

Pharmacokinetics

When given orally, aminosalicylic acid and its salts are readily absorbed, and peak plasma concentrations occur after about 1 to 4 hours.

Aminosalicylate diffuses widely through body tissues and fluids, although diffusion into the CSF occurs only if the meninges are inflamed. About 15% of the sodium salt, and 50 to 70% of the acid, is bound to plasma proteins.

Aminosalicylate is metabolised in the intestine and liver primarily by acetylation. Urinary excretion is rapid, and 80% or more of a dose is excreted within 24 hours; 50% or more of the dose is excreted as the acetylated metabolite. The half-life of aminosalicylic acid is about 1 hour.

Aminosalicylate is distributed into breast milk (see under Precautions, above, for more details).

Uses and Administration

Aminosalicylic acid and its salts are second-line antimycobacterials given orally in the treatment of multidrug-resistant tuberculosis (p.196). They should always be given with other antituberculous drugs.

Aminosalicylic acid may be given as the acid or as the sodium salt. Sodium aminosalicylate 1.38 g is equivalent to about 1 g of aminosalicylic acid. However, a usual daily oral dose is 12 g in 3 divided doses and has been recommended for products containing the acid as well as for those containing the sodium salt.

For details of doses in infants, children, and adolescents, see below.

Aminosalicylate sodium is also given rectally in the treatment of ulcerative colitis in a usual dose of 2 g once daily.

Attempts have been made in formulation to overcome the bulk and exceedingly unpleasant taste of the aminosalicylates. The salts appear to be better tolerated than the free acid and solutions in iced water prepared immediately before use may be less unpleasant to take.

Administration. A small study suggested that giving aminosalicylic acid in a dose of 4 g twice daily produced adequate serum concentrations (well in excess of 1 microgram/mL, a typical MIC against *Mycobacterium tuberculosis*) for up to 12 hours after each dose.¹ The drug was taken with an acidic beverage such as fruit juice to prevent early release in the stomach. A single 4-g dose was not sufficient to maintain serum concentrations for the full 24-hour dosage interval. The authors had subsequently changed their practice to use a twice-daily regimen for aminosalicylic acid in patients with multidrug-resistant tuberculosis.

1. Peloquin CA, *et al.* Once-daily and twice-daily dosing of p-aminosalicylic acid granules. *Am J Respir Crit Care Med* 1999; **159**: 932-4.

Administration in children. For the treatment of drug-resistant tuberculosis in infants, children, and adolescents the American Academy of Pediatrics (AAP) and WHO suggest an oral dose of para-aminosalicylic acid 200 to 300 mg/kg 2 to 4 times daily, to a maximum dose of 10 g daily.

Administration in renal impairment. It has been recommended that aminosalicylic acid should be avoided in patients with renal impairment.¹ An increase in plasma clearance of aminosalicylic acid (attributed to increased hepatic metabolism) has been noted in patients with renal impairment, hence attempting to give aminosalicylate in reduced doses to such patients may lead to subtherapeutic serum concentrations.²

- Appel GB, Neu HC. The nephrotoxicity of antimicrobial agents (first of three parts). *N Engl J Med* 1977; **296**: 663-70.
- Holdiness MR. Clinical pharmacokinetics of the antituberculosis drugs. *Clin Pharmacokinet* 1984; **9**: 511-44.

Inflammatory bowel disease. Together with corticosteroids, derivatives of 5-aminosalicylic acid are one of the mainstays of the treatment of inflammatory bowel disease (p.1697). However, aminosalicylic acid (4-aminosalicylic acid) has also been investigated, and beneficial results have been reported with both enemas¹⁻⁴ and oral dose forms⁵ in ulcerative colitis. Three patients who developed acute pancreatitis while taking mesalazine (5-aminosalicylic acid) for inflammatory bowel disease, later tolerated treatment with 4-aminosalicylic acid enemas.⁶

- Campieri M, *et al.* 4-Aminosalicylic acid (4-ASA) and 5-aminosalicylic acid (5-ASA) in topical treatment of ulcerative colitis patients. *Gastroenterology* 1984; **86**: 1039.
- Ginsberg AL, *et al.* Treatment of left-sided ulcerative colitis with 4-aminosalicylic acid enemas: a double-blind, placebo-controlled trial. *Ann Intern Med* 1988; **108**: 195-9.
- Sharma MP, Duphare HV. 4-Aminosalicylic acid enemas for ulcerative colitis. *Lancet* 1989; **i**: 450.
- O'Donnell LJD, *et al.* Double blind, controlled trial of 4-aminosalicylic acid and prednisolone enemas in distal ulcerative colitis. *Gut* 1992; **33**: 947-9.
- Beeken W, *et al.* Controlled trial of 4-ASA in ulcerative colitis. *Dig Dis Sci* 1997; **42**: 354-8.
- Daniel F, *et al.* Tolerance of 4-aminosalicylic acid enemas in patients with inflammatory bowel disease and 5-aminosalicylic acid-induced acute pancreatitis. *Inflamm Bowel Dis* 2004; **10**: 258-60.

Manganese toxicity. Intravenous aminosalicylic acid, given in a course of 6 g daily for 4 days a week, for fifteen courses, produced significant benefit in a patient with parkinsonism induced by chronic occupational manganese exposure.¹ The patient re-

mained well on prolonged follow-up. Other cases of benefit had been reported in the Chinese literature.

- Jiang Y-M, *et al.* Effective treatment of manganese-induced occupational Parkinsonism with p-aminosalicylic acid: a case of 17-year follow-up study. *J Occup Environ Med* 2006; **48**: 644-9.

Preparations

USP 31: Aminosalicylate Sodium Tablets; Aminosalicylic Acid Tablets.

Proprietary Preparations (details are given in Part 3)

Canad.: Nemasol†; **Chile:** Aflogol; **Cz.:** Quadrast†; **Fr.:** Quadrast; **Ger.:** Pas-Fatol N; **Ital.:** Quadrast†; **Sal-Pas;** **Port.:** Paramino-Corazida; **Rus.:** Pask-Akri (Паск-Акри); **Switz.:** Perfusion de PAS†; **Thai.:** PAS Sodium; **Turk.:** PAS; **USA:** Paser.

Multi-ingredient: **India:** Inapas.

