eds. Levofloxacin: an extended spectrum 4-quinolone agent. *J Antimicrob Chemother* 1999; **43** (suppl C): 1–90.

Pharmacokinetics

Levofloxacin is rapidly and almost completely absorbed after oral doses with peak plasma concentrations occurring within 1 to 2 hours. It is widely distributed into body tissues including the bronchial mucosa and lungs, but penetration into CSF is relatively poor. Levofloxacin is about 30 to 40% bound to plasma proteins. Only small amounts are metabolised, to inactive metabolites. The elimination half-life of levofloxacin is 6 to 8 hours, although this may be prolonged in patients with renal impairment. Levofloxacin is excreted largely unchanged, primarily in the urine with less than 5% as metabolites. It is not removed by haemodialysis or peritoneal dialysis.

◊ References.

1. Fish DN, Chow AT. The clinical pharmacokinetics of levofloxacin. *Clin Pharmacokinet* 1997; **32:** 101–19.
2. Piscitelli SC, *et al.* Pharmacokinetics and safety of high-dose and extended-interval regimens of levofloxacin in human immunodeficiency virus-infected patients. *Antimicrob Agents Chemother* 1999; **43:** 2323–7.

Uses and Administration

Levofloxacin is the *S*-(–)-isomer of the fluoroquinolone antibacterial ofloxacin (p.310). It is given orally, or by intravenous infusion as a 5 mg/mL solution over 30 to 90 minutes, to treat susceptible infections including tuberculosis (but see under Uses and Administration of Ciprofloxacin, p.248). Levofloxacin is given as the hemihydrate but doses are expressed in terms of the base; levofloxacin hemihydrate 256 mg is equivalent to about 250 mg of levofloxacin. Usual doses range from 250 to 500 mg once or twice daily for 7 to 14 days depending on the severity and nature of the infection. A dose of 250 mg once daily for 3 days may be given for uncomplicated urinary-tract infections. A 28-day course of treatment with a dose of 500 mg once daily should be given for chronic bacterial prostatitis. In the USA, doses of 750 mg once daily for 7 to 14 days may be used for complicated skin infections and for hospital-acquired pneumonia; a shorter course of 750 mg once daily for 5 days may be given for community-acquired pneumonia, acute bacterial sinusitis, complicated urinary-tract infections, and acute pyelonephritis. A 60-day course of treatment with a dose of 500 mg once daily is also licensed in the USA for treatment and postexposure prophylaxis of inhalation anthrax.

Doses should be reduced in patients with renal impairment (see below).

Levofloxacin is also used topically as the hemihydrate in eye drops. A solution containing the equivalent of 0.5% of levofloxacin is used for the treatment of bacterial conjunctivitis and 1.5% for corneal ulcers caused by susceptible strains of bacteria.

◊ Reviews.

1. Davis R, Bryson HM. Levofloxacin: a review of its antibacterial activity, pharmacokinetics and therapeutic efficacy. *Drugs* 1994; **4:** 677–700.
2. Martin SJ, *et al.* Levofloxacin and sparfloxacin: new quinolone antibiotics. *Ann Pharmacother* 1998; **32:** 320–36.
3. Martin SJ, *et al.* A risk-benefit assessment of levofloxacin in respiratory, skin and skin structure, and urinary tract infections. *Drugs* 2001; **24:** 199–222.
4. Croom KF, Goa KL. Levofloxacin: a review of its use in the treatment of bacterial infections in the United States. *Drugs* 2003; **63:** 2769–2802.
5. Anderson VR, Perry CM. Levofloxacin: a review of its use as a high-dose, short-course treatment for bacterial infection. *Drugs* 2008; **68:** 535–65.

Administration in children. Since fluoroquinolones can cause degenerative changes in weight-bearing joints of young *animals* they should only be used in children and adolescents where their use may be justified if the benefits outweigh the risks. Although levofloxacin is not licensed for use in this age group in either the UK or USA, a pharmacokinetic study[1] has suggested that the following doses would be needed:

- children 5 years of age and older, 10 mg/kg daily
- infants and children from 6 months to less than 5 years of age, 10 mg/kg every 12 hours

1. Chien S, *et al.* Levofloxacin pharmacokinetics in children. *J Clin Pharmacol* 2005; **45:** 153–60.

Administration in renal impairment. Although initial doses (see above) remain unchanged in patients with renal impairment, subsequent doses of levofloxacin should be adjusted according to creatinine clearance (CC).

In the UK, the following doses are recommended:

- CC 20 to 50 mL/minute: subsequent doses are halved
- CC 10 to 19 mL/minute: subsequent doses are reduced to one-quarter of the usual dose; a regimen of 250 mg daily should be reduced to 125 mg every 48 hours
- CC less than 10 mL/minute (including haemodialysis and continuous peritoneal dialysis patients): usual doses of 250 mg or 500 mg daily are reduced to 125 mg every 48 or 24 hours respectively; a regimen of 500 mg twice daily is reduced to 125 mg every 24 hours