2. Krcmery S, *et al.* Treatment of lower urinary tract infection in pregnancy. *Int J Antimicrob Agents* 2001; **17:** 279–82.
3. Wing DA. Pyelonephritis in pregnancy: treatment options for optimal outcomes. *Drugs* 2001; **61:** 2087–96.
4. Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2001 (accessed 16/05/05).
5. Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol* 2005; **32:** 749–64.
6. Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. *Urol Clin North Am* 2007; **34:** 35–42.
7. Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 07/08/08).

Women. References to urinary-tract infections in women and their management.

1. Warren JW, *et al.* Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clin Infect Dis* 1999; **29:** 745–58.
2. Hooton TM. Recurrent urinary tract infection in women. *Int J Antimicrob Agents* 2001; **17:** 259–68.
3. Fihn SD. Acute uncomplicated urinary tract infection in women. *N Engl J Med* 2003; **349:** 259–66.
4. Milo G, *et al.* Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2005 (accessed 07/08/08).
5. Nicolle L, *et al.* Uncomplicated urinary tract infection in women: current practice and the effect of antibiotic resistance on empiric treatment. *Can Fam Physician* 2006; **52:** 612–8.
6. Foster RT. Uncomplicated urinary tract infections in women. *Obstet Gynecol Clin North Am* 2008; **35:** 235–48.
7. André M, Mölstad S. Nya riktlinjer för urinvägsinfektion hos kvinnor. *Lakartidningen* 2008; **105:** 1107–9.

Whipple's disease

Whipple's disease is a rare chronic systemic condition associated with infection with *Tropheryma whippelii*.[1-4] It was once considered to be a disease predominantly involving the small intestine and resulting in malabsorption, but may affect virtually all organs. There is probably CNS involvement in all patients with Whipple's disease, although it may only be evident in 10 to 20%. Before the use of antibacterial therapy the disease was invariably fatal. The treatment generally recommended is either benzylpenicillin (sometimes given as procaine benzylpenicillin) and streptomycin, or ceftriaxone, parenterally for two weeks, followed by co-trimoxazole orally for at least one year.[2,3,5,6] Such long-term treatment with co-trimoxazole, a drug that crosses the blood-brain barrier, is advisable because of the relatively high frequency and seriousness of CNS relapse. These relapses respond less well to antibacterial treatment; chloramphenicol has been used in those not responding to the above regimen and a patient with CNS relapse improved on ceftriaxone given intravenously.[7] Further alternatives may be a tetracycline[8] or cefixime.[6] A patient intolerant of co-trimoxazole was given phenoxymethylpenicillin and probenecid after the initial 14-day course of benzylpenicillin and streptomycin.[9] There has also been a report of benefit in a penicillin-allergic patient treated with erythromycin.[10] A combination of doxycycline with hydroxychloroquine may be tried in patients without neurological involvement.[3]

1. Relman DA, *et al.* Identification of the uncultured bacillus of Whipple's disease. *N Engl J Med* 1992; **327:** 293–301.
2. Marth T, Raoult D. Whipple's disease. *Lancet* 2003; **361:** 239–46.
3. Fenollar F, *et al.* Whipple's disease. *N Engl J Med* 2007; **356:** 55–66.
4. Schneider T, *et al.* Whipple's disease: new aspects of pathogenesis and treatment. *Lancet Infect Dis* 2008; **8:** 179–90.
5. Singer R. Diagnosis and treatment of Whipple's disease. *Drugs* 1998; **55:** 699–704.
6. Maiwald M, Relman DA. Whipple's disease and Tropheryma whippelii: secrets slowly revealed. *Clin Infect Dis* 2001; **32:** 457–63.
7. Adler CH, Galetta SL. Oculo-facial-skeletal myorhythmia in Whipple disease: treatment with ceftriaxone. *Ann Intern Med* 1990; **112**: 467–9.
8. Abramowicz M, ed. The choice of antibacterial drugs. In: *Handbook of antimicrobial therapy.* 18th ed. New Rochelle NY: The Medical Letter, 2008: 72.
9. Rickman LS, *et al.* Brief report: uveitis caused by Tropheryma whippelii (Whipple's bacillus). *N Engl J Med* 1995; **332:** 363–6.
10. Bowles KM, *et al.* A 35-year-old with swollen knees who had recurrent fever and pericarditis, then diarrhoea before getting better. *Lancet* 1996; **348:** 1356.