Amoxicillin (BAN, rINN)

Amoksisilin; Amoksisilini; Amoxicilina; Amoxicilline; Amoxicillinum; Amoxycillin. (6R)-6-[α-D-(4-Hydroxyphenyl)glycylamino]penicillanic acid.

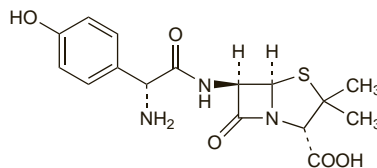
АМОКСИЦИЛИН

$C_{16}H_{19}N_3O_5S = 365.4$.

CAS — 26787-78-0.

ATC — J01CA04.

ATC Vet — QG51AX01; QJ01CA04.



Amoxicillin Sodium (BANM, USAN, rINNM)

Amoksisilino natrio druska; Amoksisilin Sodyum; Amoksisilini-natrium; Amokscylina sodowa; Amoxicilin sodná sůl; Amoxicilina sódica; Amoxicilline sodique; Amoxicillinatium; Amoxicillin-nátrium; Amoxicillinum natrium; Amoxycillin Sodium; BRL-2333AB-B; Natrii Amoxicillinum.

Натрий АМОКСИЦИЛИН

$C_{16}H_{18}N_3NaO_5S = 387.4$.

CAS — 34642-77-8.

ATC — J01CA04.

ATC Vet — QJ01CA04.

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

Ph. Eur. 6.2 (Amoxicillin Sodium). A white or almost white, very hygroscopic powder. Very soluble in water; sparingly soluble in dehydrated alcohol; very slightly soluble in acetone. A 10% solution in water has a pH of 8.0 to 10.0. Store in airtight containers.

Amoxicillin Trihydrate (BANM, rINNM)

Amoksisilinas trihidratas; Amoksisilin Trihidrat; Amoksisilini-trihidraatti; Amokscylina trójwodna; Amoxicilin trihidrát; Amoxicilina trihidrat; Amoxicillin (USAN); Amoxicilline trihydraté; Amoxicillin-trihidrat; Amoxicillintrihidrat; Amoxicillinum trihydricum; Amoxycillin Trihydrate; BRL-2333.

АМОКСИЦИЛИН Тригидрат

$C_{16}H_{19}N_3O_5S \cdot 3H_2O = 419.4$.

CAS — 61336-70-7.

ATC — J01CA04.

ATC Vet — QJ01CA04.

NOTE. Compounded preparations of amoxicillin may be represented by the following names:

- Co-amoxiclav *x/y* (BAN)—amoxicillin (as the trihydrate or the sodium salt) and potassium clavulanate; *x* and *y* are the strengths in milligrams of amoxicillin and clavulanate acid respectively
- Co-amoxiclav (PEN)—amoxicillin trihydrate and potassium clavulanate.

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

Ph. Eur. 6.2 (Amoxicillin Trihydrate). A white or almost white, crystalline powder. Slightly soluble in water; very slightly soluble in alcohol; practically insoluble in fatty oils. It dissolves in dilute acids and in dilute solutions of alkali hydroxides. A 0.2% solution in water has a pH of 3.5 to 5.5. Store in airtight containers.

USP 31 (Amoxicillin). A white, practically odorless crystalline powder. Slightly soluble in water and in methyl alcohol; insoluble in carbon tetrachloride, in chloroform, and in benzene. pH of a 0.2% solution in water is between 3.5 and 6.0. Store in airtight containers.

Adverse Effects and Precautions

As for Ampicillin, p.204.

The incidence of diarrhoea is less with amoxicillin than ampicillin.

Hepatitis and cholestatic jaundice have been reported with amoxicillin plus clavulanic acid; the clavulanic acid component has been implicated. Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and exfoliative dermatitis have also been attributed occasionally to the use of amoxicillin with clavulanic acid.

Breast feeding. Although amoxicillin is excreted in breast milk in small amounts,¹ the American Academy of Pediatrics considers that it is usually compatible with breast feeding.²

- Kafetzis DA, *et al.* Passage of cephalosporins and amoxicillin into the breast milk. *Acta Paediatr Scand* 1981; **70**: 285-8.
- 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 24/05/04)

Effects on the liver. Hepatitis and cholestatic jaundice associated with the combination amoxicillin with clavulanic acid (co-amoxiclav) have been reported¹⁻⁴ and by 1993 the UK CSM had received 138 reports of hepatobiliary disorders, 3 of which were fatal.⁵ It warned that, although usually reversible, the reaction often occurred after stopping therapy with a delay of up to 6 weeks. It appeared that the clavulanic acid was probably responsible. Retrospective analysis of cases reported in Australia⁶ and a cohort study in the UK⁷ found increasing age and prolonged treatment to be major risk factors for jaundice after co-amoxiclav; male sex is also a risk factor. By 1997 the CSM considered that cholestatic jaundice occurred with a frequency of about 1 in 6000 adult patients and that the risk of acute liver injury was about 6 times greater with co-amoxiclav than with amoxicillin alone. Therefore it recommended that co-amoxiclav should be reserved for bacterial infections likely to be caused by amoxicillin-resistant strains, and that treatment should not usually exceed 14 days.⁸

- Stricker BHC, *et al.* Cholestatic hepatitis due to antibacterial combination of amoxicillin and clavulanic acid (Augmentin). *Dig Dis Sci* 1989; **34**: 1576-80.
- Wong FS, *et al.* Augmentin-induced jaundice. *Med J Aust* 1991; **154**: 698-701.
- Larrey D, *et al.* Hepatitis associated with amoxycillin-clavulanic acid combination report of 15 cases. *Gut* 1992; **33**: 368-71.
- Hebbard GS, *et al.* Augmentin-induced jaundice with a fatal outcome. *Med J Aust* 1992; **156**: 285-6.
- Committee on Safety of Medicines/Medicines Control Agency. Cholestatic jaundice with co-amoxiclav. *Current Problems* 1993; **19**: 2. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024454&RevisionSelectionMethod=LatestReleased (accessed 28/07/08)
- Thomson JA, *et al.* Risk factors for the development of amoxycillin-clavulanic acid associated jaundice. *Med J Aust* 1995; **162**: 638-40.
- Rodríguez LAG, *et al.* Risk of acute liver injury associated with the combination of amoxicillin and clavulanic acid. *Arch Intern Med* 1996; **156**: 1327-32.
- Committee on Safety of Medicines/Medicines Control Agency. Revised indications for co-amoxiclav (Augmentin). *Current Problems* 1997; **23**: 8. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023230&RevisionSelectionMethod=LatestReleased (accessed 11/07/06)

Effects on the teeth. A report of tooth discoloration in 3 children associated with the use of amoxicillin with clavulanic acid.¹

- García-López M, *et al.* Amoxycillin-clavulanic acid-related tooth discoloration in children. *Pediatrics* 2001; **108**: 819-20.

