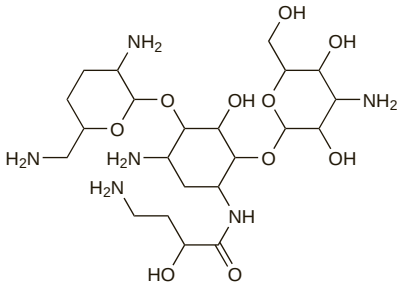
Arbekacin Sulfate *(rINNM)*

ABK (arbekacin); AHB-DBK (arbekacin); Arbekacin Sulphate; Arbékacine, Sulfate d'; Arbekacini Sulfas; HABA-Dibekacin (arbekacin); Sulfato de arbekacina. *O*-3-Amino-3-deoxy-α-D-glucopyranosyl-(1→4)-*O*-[2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranosyl-(1→6)]-*N*′-[(2*S*)-4-amino-2-hydroxybutyryl]-2-deoxy-L-streptamine sulphate.

Арбекацина Сульфат

$C_{22}H_{44}N_6O_{10}.xH_2SO_4$.
CAS — 51025-85-5 (arbekacin).



(arbekacin)

Pharmacopoeias. In *Jpn*.

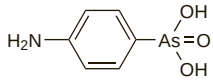
Profile
Arbekacin is an aminoglycoside derived from dibekacin and has general properties similar to those of gentamicin (p.282). It has been used as the sulfate in the treatment of serious infections due to meticillin-resistant *Staphylococcus aureus*.

Arsanilic Acid *(BAN, rINN)*

Acide Arsanilique; Ácido arsanílico; Acidum Arsanilicum; Aminarsonic Acid; AS-101. *p*-Aminobenzenearsonic acid; 4-Aminophenylarsonic acid.

Арсаниловая Кислота

$C_6H_8AsNO_3$ = 217.1.
CAS — 98-50-0.



NOTE. The code AS-101 has also been used for an immunomodulator investigated as an antineoplastic and antiviral.

Pharmacopoeias. In *US* for veterinary use only.
USP 31 (Arsanilic Acid). A white to off-white crystalline powder. Soluble in hot water, in amyl alcohol, and in solutions of alkali carbonates; slightly soluble in cold water, in alcohol, and in acetic acid; insoluble in acetone, in chloroform, in ether, in benzene, and in dilute mineral acids; sparingly soluble in concentrated mineral acids.

Sodium Arsanilate *(BANM, rINNM)*

Arsanilate de Sodium; Arsanilato sódico; Natrii Arsanilas; Sodium Aminarsonate; Sodium Anilarsonate. Sodium 4-aminophenylarsonate.

Натрий Арсанилат

$C_6H_7AsNNaO_3$ = 239.0.
CAS — 127-85-5.

Pharmacopoeias. *Fr.* includes the anhydrous substance and the trihydrate.

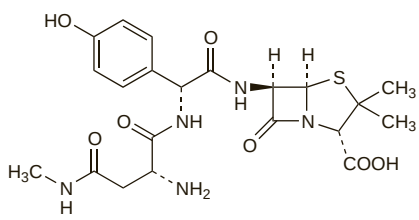
Profile
Arsanilic acid and sodium arsanilate are used in veterinary medicine for the prophylaxis and treatment of enteric infections in pigs and also as growth-promoting agents.

Aspoxicillin *(rINN)*

Aspoxicilina; Aspoxicilline; Aspoxicillinum; TA-058. (2*S*,5*R*,6*R*)-6-{(2*R*)-2-[(2*R*)-2-Amino-3-(methylcarbamoyl)propionamido]-2-(*p*-hydroxyphenyl)acetamido}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]-heptane-2-carboxylic acid.

Аспоксициллин

$C_{21}H_{27}N_5O_7S$ = 493.5.
CAS — 63358-49-6.



Pharmacopoeias. *Jpn* includes the trihydrate.

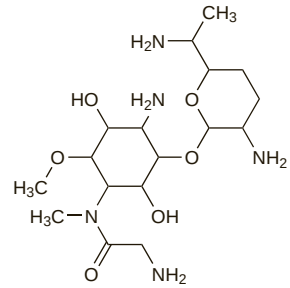
Profile
Aspoxicillin is a ureidopenicillin that has been given intravenously in the treatment of susceptible infections.