Yaws

See under Syphilis, p.192.

Yersinia enteritis

See p.174.

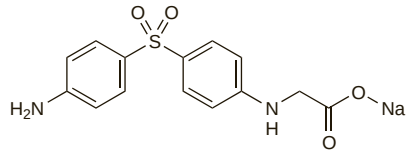
Acediasulfone Sodium *(rINN)*

Acediasulfona sódica; Acédiasulfone Sodique; Acediasulfonnatrium; Acediasulfonum Natricum; Asediasulfoninatrium; Sodium Diaphenylsulphonacetate. *N-p*-Sulphanilylphenylglycine sodium.

Ацедиасульфон Натрий

$C_{14}H_{13}N_2NaO_4S$ = 328.3.

CAS — 127-60-6.



Profile

Acediasulfone sodium is reported to have antibacterial properties and is an ingredient of preparations used topically in the treatment of local infections of the ear.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Ciloprin cum Anaesthetico†; ***Fin.:*** Ciloprin cum Anaesthetico†; ***India:*** Otogesic; ***Switz.:*** Ciloprin ca†.

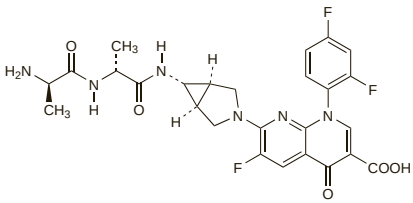
Alatrofloxacin Mesilate *(rINNM)*

Alatrofloxacin Mesylate *(USAN)*; Alatrofloxacine, Mésilate d'; Alatrofloxacini Mesilas; CP-116517-27; Mesilato de alatrofloxacino. 7-{(1*R*,5*S*,6*s*)-6-[(*S*)-2-((*S*)-2-Aminopropionamido)propionamido]-3-azabicyclo[3.1.0]hex-3-yl}-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid monomethanesulphonate.

Алатрофлоксацина Мезилат

$C_{26}H_{25}F_3N_6O_5,CH_3SO_3H$ = 654.6.

CAS — 157182-32-6 (alatrofloxacin); 157605-25-9 (alatrofloxacin mesilate).



(alatrofloxacin)

Profile

Alatrofloxacin is a prodrug of the fluoroquinolone antibacterial trovafloxacin (p.357) and has been used intravenously as the mesilate in the treatment of susceptible infections.

Alatrofloxacin and trovafloxacin preparations were withdrawn worldwide after reports of unpredictable severe hepatic adverse effects, including some fatalities.

Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Trovan†; ***USA:*** Trovan†.

Amikacin *(BAN, rINN)*

Amicacina; Amikacina; Amikacinas; Amikacine; Amikacinum; Amikacyna; Amikasiini. 6-*O*-(3-Amino-3-deoxy-α-D-glucopyranosyl)-4-*O*-(6-amino-6-deoxy-α-D-glucopyranosyl)-*N*^{1}-[(2*S*)-4-amino-2-hydroxybutyryl]-2-deoxystreptamine.

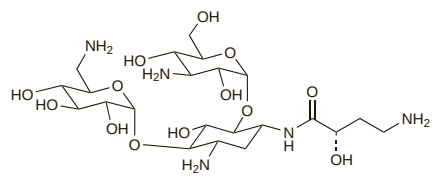
Амикацин

$C_{22}H_{43}N_5O_{13}$ = 585.6.

CAS — 37517-28-5.

ATC — D06AX12; J01GB06; S01AA21.

ATC Vet — QD06AX12; QJ01GB06; QS01AA21.



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

Ph. Eur. 6.2 (Amikacin). An antimicrobial substance obtained from kanamycin A. A white or almost white powder. Sparingly soluble in water; practically insoluble in alcohol and in acetone; slightly soluble in methyl alcohol. A 1% solution in water has a pH of 9.5 to 11.5.