Sodium content. Each g of amoxicillin sodium contains about 2.6 mmol of sodium.

Interactions

As for Ampicillin, p.204.

Antimicrobial Action

As for Ampicillin, p.204.

Amoxicillin has been reported to be more active *in vitro* than ampicillin against *Enterococcus faecalis*, *Helicobacter pylori*, and *Salmonella* spp., but less active against *Shigella* spp.

Amoxicillin is inactivated by beta lactamases and complete cross-resistance has been reported between amoxicillin and ampicillin. The spectrum of activity of amoxicillin may be extended by use with a beta-lactamase inhibitor such as clavulanic acid (p.250). As well as reversing resistance to amoxicillin in beta-lactamase-producing strains of species otherwise sensitive, clavulanic acid has also been reported to enhance the activity of amoxicillin against several species not generally considered sensitive. These have included *Bacteroides*, *Legionella*, and *Nocardia* spp., *Haemo-*

philus influenzae, *Moraxella catarrhalis* (*Branhamella catarrhalis*), and *Burkholderia pseudomallei* (*Pseudomonas pseudomallei*). However, *Ps. aeruginosa*, *Serratia marcescens*, and many other Gram-negative bacteria remain resistant. Transferable resistance has been reported in *H. pylori*.

Pharmacokinetics

Amoxicillin is resistant to inactivation by gastric acid. It is more rapidly and more completely absorbed than ampicillin when given orally. Peak plasma-amoxicillin concentrations of about 5 micrograms/mL have been observed 1 to 2 hours after a dose of 250 mg, with detectable amounts present for up to 8 hours. Doubling the dose can double the concentration. The presence of food in the stomach does not appear to diminish the total amount absorbed.

Concentrations of amoxicillin after intramuscular injection are similar to those achieved with oral doses.

About 20% is bound to plasma proteins and plasma half-lives of 1 to 1.5 hours have been reported. The half-life may be prolonged in neonates, the elderly, and patients with renal impairment; in severe renal impairment the half-life may be 7 to 20 hours. Amoxicillin is widely distributed at varying concentrations in body tissues and fluids. It crosses the placenta; small amounts are distributed into breast milk. Little amoxicillin passes into the CSF unless the meninges are inflamed.

Amoxicillin is metabolised to a limited extent to penicilloic acid which is excreted in the urine. About 60% of an oral dose of amoxicillin is excreted unchanged in the urine in 6 hours by glomerular filtration and tubular secretion. Urinary concentrations above 300 micrograms/mL have been reported after a dose of 250 mg. Probenecid reduces renal excretion. Amoxicillin is removed by haemodialysis. High concentrations have been reported in bile; some may be excreted in the faeces.

Amoxicillin with clavulanic acid. The pharmacokinetics of amoxicillin and clavulanic acid are broadly similar and neither appears to affect the other to any great extent.

Uses and Administration

Amoxicillin is the 4-hydroxy analogue of ampicillin (p.205) and is used similarly in susceptible infections. These include actinomycosis, anthrax, biliary-tract infections, bronchitis, endocarditis (particularly for prophylaxis), gastro-enteritis (including salmonella enteritis, but not shigellosis), gonorrhoea, Lyme disease, mouth infections, otitis media, pneumonia, spleen disorders (pneumococcal infection prophylaxis), typhoid and paratyphoid fever, and urinary-tract infections. The beta-lactamase inhibitor clavulanic acid (p.250) widens amoxicillin's antimicrobial spectrum and a combined preparation (co-amoxiclav) can be used when resistance to amoxicillin is prevalent, for example in respiratory-tract infections due to *Haemophilus influenzae* or *Moraxella catarrhalis* (*Branhamella catarrhalis*), in the empirical treatment of animal bites, or in melioidosis. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Amoxicillin is also given as part of treatment regimens to eradicate *Helicobacter pylori* infection in patients with peptic ulcer disease (p.1702).

Administration and dosage. Amoxicillin is given orally as the trihydrate and by injection as the sodium salt. Doses are expressed in terms of the equivalent amount of amoxicillin; 1.06 g of amoxicillin sodium and 1.15 g of amoxicillin trihydrate are each equivalent to about 1 g of amoxicillin.

The usual oral dose is 250 to 500 mg every 8 hours, or 500 to 875 mg every 12 hours. Children up to 10 years of age may be given 125 to 250 mg every 8 hours; for those under 40 kg, a dose of 20 to 40 mg/kg daily in divided doses every 8 hours, or 25 to 45 mg/kg daily in divided doses every 12 hours, may be used; in infants

less than 3 months old, the maximum dose should be 30 mg/kg daily in divided doses every 12 hours.

Higher oral doses of amoxicillin, either as a single dose or in short courses, are used in some conditions. For example, a dose of 3 g repeated once after 8 hours may be used for dental abscesses. A 3-g dose may be given for uncomplicated acute urinary-tract infections, and repeated once after 10 to 12 hours.

A high-dose regimen of 3 g twice daily may be used in patients with severe or recurrent infections of the respiratory tract. If necessary, children aged 3 to 10 years with otitis media may be given 750 mg twice daily for 2 days. Amoxicillin has also been given as a single dose of 3 g, with probenecid 1 g, in the treatment of uncomplicated gonorrhoea in areas where gonococci remain sensitive.

For the prophylaxis of endocarditis in patients at risk, amoxicillin 2 or 3 g is given about 1 hour before dental procedures.

For the eradication of *H. pylori*, amoxicillin is given with either metronidazole or clarithromycin as a proton pump inhibitor; usual doses of amoxicillin are 0.75 or 1 g twice daily or 500 mg three times daily.

An extended release formulation containing 775 mg of amoxicillin as the trihydrate is available in the USA for the treatment of tonsillitis and pharyngitis due to *Streptococcus pyogenes* in patients aged 12 years or older. It is given orally in a dose of 775 mg daily for 10 days.