Astromicin Sulfate *(USAN, pINNM)*

Abbott-44747; Astromicin Sulphate; Astromicine, Sulfate d'; Astromicini Sulfas; Fortimicin A Sulphate; KW-1070; Sulfato de astromicina. 4-Amino-1-(2-amino-*N*-methylacetamido)-1,4-dideoxy-3-*O*-(2,6-diamino-2,3,4,6,7-pentadeoxy-β-L-*lyxo*-heptopyranosyl)-6-*O*-methyl-L-*chiro*-inositol sulphate.

Астромицина Сульфат

$C_{17}H_{35}N_5O_6.2H_2SO_4$ = 601.6.
CAS — 55779-06-1 (astromicin); 72275-67-3 (astromicin sulfate); 66768-12-5 (xH_2SO_4).



(astromicin)

Pharmacopoeias. In *Jpn*.

Profile
Astromicin is an aminoglycoside antibiotic produced by *Micromonospora* spp. and with actions and uses similar to those of gentamicin (p.282). Astromicin sulfate has been given by intramuscular injection or intravenous infusion. Dosage should be adjusted based on serum-astromicin concentration monitoring.

Preparations

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

Avilamycin *(BAN, USAN, rINN)*

Avilamicina; Avilamycine; Avilamycinum; LY-048740 (avilamycin or avilamycin A).

Авиламицин

$C_{61}H_{88}Cl_2O_{32}$ (avilamycin A) = 1404.2.
CAS — 11051-71-1 (avilamycin); 69787-79-7 (avilamycin A); 69787-80-0 (avilamycin C).

Profile
Avilamycin is an antibacterial that has been used in veterinary medicine as a growth promotor.

Avoparcin *(BAN, USAN, rINN)*

Avoparcina; Avoparcine; Avoparcinum; Compound 254.

Авопарцин

CAS — 37332-99-3.

Profile
Avoparcin is a glycopeptide antibiotic usually produced by *Amycolatopsis coloradensis* (*Streptomyces candidus*). It has been incorporated into animal feedstuffs to promote growth.

◊ There is evidence of cross-resistance between avoparcin and vancomycin.[1] Suggestions that vancomycin-resistant organisms could enter the human population from the food chain as a result of the use of avoparcin as a growth promotor in animals[2,3] were disputed by the manufacturers of avoparcin.[4,5] After a ban in the EU on the use of avoparcin as a growth promotor in animals there has been some evidence[6] of a decrease in the occurrence of vancomycin-resistant enterococci in poultry meat.

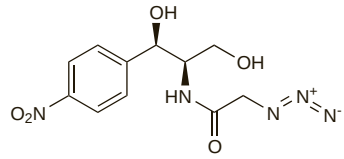
1. Klare I, *et al*. vanA-mediated high-level glycopeptide resistance in Enterococcus faecium from animal husbandry. *FEMS Microbiol Lett* 1995; **125:** 165–72.
2. Howarth F, Poulter D. Vancomycin resistance: time to ban avoparcin? *Lancet* 1996; **347:** 1047.
3. Wise R. Avoparcin and animal feedstuff. *Lancet* 1996; **347:** 1835.
4. Mudd A. Vancomycin resistance and avoparcin. *Lancet* 1996; **347:** 1412.
5. Mudd AJ. Is it time to ban all antibiotics as animal growth-promoting agents? *Lancet* 1996; **348:** 1454–5.
6. Pantosti A, *et al*. Decrease of vancomycin-resistant enterococci in poultry meat after avoparcin ban. *Lancet* 1999; **354:** 741–2.

Azidamfenicol *(BAN, rINN)*

Azidamfénicol; Azidamfenicolum; Azidamphenicol; Azidanfenicol; Azidoamphenicol; Bayer-52910. 2-Azido-*N*-[(α*R*,β*R*)-β-hydroxy-α-hydroxymethyl-4-nitrophenethyl]acetamide.

Азидамфеникол

$C_{11}H_{13}N_5O_5$ = 295.3.
CAS — 13838-08-9.
ATC — S01AA25.
ATC Vet — QS01AA25.



Profile
Azidamfenicol is an antibiotic that is related structurally to chloramphenicol (p.239). It is used as 1% eye drops or eye ointment in the treatment of bacterial eye infections.

Preparations

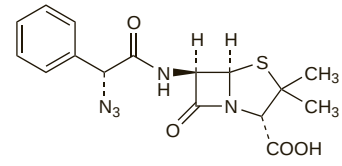
Proprietary Preparations (details are given in Part 3)
Cz.: Ophthalmo-Azaphenicol†; ***Ger.:*** Berlicetin; Posifenicol; Thilocanfol; ***Gr.:*** Thilocof.