USP 31 (Amikacin). A white crystalline powder. Sparingly soluble in water. pH of a 1% solution in water is between 9.5 and 11.5. Store in airtight containers.

Amikacin Sulfate *(USAN, rINNM)*

Amikacin Sulphate *(BANM)*; Amikacin-disulfát; Amikacine, sulfate d'; Amikacini Disulfas; Amikacini sulfas; Amikacino sulfatas; Amikacinsulfat; Amikacin-szulfát; Amikacyny siarczan; Amikasiinisulfaatti; Amikasin Sülfat; BB-K8; Sulfato de amikacina.

Амикацина Сульфат

$C_{22}H_{43}N_5O_{13},2H_2SO_4$ = 781.8.

CAS — 39831-55-5.

ATC — D06AX12; J01GB06; S01AA21.

ATC Vet — QD06AX12; QJ01GB06; QS01AA21.

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

Ph. Eur. 6.2 (Amikacin Sulphate). A white or almost white powder. It loses not more than 13.0% of its weight on drying. Freely soluble in water; practically insoluble in alcohol and in acetone. The pH of a 1% solution in water is between 2.0 and 4.0. Store in airtight containers.

USP 31 (Amikacin Sulfate). Amikacin sulfate having a molar ratio of amikacin to H_2SO_4 of 1:2 contains the equivalent of not less than 674 micrograms and not more than 786 micrograms of amikacin per mg, calculated on the dried basis. Amikacin sulfate having a molar ratio of amikacin to H_2SO_4 of 1:1.8 contains the equivalent of not less than 691 micrograms and not more than 806 micrograms of amikacin per mg, calculated on the dried basis.

A white crystalline powder. Freely soluble in water. pH of a 1% solution in water is between 2.0 and 4.0 (1:2 salt) and 6.0 to 7.3 (1:1.8 salt). Store in airtight containers.

Incompatibility. For discussion of the incompatibility of aminoglycosides, including amikacin, with beta lactams, see under Gentamicin Sulfate, p.282. Amikacin is also reported to be incompatible with various other drugs. However, reports are contradictory in many cases, and other factors, such as the strength and composition of the vehicles used, may play a role.

Stability. Solutions may darken from colourless to pale yellow but this does not indicate a loss of potency.

Adverse Effects, Treatment, and Precautions

As for Gentamicin Sulfate, p.282. Peak plasma concentrations of amikacin greater than 30 to 35 micrograms/mL or trough concentrations greater than 5 to 10 micrograms/mL should be avoided. Amikacin affects auditory (cochlear) function to a greater extent than gentamicin.

Effects on the eyes. A report of retinal damage after intravitreal injection of amikacin.[1]

1. Jackson TL, Williamson TH. Amikacin retinal toxicity. *Br J Ophthalmol* 1999; **83:** 1199–1200.

Interactions

As for Gentamicin Sulfate, p.283.

Antimicrobial Action

As for Gentamicin Sulfate, p.283. Amikacin is active against a similar range of organisms although it is also reported to have some activity against *Nocardia asteroides*, *Mycobacterium tuberculosis*, and some atypical mycobacterial strains. Amikacin is not degraded by many of the common enzymes often responsible for acquired aminoglycoside resistance. In consequence, cross-resistance with gentamicin and other aminoglycosides is infrequent and amikacin may be effective against strains resistant to other aminoglycosides. However, resistant strains of Gram-negative bacteria and staphylococci have been reported, and it is generally reserved for infections resistant to other aminoglycosides, although reports differ as to the extent and speed of the development of amikacin resistance where it has been widely used.

◊ References.

1. Ho YII, *et al.* In-vitro activities of aminoglycoside-aminocyclitols against mycobacteria. *J Antimicrob Chemother* 1997; **40:** 27–32.

Pharmacokinetics

As for Gentamicin Sulfate, p.284.

On intramuscular injection, peak plasma-amikacin concentrations of about 20 micrograms/mL are achieved 1 hour after a 500-mg dose, reducing to about