Amoxicillin is given by intramuscular or slow intravenous injection in doses of 500 mg every 8 hours. In severe infections, 1 g of amoxicillin may be given every 6 hours by slow intravenous injection over 3 to 4 minutes or by infusion over 30 to 60 minutes. Children up to 10 years of age may be given 50 to 100 mg/kg daily by injection in divided doses.

Doses may need to be reduced in moderate to severe renal impairment (see below).

Amoxicillin with clavulanic acid. Amoxicillin combined with clavulanic acid (co-amoxiclav) is given by mouth in a ratio of amoxicillin (as the trihydrate) 2, 4, 7, or 14 parts to 1 part of clavulanic acid (as the potassium salt), or intravenously in a ratio of 5 parts of amoxicillin (as the sodium salt) to 1 part of clavulanic acid (as the potassium salt). Doses of the combination, calculated on amoxicillin content, are similar to those for amoxicillin used alone.

References.

1. Speller DCE, *et al.*, eds. Clavulanate/β-lactam antibiotics: further experience. *J Antimicrob Chemother* 1989; **24** (suppl B): 1-226.
2. Todd PA, Benfield P. Amoxicillin/clavulanic acid: an update of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1990; **39**: 264-307.
3. Easton J, *et al.* Amoxicillin/clavulanic acid: a review of its use in the management of paediatric patients with acute otitis media. *Drugs* 2003; **63**: 311-40.
4. McCormack PL, Keating GM. Amoxicillin/clavulanic acid 2000mg/125mg extended release (XR): a review of its use in the treatment of respiratory tract infections in adults. *Drugs* 2005; **65**: 121-36.

Administration in renal impairment. Doses of amoxicillin should be reduced in patients with moderate to severe renal impairment according to creatinine clearance (CC):

- CC 10 to 30 mL/minute: 250 to 500 mg every 12 hours
- CC less than 10 mL/minute: 250 to 500 mg every 24 hours
- haemodialysis patients: 250 to 500 mg every 24 hours and an additional dose both during and after the dialysis session.

Preparations

BP 2008: Amoxicillin Capsules; Amoxicillin Injection; Amoxicillin Oral Suspension; Co-Amoxiclav Injection; Co-Amoxiclav Tablets;

USP 31: Amoxicillin and Clavulanate Potassium for Oral Suspension; Amoxicillin and Clavulanate Potassium Tablets; Amoxicillin Capsules; Amoxicillin for Oral Suspension; Amoxicillin Tablets; Amoxicillin Tablets for Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Arg: Abiotyl; Almosan; Amixen; Amox-G; Amoxi; Amoxibiot; Amoxicilina Duo; Amoxicina; Amoxicler; Amoxidol; Amoxidol Duo; Amoxigrand; Amoxipenil; Amoxipoten; Amoxiten; Amoxol; Antiamox; Antibiotina; Antibiotocina; Apracur Biotic; Ardin; Atrival; Biotamoxal; Bioxilina; Clafamox; Darzil; Dunox; Fabamox; Flenoxon; Fullcina; Fullcina Duo; Grinsil; Grinsil Duo; Mixcilin; Moxitral; Nobactam; Optamox; Oximar; Plamox; Telmo; Trifamox; Trifamox Duo; Xalotin; **Austral:** Alphamox; Amohexal; Amoxil; Bgramin; Cilamox; Fismox; Ibiomox; Maxamox; Moxacin; **Austria:** Amoxal; Amoxihexal; Amoxilan; Amoxistad; Antibiotid; Clamoxyl; Eramox; Ospamox; Supramox; **Belg:** Amoxip; Amoxypen; Bactimed; Clamoxyl; Docamoxil; Flenoxin; Hiconil; Moxalinet; Moxitop; Nobavritine; **Braz:** Amoflux; Amox; Amoxadene; Amoxi-Ped; Amoxibron; Amoxicap; Amoxicin; Amoxidil; Amoxiflar; Amoxil; Amoximed; Amoxi-