Azidocillin Sodium *(BANM, rINNM)*

Azidobenzylpenicillin Sodium; Azidocilina sódica; Azidocilline Sodique; Natrii Azidocillinum. Sodium (6*R*)-6-(D-2-azido-2-phenylacetamido)penicillanate.

Натрий Азидоциллин

$C_{16}H_{16}N_5NaO_4S$ = 397.4.
CAS — 17243-38-8 (azidocillin); 35334-12-4 (azidocillin sodium).
ATC — J01CE04.
ATC Vet — QJ01CE04.



(azidocillin)

Profile
Azidocillin is a semisynthetic penicillin with actions and uses similar to those of phenoxymethylpenicillin (p.314). It is given orally as the sodium salt; doses, expressed in terms of the base, are 750 mg twice daily in the treatment of susceptible infections. The potassium salt has also been used.

Preparations
Proprietary Preparations (details are given in Part 3)
Ger.: InfectoBicillin H.

Azithromycin *(BAN, USAN, rINN)*

Atsitromysiini; Azithromycine; Azithromycinum; Azitromicina; Azitromicinas; Azitromisin; Azitromycin; Azytromycyna; CP-62993; XZ-450. (2*R*,3*S*,4*R*,5*R*,8*R*,10*R*,11*R*,12*S*,13*S*,14*R*)-13-(2,6-Dideoxy-3-*C*-3-*O*-dimethyl-α-L-*ribo*-hexopyranosyloxy)-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-11-(3,4,6-trideoxy-3-dimethylamino-β-D-*xylo*-hexopyranosyloxy)-1-oxa-6-azacyclopentadecan-15-one dihydrate; 9-Deoxo-9a-aza-9a-methyl-9a-homoerythromycin A dihydrate.

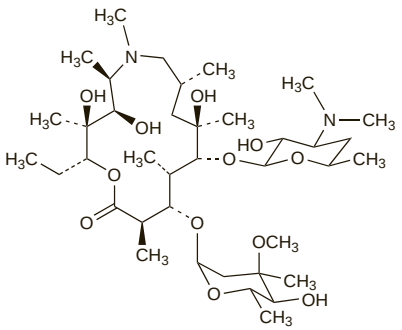
Азитромицин

$C_{38}H_{72}N_2O_{12},2H_2O$ = 785.0.

CAS — 83905-01-5 (anhydrous azithromycin); 117772-70-0 (azithromycin dihydrate).

ATC — J01FA10; S01AA26.

ATC Vet — QJ01FA10; QS01AA26.



Pharmacopoeias. In *Chin.* and *Jpn.*
Eur. (see p.vii) includes the anhydrous form.
US includes the monohydrate and the dihydrate.
Ph. Eur. 6.2 (Azithromycin). A white or almost white powder. Practically insoluble in water; freely soluble in dehydrated alcohol and in dichloromethane. A 0.2% solution in a mixture of methyl alcohol and water (1:1) has a pH of 9.0 to 11.0. Store in airtight containers.
USP 31 (Azithromycin). It is anhydrous or contains one or two molecules of water of hydration. pH of a 0.2% solution in a mixture of methyl alcohol and water (1:1) is between 9.0 and 11.0. Store in airtight containers.

Adverse Effects and Precautions
As for Erythromycin, p.270.

Gastrointestinal disturbances are the most frequent adverse effect of azithromycin but are usually mild and less frequent than with erythromycin. Headache, somnolence, and taste disturbances may occur. Severe hypersensitivity reactions occur rarely but may be prolonged. Thrombocytopenia and mild transient neutropenia have been rarely reported in patients receiving azithromycin. Pain and inflammation may occur at the site of intravenous infusions particularly at high concentrations.

Licensed product information states that azithromycin should be used with caution in patients with hepatic or renal impairment. It should not be given to those with severe hepatic impairment as safety has not been established. Although plasma concentrations may be increased in renal impairment dosage adjustment is not usually required.

Incidence of adverse effects. In patients receiving azithromycin daily long-term for mycobacterial infections,[1] gastrointestinal disorders occurred in 32 of 39 patients (82%), hearing impairment in 10 patients (26%), tinnitus in 18 patients (46%), and poor balance or dizziness in 11 patients (28%). In general, adverse effects were associated with higher serum-azithromycin concentrations.