na; Amoxipen; Amoxitan; Amplaf; Amplamox; Aproxipax; Bimoxin; Camoxin; Duzimic; Farnoxil; Flenoxon; Hiconil; Hincamox; Ibiomox; Ili; Liclon; Lifamox; Moxipilus; Nemoxyl; Neo Moxilin; Novocit; Novoclin; Novoxil; Ocylin; Penicilinet; Pharnox; Polibac; Polimoxil; Probenil; Prodoxil; Resciline; Trimox; Ultramox; Uni Amox; Velamox; **Canada:** Apo-Amox; Lin-Amoxil; Novamoxin; Nu-Amox; **Chile:** Abiolex; Amobiot; Amoval; Amoval Duo; Amoxipenil; Moxilina; Optamox; **Cz:** Amoclen; Amogal; Amoxihexal; Apo-Amoxil; Duomox; Gonoform; Grunamox; Infecto-Mox; Ospamox; **Denm:** Flenoxin; Imacilin; Imadraz; **Fin:** Amorion; Amoxin; Clamox; Flenoxin; Penafit; **Fr:** A-Gram; Amode; Bactox; Bristamox; Clamoxyl; Flenoxin; Gramidil; Hiconil; **Ger:** Amagesan; Amc-Puren; Amoxi; Amoxi-Diolan; Amoxi-Hela; Amoxi-Puren; Amoxi-Tablinen; Amoxi-Wolff; Amoxibeta; Amoxidox; Amoxihexal; Amoxillat; Amoximerck; Amoxypen; Clamoxyl; espa-moxin; Flui-Amoxicillin; Infecto-Mox; Jutamox; Pharnox; Apo-Amoxi; Aroxin; Betamox; Amoxil; Aproxal; Flenoxin; Ospamox; Paradoxil; Stevendil; Triodanin; **Hong Kong:** Amolin; Amoxil; Amoxapen; Apo-Amoxi; Aroxin; Betamox; Edamox; Farnoxilin; Moxilin; Moxlin; Ospamox; Promox; Ranoxyl; Reichamox; Unimox; **Hung:** Clonamox; Duomox; Humamoxin; Ospamox; **India:** Amoxil; Amoxivan; Aristomox; Biomoxil; Damoxyl; Flenoxin; Genomox; Hipen; Imox; Loxyn; Mokcan; Mox; Moxycarb; Novamox; Ronemox; Symoxyl; **Indon:** Abdiox; Adlam; Amobiotic; Amosine; Amoxil; Amoxilin; Amoxsan; Arcamox; Bellacid; Bintamox; Bioxylin; Corsamox; Danoxil; Dexymox; Erphamox; Ethimox; Farnoxyl; Ikamoxyl; Intermoxil; Kalmoxilin; Kimoxil; Lapimox; Leonoxyl; Medimox; Medoxyl; Mestamox; Mexilin; Mokbios; Moxlin; Moxlid; Nufamox; Opimox; Ospamox; Penmox; Primoxil; Pritamox; Robamox; Scannoxyl; Silamox; Solpenox; Supramox; Topillin; Vibriamox; Wiomox; Wilecillin; Xiltrop; **Irl:** Amoxil; Clonamox; Galenamox; Geramox; Oramox; Pinamox; **Israel:** Amoxi; Hiconil; Moxypen; Moxxyvit; **Ital:** Alfamox; Amocin; Amoflux; Amosol; Amoxi; Amoxilin; Amoxina; Bradimox; Dodemox; Erremox; Genimox; Hydramox; Ibiomox; Isomoxin; Majorpen; Mopen; Moxiren; Neo-Amplex; Neotetrax; Oralmox; Pamoxil; Progemox; Sievert; Sirmoxil; Simplexoxil; Sintopen; Velamox; Zimox; **Jpn:** Pasetocin; **Malaysia:** Beamox; Moxacil; Moxilin; Moxipen; Ospamox; Setmoxil; **Mex:** Acimox; Acroxil; Amecina; Amicil; Amobay; Amoxifur; Amoxin; Amoxinovag; Amoxisol; Amoxivet; Ampiliron; Amoxilina; AMX; Ardin; Amoxin; Betabiot; Bimoxan; Biocam; Brenoxil; Dimopen; Dexamil; Examol; Flenoxin; Gimbaxina; Grunicina; Hidramox; Limoxin; Lorexil M; Lumox; Micro Mox; Mocimed; Moxiclin; Moxlin; Penamox; Pentidox; Polymox; Prodomox; Servamox; Servamox-F; Solcilina; Vandix; Xalyn-Or; Xiprocant; **Neth:** Amoxi; Amoxilag; Clamoxyl; Flenoxin; **Norw:** Amoxilin; Imacilin; **NZ:** Alpha-Amoxi; Amoxil; Apo-Amoxi; Flenoxin; Ibiomox; Ospamox; **Philipp:** Amelox; Amoxil; Amusa; Bactigen; Bradoxil; Cartrimox; Clamox; Clifam; Clearamox; Daisamox; Eleomox; Essenmox; Gexcil; Globamox; Globapen; Himox; Kramollex; Lewixin; Littmox; Maelenoxyl; Medimoxil; Medviox; Megamox; Montramox; Moxillin; Moxipen; Neomox; Novamox; Pediamox; Penbiosyn; Promox; Roddexil; Sumoxil; Syndoxil; Telsimox; Teramoxil; Termox; Trexil; Valmox; Vastamox; Vaxman; Westmox; Yugoxil; Zerrmox; Zymoxyl; **Pol:** Amotaks; Apo-Amoxi; Duomox; Grunamox; Hiconil; Novamox; Ospamox; **Port:** Amplamox; Bodisan; Cipamox; Clamoxyl; Flenoxin; Moxadent; Moxipen; Oramina; Ospamox; Penamox; **Rus:** Amosin (Амосин); Flenoxin (Фленоксин); Hiconil (Хиконил); Ospamox (Оспамокс); **S.Afr:** A-Lennon; Acucil; Amocillin; Amoxil; Amoxyl; Betamox; C-Mox; Ipcamox; Maxcil; Moxan; Moxypen; Penmox; Promoxil; Ramoxyl; Spectramox; Xeracil; Zoxil; **Singapore:** Amoxa; Amoxapen; Amoxicap; Amoxigran; Amoxil; Apo-Amoxi; Aroxin; Moxilin; Moxipen; Ospamox; Unimox; **Spain:** Actimoxil; Agerpen; Amritron; Amoflamisan; Amoxaren; Amoxi Gobens; Amoxibacter; Amoximedical; Apamox; Ardin; Blenox; Bolchipen; Borbalan; Britamox; Bronid; Clamoxyl; Co Amoxin; Dobridicil; Edoxil; Eupen; Flubiotic NF; Hosboral; Inexbron; Morgexil; Reloxyl; Remisan; Salvapen; Tolodina; **Swed:** Amimox; Imacilin; **Switz:** amoxi-basant; Amoxi-Cophar; Amoxi-Mepha; Amoximex; Antiotict; Aziline; Clamoxyl; Escamox; Flenoxin; Penimox; Spectroxy; Supramox; **Thai:** Acticillin; Amacin; Amox; Amoxa; Amoxillin; Amoxi; Amoxil; Amoxy; Amoxylin; Asiama; Coamox; Ibiomox; Kamoxin; Kenya-Mox; Manmox; Mexil; Milamox; Moxapen; Moxcil; Moxlin; Moxilcap; Moxilin; Moximed; Moxipant; Moxitab; Pondnoxil; Pulmoxil; Rancil; Ranoxyl; Samox; Samoxin; Servamox; Sia-Mox; Sil-A-Mox; TVMox; Unimox; **Turk:** Alfoxil; Amokslay; Amokslin; Amoksina; Amosin; Atokslin; Demoksil; Largopen; Moksilin; Remoxil; Topramox; **UAE:** Iulphamox; **UK:** Amox; Amoram; Amoxident; Amoxil; Galenamox; Rimoxilin; **USA:** Amoxil; Disper-Mox; Moxatag; Trimox; **Venez:** Amitrexyl; Amofar; Amoxal; Amoxiduo; Amoxiga; Amoxilan; Amoxipen; Amoxival; Amrylin; Bactamox; Fibramox; Flenoxon; Ofamix; Ospamox; Sentapen; Strimox; Sumopen; Trimoxil.

Multi-ingredient Arg: Acemux Biotic; Adlav; Albesine Biotic; Amixen Clavulanate; Amixen Plus; Amoclav; Amox-G Bronquial; Amoxi Plus; Amoxi Respiratorio; Amoxidol Respiratorio; Amoxidol Respiratorio Duo; Amoxigrand Bronquial; Amoxigrand Compuesto; Amoxipenil Bronquial; Amoxitenk Plus; Amoxitenk Respiratorio; Aseptobron Respiratorio; Bi Moxal; Bi Moxal Duo; Bioclad; Bioclinia Plus; Clavulox; Clavulox Duo; Cloximar Duo; Darzil Plus; Darzil SB; Desinfam Biotic; Dibional; Fluimucil Biotic; Fullcina Plus; Glifapen; Grinsil Clavulanate; Grinsil Respiratorio; Heliklar; Klonamox; Lertus Biotic; Mucos Dosodos Biotic; No-Tos Biotic; Nobactam Bronquial; Oximar Respiratorio; Rodnac Biotic; Trexlor NF; Trifamox Bronquial; Trifamox Bronquial Duo; Trifamox IBL; **Austral:** Augmentin; Ausclav; Clamohexal; Clamoxyl; Clavulin; Curam; Klacid HP 7; Loxec Hp 7; Nexium Hp; Pylorid-KA; Soma-Ma; **Austria:** Amoclan; Amoxicillin comp; AmoxiClavulan; Amoxicomp; Amoxipus; Amoxidat plus; Augmentin; Bendav; Benomox; Betamoclav; Clavamox; Clavex; Clavolek; Clavoplus; Clavulanex; CombAmox; Curam; Helicocin; Helipac; Lanoclav; Lekomoxilav; Oxycilav; Xiclav; **Belg:** Amoclan; Augmentin; Clavucid; Co-Amoxi; Co-Amoxilan; Docamoclat; **Braz:** Anzopac; Augmentin; Betadav; Bronco-Amoxil; Bronco-Polimoxil; Clav-Air; Clavoxil; Clavulin; Erradic; H-Bacter; Helicoid; Triplecic; Helicopac; Heliklar; Novamox; Omepiramix; Policlavumoxil; Pylorik; Pyloripac; Pyloritrag; Sigma Clav; Sulbamox; **Canada:** Apo-Amoxi Clav; Clavulin; Hp-Pac; Loxec 1-2-3 A; Novo-Clavamoxin; ratio-Aclavulanate; **Chile:** Ambilan; Ambilan Bid; Amolex; Augmentin; Augmentin Bid; Clavine; Clavine Duo; Clavoxilina Bid; Sulbamox; **Cz:** Amokslav; Augmentin; Augmentin Duo; Betaklav; Curam; Enhancin; Forcid; Klamoxylin; Megamox; **Denm:** Bioclad; Spektramox; **Fin:** Amoxin Comp; Augmentin; Bioclad; Clapharin Comp; Clavurion; Clavuxil; Forcid; Helipak A; Helipak K; Loxec Helirag; Spektramox; **Fr:** Augmentin; Cilor; **Ger:** Abiclav; Amoclav; Amoxclav; Amoxi-Clavulan; Amoxi-saar plus; Amoxicillin comp; Amoxiclav; Amoxidura Plus; Amoxillat-Clav; Amocil; Augmentan; Flanamox; Zactac; **Gr:** Augmentin; Bioclad; Forcid; Fugentin; Moxiclav; Tenevar; **Hong Kong:** Amokslav; Augmentin; Clamovid; Curam; Fleming; Moxiclav; Quali-Mentin; **Hung:** Akti; Amoclan; Amoclar; Augmentin; Augmentin Duo; Augmentin-Extra; Clavumox; Co-Amoxi; Curam; Enhancin; **India:** ABClo; Amclod; Augmentin; Bidal; Biomoxil-LB; Boostin; Bromolin; Carbomox; Helipac; Hipenox; Imox-Clo; Imox-Clo LB; LMX; Moxycarb-DT; Novadav; Novadav; Novadav-LB; Novamox AX; Novamox LB; Nuclav; Rapidav; Respirom; Symbiotic; Symoxyl-LB; **Indon:** Amocomb; Ancia; Augmentin; Amoxicil; Bellamox; Betacilav; Biditin; Capsinat; Clabat; Claneaks; Clavamox; Comsika; Danoclav; Daxet; Dexycil; Improv; Lansiclav; Nufadav; Nuvo-

The symbol † denotes a preparation no longer actively marketed

clav; Prafamox; Protamox; Surpas; Syneclav; Viaclav; Vulamox; Zumafer. **Int.:** Augmentin; Clavamel; Germentin; Pinadav. **Israel:** Amoxiclav; Augmentin; Clavamox. **Ital.:** Abba; Anival; Augmentin; Clavulin; Neoduplamox; Xl-namox. **Malaysia:** Augmentin; Caprom; Clamovid; Curam; Enhancin; Klacid HP 7; Moxiclav; Vestaclov. **Mex.:** Acarboxin; Acimox AC; Acimox-Ex; Acroxil-C; Alvi-Tec; Ambrexin; Ambobay CL; Amoxibron; Amoxiclav; Amoxiclide; Apoclavox; Augmentin; Avuxilan; Biocivam; Ex; Bolbamox; Bromel; Bromixen; Bromoxil; Broxilom-AM; Brumax; Cibronal; Clambusil; Clamoxin; Clavant; Clavacyd; Clavulin; Clavuser; Enhancin; Esteclin Bac; Ferlex; Gimabrol; Gramaxin; Hidramox-M; Loexom FC; Loexom FS; Lumox-bron S; Maxint; Megamox; Moxlin CLV; Mucovibrol Amoxi; Mucoxina; Penamox M; Penbiritin Ex; Pentibroxil; Pylopac; Ravotaf; Riclasip; Sekretovit Amoxi; Septacin Amoxi; Sermoxol; Seryamox CLV; Sinufin; Solcibrol; Toxol; Trifamox IBL; Valclan; Vanmoxol. **Neth.:** Amoclan; Amucan; Augmentin; Bioclavid; Forcid; PantoPAC. **Norw.:** Bremide; **NZ:** Alpha-Amoxyclov; Augmentin; Klacid HP 7; Loxec; Hp 7; Synermox. **Philipp.:** Amoclav; Augmentin; Augmex; Augurcin; Bactiv; Bactodav; Bioclavid; Clamovid; Claneke; Claventin; Clavoxel; Clovimax; Enhancin; Exten; Klavic; Natravox; OAC Hp7; Proxilin; Sullivan; Suplestin; Valmoxel; Xlclanic. **Pol.:** Amoksklav; Augmentin; Curam; Forcid; Ramoclav; Taromentin. **Port.:** Amoclavam; Amplamox Plus; Augmentin; Betamox; Clavamox; Clavepen; Forcid; Noprilam; Penilam; **Rus.:** Amoclan (Амоклан); Amoksklav (Амоксилава); Augmentin (Аугментин); Flemoclav (Флемоклав); Medoclav (Медоклав); Paniklav (Паниклав); Rapiclav (Раниклав); Trifamox IBL (Трифамокс ИБЛ). **S.Afr.:** Adco-Amoclav; Augmaxil; Augmentin; Bio-Amoksklav; Clamentin; Clavumox; Co-Amoxyclov; Curam; Forcid; Hiconid-NS; Loxec 20 Triple; Macro-pen; Megapen; Moxyclov; Randav; Rolab-Amoclav; Suprapen; **Singapore:** Amocla; Augmentin; Augmex; Clamonex; Clamovid; Curam; Enhancin; Fugentin; Moxiclav. **Spain:** Amo Resant; Amoclav; Amoxi Gobens Mucolitico; Amoxylus; Aridine Bronqual; Aridneclav; Augmentine; Bigpen; Bronco Tonic; Burmicin; Clamoxyl Mucolitico; Clavepen; Clavucid; Clavumox; Duonasa; Edoxil Mucolitico; Eupelclanic; Eupen Bronqual; Immu-pent; Kelsopen; Pulmo Borbalan; Reloxyl Mucolitico; Remisan Mucolitico; Salvapen Mucolitico. **Swed.:** Bioclavid; Nexium Hp; Spektramox. **Switz.:** Amicosol; Augmentin; Aziclav; Clavamox; clavu-basan; Co-Amoxi; Co-Amoxicillin. **Thai.:** Amocla; Amoksklav; Augclav; Augmentin; Augpen; Cavumox; Curam; Klamox; Moxiclav; Moxicle; Penda; Randav. **Turk.:** Amok-lavin; Augmentin; Bioment; Croxilex; Helipak; Klamox; Klavunat; Klavupen; **UAE:** Julmentin; **UK:** Amiclav; Augmentin; Augmentin-Duo; Heliclear; **USA:** Amoclan; Augmentin; Prevpac. **Venez.:** Augmentin; Augmentin Bid; Clavumox; Curam; Fulgram.