1. Brown BA, *et al.* Relationship of adverse events to serum drug levels in patients receiving high-dose azithromycin for mycobacterial lung disease. *Clin Infect Dis* 1997; **24:** 958–64.

Effects on the ears. Reversible sensorineural hearing loss was reported in 3 patients given oral azithromycin 500 mg daily with clofazimine and ethambutol for the treatment of disseminated *Mycobacterium avium* complex infection.[1] Irreversible hearing loss has also been reported after low-dose exposure to oral azithromycin.[2,3] A patient who had had 8 days of treatment with intravenous azithromycin 500 mg daily for pneumonia reported complete deafness, which had resolved 20 days after stopping the drug.[4]

See also Incidence of Adverse Effects, above.

1. Wallace MR, *et al.* Ototoxicity with azithromycin. *Lancet* 1994; **343:** 241.
2. Ress BD, Gross EM. Irreversible sensorineural hearing loss as a result of azithromycin ototoxicity: a case report. *Ann Otol Rhinol Laryngol* 2000; **109:** 435–7.
3. Mick P, Westerberg BD. Sensorineural hearing loss as a probable serious adverse drug reaction associated with low-dose oral azithromycin. *J Otolaryngol* 2007; **36:** 257–63.
4. Bizjak ED, *et al.* Intravenous azithromycin-induced ototoxicity. *Pharmacotherapy* 1999; **19:** 245–8.

Effects on fluid and electrolyte homoeostasis. The syndrome of inappropriate antidiuretic hormone secretion was associated with azithromycin treatment in a patient.[1,2]

1. Cadle RM, *et al.* Symptomatic syndrome of inappropriate antidiuretic hormone secretion associated with azithromycin. *Ann Pharmacother* 1997; **31:** 1308–10.
2. Kintzel PE. Correction: symptomatic syndrome of inappropriate antidiuretic hormone secretion associated with azithromycin. *Ann Pharmacother* 1998; **32:** 388.

Effects on the kidneys. Acute interstitial nephritis leading to irreversible renal failure has been reported[1] in a patient who received azithromycin for 9 days. A later report[2] described a patient who developed recurrent acute interstitial nephritis after courses of azithromycin. Repeated exposure resulted in persistent renal damage; leucocytosis and eosinophilia were still present 1 year later.

1. Mansoor GA, *et al.* Azithromycin-induced acute interstitial nephritis. *Ann Intern Med* 1993; **119:** 636–7.
2. Soni N, *et al.* Recurrent acute interstitial nephritis induced by azithromycin. *Pediatr Infect Dis J* 2004; **23:** 965–6.

Eosinophilia. A syndrome characterised by eosinophilia, arthralgia, fever, and rash was associated with azithromycin or roxithromycin treatment in a patient on separate occasions.[1] The original authors believed the condition represented the Churg-Strauss syndrome, although this was disputed in correspondence[2] and attributed to the eosinophilia-myalgia syndrome.

1. Hübner C, *et al.* Macrolide-induced Churg-Strauss syndrome in a patient with atopy. *Lancet* 1997; **350:** 563.
2. Kränke B, Aberer W. Macrolide-induced Churg-Strauss syndrome in patient with atopy. *Lancet* 1997; **350:** 1551–2.

Overdosage. Bradycardia with complete heart block was reported[1] in a 9-month-old infant who had been inadvertently given about 50 mg/kg of azithromycin intravenously.

1. Tilelli JA, *et al.* Life-threatening bradyarrhythmia after massive azithromycin overdose. *Pharmacotherapy* 2006; **26:** 147–50.

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

Giving azithromycin with antacids containing aluminium or magnesium salts can reduce the rate, but not the extent, of its absorption; azithromycin should be given at least 1 hour before or 2 hours after the antacid.

Nelfinavir. Azithromycin serum concentrations are markedly increased when it is given with nelfinavir,[1] but the clinical significance of this is uncertain. US licensed product information for azithromycin states that dosage adjustment is not required although the patient should be closely monitored for adverse effects.

1. Amsden GW, *et al.* A study of the pharmacokinetics of azithromycin and nelfinavir when coadministered in healthy volunteers. *J Clin Pharmacol* 2000; **40:** 1522–7.