Ampicillin (BAN, USAN, rINN)

Aminobenzylpenicillin; Ampicilin; Ampicilina; Ampicilinas, bev-andenis; Ampicillin, vattenfritt; Ampicilline; Ampicilline anhydrous; Ampicillinum; Ampicillinum anhydricum; Ampicilina bezwodna; Ampisilin; Ampisilini; Ampisilini, vedet-50; Anhydrous Ampicillin; AY-6108; BRL-1341; NSC-528986; P-50; Vízmentes ampicillin. (6R)-6-(α -D-Phenylglycylamino)penicillanic acid.

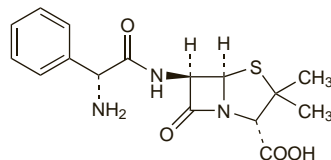
АМПИЦИЛИН

$C_{16}H_{19}N_3O_4S = 349.4$.

CAS — 69-53-4.

ATC — J01CA01; S01AA19.

ATC Vet — QJ01CA01; QJ51CA01; QS01AA19.



NOTE: Compounded preparations of ampicillin may be represented by the following names:

- Co-fluampicillin (BAN)—flucloxacillin 1 part and ampicillin 1 part (w/w).

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

Int. and *US* permit anhydrous or the trihydrate.

Ph. Eur. 6.2 (Ampicillin, Anhydrous; Ampicillin BP 2008). A white or almost white, crystalline powder. It exhibits polymorphism. Sparingly soluble in water; practically insoluble in alcohol, in acetone, and in fatty oils. It dissolves in dilute solutions of acids and of alkali hydroxides. A 0.25% solution in water has a pH of 3.5 to 5.5. Store at a temperature not exceeding 30° in airtight containers.

USP 31 (Ampicillin). It is anhydrous or contains three molecules of water of hydration. A white, practically odourless crystalline powder. Slightly soluble in water and in methyl alcohol; insoluble in carbon tetrachloride, in chloroform, and in benzene. pH of a 1% solution in water is between 3.5 and 6.0. Store in airtight containers.

Ampicillin Sodium (BANM, USAN, rINN)

Aminobenzylpenicillin Sodium; Ampicilin sodná sůl; Ampicilina sodica; Ampicilino natrio druska; Ampicilline sodique; Ampicillin-natrium; Ampicillin-natrium; Ampicillinum natrium; Ampicilina sodowa; Ampisilininatrium; Natrii Ampicillinum; Sodyum Ampisilini.

Натрий Ампициллин

$C_{16}H_{18}N_3NaO_4S = 371.4$.

CAS — 69-52-3.

ATC — J01CA01; S01AA19.

ATC Vet — QJ01CA01; QS01AA19.

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

Ph. Eur. 6.2 (Ampicillin Sodium). A white or almost white hygroscopic powder. Freely soluble in water; sparingly soluble in acetone; practically insoluble in liquid paraffin and in fatty oils. A 10% solution in water has a pH of 8.0 to 10.0. Store in airtight containers.

USP 31 (Ampicillin Sodium). A white to off-white, odourless or practically odourless, hygroscopic, crystalline powder. Very soluble in water and in isotonic sodium chloride and glucose solutions. pH of a solution in water containing the equivalent of ampicillin 1% is between 8.0 and 10.0. Store in airtight containers.

Incompatibility. The incompatibility of ampicillin sodium and aminoglycosides is well established. Incompatibilities have also been reported with a wide range of other drugs, including other antibacterials, and appear to be more pronounced at higher concentrations and in solutions also containing glucose.

Stability. The stability of solutions of ampicillin sodium is dependent on many factors including concentration, pH, temperature, and the nature of the vehicle. Stability decreases in the presence of glucose, fructose, invert sugar, dextrans, hetastarch, sodium bicarbonate, and lactate. It is recommended that reconstituted solutions of ampicillin sodium for injection should be given within 24 hours of preparation, and should be stored at 2° to 8° but should not be frozen. Solutions for infusion are stable for varying periods and details are given in licensed product information.

References.

1. Lynn B. The stability and administration of intravenous penicil-lins. *Br J Intraven Ther* 1981; 2(Mar): 22–39.

Ampicillin Trihydrate (BANM, rINN)

Ampicilin trihidrát; Ampicilina trihidrato; Ampicilinas trihidratas; Ampicillin; Ampicilline trihydraté; Ampicillin-trihidrát; Ampicil-lintrihidrat; Ampicillinum trihydricum; Ampicilina trójwodna; Ampisiliniintrihidraatti.