Antimicrobial Action
As for Erythromycin, p.271. Azithromycin is less active than erythromycin against streptococci and staphylococci, but has greater activity than erythromycin *in vitro* against some Gram-negative organisms such as *Haemophilus influenzae* and *Moraxella catarrhalis* (*Branhamella catarrhalis*), as well as having activity against some of the Enterobacteriaceae such as *Escherichia coli* and *Salmonella* and *Shigella* spp. Azithromycin is also more active than erythromycin against *Chlamydia trachomatis* and *Ureaplasma urealyticum*, and some opportunistic mycobacteria, including *Mycobacterium avium* complex. It has activity against the protozoa *Toxoplasma gondii* and *Plasmodium falciparum*.

Resistance. The pattern of resistance to azithromycin is similar to that seen with clarithromycin (p.249).

Pharmacokinetics
Azithromycin given orally is rapidly absorbed and about 40% bioavailable. Absorption from capsules, but not tablets or suspension, is reduced by food. Peak plasma concentrations occur 2 to 3 hours after an oral dose and 1 to 2 hours after intravenous dosage. However, azithromycin is extensively distributed into the tissues, and tissue concentrations subsequently remain much higher than those in the blood; in contrast to most other antibacterials, plasma concentrations are therefore of little value as a guide to efficacy. High concentrations are taken up into white blood cells. There is little diffusion into the CSF when the meninges are not inflamed. Data from *animal* studies indicate that azithromycin crosses the placenta. Small amounts of azithromycin are demethylated in the liver, and it is excreted in bile mainly as unchanged drug and a number of inactive metabolites have also been detected. About 6% of an oral dose (representing about 20% of the amount in the systemic circulation) is excreted in the urine. The terminal elimination half-life is about 68 hours.

◊ Reviews and references.

1. Lalak NJ, Morris DL. Azithromycin clinical pharmacokinetics. *Clin Pharmacokinet* 1993; **25:** 370–4.
2. Luke DR, *et al.* Safety, toleration, and pharmacokinetics of intravenous azithromycin. *Antimicrob Agents Chemother* 1996; **40:** 2577–81.
3. Rapp RP. Pharmacokinetics and pharmacodynamics of intravenous and oral azithromycin: enhanced tissue activity and minimal drug interactions. *Ann Pharmacother* 1998; **32:** 785–93.
4. Chandra R, *et al.* Clinical pharmacokinetics and gastrointestinal tolerability of a novel extended-release microsphere formulation of azithromycin. *Clin Pharmacokinet* 2007; **46:** 247–59.

Uses and Administration
Azithromycin is a nitrogen-containing macrolide (azalide) with actions and uses similar to those of erythromycin (p.272). It is given in the treatment of respiratory-tract infections (including otitis media), in skin and soft-tissue infections, and in uncomplicated genital infections. Azithromycin may also be used for the prophylaxis, and as a component of regimens in the treatment, of *Mycobacterium avium* complex (MAC) infections. It is used in some countries for the prophylaxis of endocarditis in at-risk patients unable to take penicillin. It is also used in the management of trachoma and typhoid.

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

Azithromycin has been tried in protozoal infections such as babesiosis (below), crytosporidiosis (p.823), and toxoplasmosis (p.826).

It is given orally or by intravenous infusion usually as the dihydrate; doses are expressed in terms of the anhydrous substance. Azithromycin dihydrate 524 mg is equivalent to about 500 mg of anhydrous azithromycin. The capsule formulation should be given at least 1 hour before, or 2 hours after, meals.

The usual oral adult dose of azithromycin is 500 mg as a single dose daily for 3 days. Alternatively, an initial dose of 500 mg may be followed by 250 mg daily for a further 4 days.

For uncomplicated genital infections caused by *Chlamydia trachomatis* and for chancroid, 1 g of azithromycin is given as a single dose. A single dose of 2 g has been given for uncomplicated gonorrhoea. For the treatment of granuloma inguinale, an initial dose of 1 g followed by 500 mg daily may be given, or 1 g may be given once a week for at least 3 weeks, until all lesions have completely healed.

In the USA, a modified-release preparation given as an oral suspension is available. The product delivers a single dose of 2 g and should also be taken on an empty stomach. It is licensed for the treatment of acute bacterial sinusitis or community-acquired pneumonia in adults.

For prophylaxis of disseminated MAC infections, azithromycin 1.2 g may be given once weekly. For treatment or secondary prophylaxis, 500 mg once daily should be given with other antimycobacterials.