АМПИЦИЛИН Тригидрат

$C_{16}H_{19}N_3O_4 \cdot 3H_2O = 403.5$.

CAS — 7177-48-2.

ATC — J01CA01; S01AA19.

ATC Vet — QJ01CA01; QS01AA19.

Pharmacopoeias. In *Eur.* (see p.vii) and *Viet.* In *Chin.* and *Jpn* under the title Ampicillin. *Int.* and *US* permit anhydrous or the trihydrate under the title Ampicillin.

Ph. Eur. 6.2 (Ampicillin Trihydrate). A white or almost white, crystalline powder. Slightly soluble in water; practically insoluble in alcohol and in fatty oils. It dissolves in dilute solutions of acids and of alkali hydroxides. A 0.25% solution in water has a pH of 3.5 to 5.5. Store in airtight containers.

USP 31 (Ampicillin). It is anhydrous or contains three molecules of water of hydration. A white, practically odourless crystalline powder. Slightly soluble in water and in methyl alcohol; insoluble in carbon tetrachloride, in chloroform, and in benzene. pH of a 1% solution in water is between 3.5 and 6.0. Store in airtight containers.

Adverse Effects

As for Benzylpenicillin, p.213.

Skin rashes are among the most common adverse effects and are generally either urticarial or maculopapular; the urticarial reactions are typical of penicillin hypersensitivity, while the erythematous maculopapular eruptions are characteristic of ampicillin and amoxicillin and often appear more than 7 days after commencing treatment. Such rashes may be due to hypersensitivity to the beta-lactam moiety or to the amino group in the side-chain, or to a toxic reaction. The occurrence of a maculopapular rash during ampicillin use does not necessarily preclude the subsequent use of other penicillins. However, since it may be difficult in practice to distinguish between hypersensitive and toxic responses, skin testing for hypersensitivity may be advisable before another penicillin is used in patients who have had ampicillin rashes. Most patients with infectious mononucleosis develop a maculopapular rash when treated with ampicillin, and patients with other lymphoid disorders such as lymphatic leukaemia, and possibly those with HIV infection, also appear to be at higher risk. More serious skin reactions may occur and erythema multiforme associated with ampicillin has occasionally been reported.

Gastrointestinal adverse effects, particularly diarrhoea and nausea and vomiting, occur quite often, usually after oral use. Pseudomembranous colitis has also been reported.

Precautions

As for Benzylpenicillin, p.214.

Ampicillin should be stopped if a skin rash occurs. It should preferably not be given to patients with infectious mononucleosis since they are especially susceptible to ampicillin-induced skin rashes; patients with lymphatic leukaemia or possibly HIV infection may also be at increased risk of developing skin rashes.

Myasthenia gravis. The symptoms of a woman with myasthenia gravis were exacerbated when she was given ampicillin.¹

1. Argov Z, *et al.* Ampicillin may aggravate clinical and experimental myasthenia gravis. *Arch Neurol* 1986; 43: 255–6.

Sodium content. Each g of ampicillin sodium contains about 2.7 mmol of sodium.

Interactions

As for Benzylpenicillin, p.214.

Allopurinol. An increased frequency of skin rashes has been reported in patients receiving ampicillin or amoxicillin, with allopurinol, compared with those receiving the antibacterial alone,¹ but this could not be confirmed in a subsequent study.²

1. Jick H, Porter JB. Potentiation of ampicillin skin reactions by allopurinol or hyperuricemia. *J Clin Pharmacol* 1981; 21: 456–8.
2. Hoigne R, *et al.* Occurrence of exanthems in relation to amipenicillin preparations and allopurinol. *N Engl J Med* 1987; 316: 1217.

Chloroquine. The absorption of ampicillin has been reduced in healthy subjects taking chloroquine.¹

1. Ali HM. Reduced ampicillin bioavailability following oral coadministration with chloroquine. *J Antimicrob Chemother* 1985; 15: 781–4.

Antimicrobial Action

Ampicillin is a beta-lactam antibiotic. It is bactericidal and has a similar mode of action to that of benzylpenicillin (p.214), but as an aminopenicillin with an amino group side-chain attached to the basic penicillin structure, ampicillin is better able to penetrate the outer membrane of some Gram-negative bacteria and has a broader spectrum of activity.

Spectrum of activity. Ampicillin resembles benzylpenicillin in its action against Gram-positive organisms, including *Streptococcus pneumoniae* and other streptococci, but, with the possible exception of activity against *Enterococcus faecalis*, it is slightly less potent than benzylpenicillin. *Listeria monocytogenes* is highly sensitive. The Gram-negative cocci *Moraxella catarrhalis* (*Branhamella catarrhalis*), *Neisseria gonorrhoeae*, and *N. meningitidis* are sensitive. Ampicillin is more active than benzylpenicillin against some Gram-negative bacilli, including *Haemophilus influenzae* and Enterobacteriaceae such as *Escherichia coli*, *Proteus mirabilis*, *Salmonella* and *Shigella* spp. It is inactive against *Pseudomonas aeruginosa*. Ampicillin also has activity similar to benzylpenicillin against other organisms including many anaerobes and *Actinomyces* spp.

Activity with other antimicrobials. There is synergy against some beta-lactamase-producing organisms between ampicillin and beta-lactamase inhibitors such as clavulanic acid or sulbactam, and also penicillinase-stable drugs such as cloxacillin or flucloxacillin. Synergy has also been shown between ampicillin and aminoglycosides against a range of organisms, including enterococci. Variable effects ranging from synergy to antagonism have been reported between ampicillin and other beta lactams, bacteriostatic drugs such as chloramphenicol, and rifampicin.

Resistance. Like benzylpenicillin, ampicillin is inactivated by beta lactamases, although other mechanisms may be responsible for resistance in some species. There are geographical variations in the incidence of resistance, but most staphylococci and many strains of *E. coli*, *H. influenzae*, *M. catarrhalis*, *N. gonorrhoeae*, and *Salmonella* and *Shigella* spp. are resistant.

Pharmacokinetics

Ampicillin is relatively resistant to inactivation by gastric acid and is moderately well absorbed from the gastrointestinal tract after oral doses. Food can interfere with the absorption of ampicillin so doses should pref-