

dav; Pramox; Protamox; Surpas; Syneclav; Vlaclav; Vulamox; Zumafen; **Irl.:** Augmentin; Clavamel; Germentin; Pinadav; **Israel:** Amoxiclav; Augmentin; Clavamox; **Ital.:** Abba; Anival; Augmentin; Clavulin; Neoduplamox; Xilnamod; **Malaysia:** Augmentin; Cavimox; Clamovid; Curam; Enhancin; Klacid HP 7; Moxiclav; Vestaclav; **Max.:** Acarboxin; Acimox AC; Acimox-E; Acroxil-C; Alvi-Tec; Ambrexin; Amobax; Amoxibron; Amoxiclav; Amoxiclide; Apoclavox; Augmentin; Avubax; Bioclam; Ex; Bollamox; Bromel; Bromixen; Bromoxil; Broxilom-AM; Brumax; Cibronal; Clambusil; Clamoxin; Clavant; Clavuoyd; Clavulin; Clavuser; Enhancin; Esteclin Bac; Ferlex; Gimabrol; Gramaxin; Hidramox-M; Loexom FC; Loexom FS; Lumoxbron S; Maxint; Mlegamox; Moxlin CLV; Mucovibrol Amoxi; Mucovina; Penamox M; Penbritin Ex; Pentibroxil; Pylapac; Ravotaf; Riclesip; Sekretovit Amoxi; Septacin Amoxi; Sermoxol; Servamox CLV; Sinufin; Solcibrol; Toxol; Trifamox IBL; Valclan; Vanmoxil; **Neth.:** Amoclan; Amuclan; Augmentin; Bioclavid; Forcid; PantopAC; **Norw.:** Bremide; **NZ:** Alpha-Amoxycylav; Augmentin; Klacid HP 7; Losec Hp 7; Synermox; **Philipp.:** Amoclav; Augmentin; Augmex; Augurcin; Bactiv; Bactoclav; Bioclavid; Clamovid; Claneke; Claventin; Clavoxel; Clovimax; Enhancin; Exten; Klavic; Natravox; OAC Hp7; Poxiclav; Sullivan; Suplestin; Valmoxil; Xilanic; **Pol.:** Amoksilav; Augmentin; Curam; Forcid; Ramoclav; Taromentin; **Port.:** Amoclavam; Amplamox Plus; Augmentin; Betamox; Clavamox; Clavepen; Forcid; Noprilam; Penilam; **Rus.:** Amoclan (Амоклан); Amoksilav (Амоксилава); Augmentin (Аугментин); Flemoclin (Флемоклав); Medoclav (Медоклав); Panclav (Панклава); Rapiclav (Рапикава); Trifamox IBL (Трифамокс ИБЛ); **S.Afr.:** Adco-Amoclav; Augmaxil; Augmentin; Bio-Amoksilav; Clamentin; Clavromox; Co-Amoxycylav; Curam; Forcid; Hiconil-NS; Losec 20 Triple; Macropep; Megapen; Moxycylav; Ranclav; Rolab-Amoclav; Suprapen; **Singapore:** Amocla; Augmentin; Augmex; Clamonex; Clamovid; Curam; Enhancin; Fugentin; Moxiclav; **Spain:** Amo Resan; Amoclav; Amoxi Gobens Mucolitico; Amoxylupis; Aridine Bronqual; Aridneclav; Augmentine; Bigpen; Bronco Tonic; Burmicin; Clamoxyl Mucolitico; Clavepen; Clavucid; Clavumox; Duonas; Edoxil Mucolitico; Eupelanclav; Eupen Bronqual; Imupen; 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; Amoksilav; Augclav; Augmentin; Augpen; Cavumox; Curam; Klamox; Moxiclav; Moxicle; Pencla; Randlav; **Turk.:** Amoklav; Augmentin; Bioment; Croxilex; Helipac; Klamox; Klavunat; Klavupen; **UAE:** Julmentin; **UK:** Amiclav; Augmentin; Augmentin-Duo; Heliclear; **USA:** Amoclan; Augmentin; Prevpac; **Venez.:** Augmentin; Augmentin Bid; Clavamox; Curam; Fulgram.

## Ampicillin (BAN, USAN, rINN)

Aminobenzylpenicillin; Ampicilin; Ampicilina; Ampicilinas; bevandenis; Ampicillin, vattenfritt; Ampicilline; Ampicilline anhydrous; Ampicillinum; Ampicillinum anhydricum; Ampicilina bezwodna; Ampisilin; Ampisilliini; Ampisilliini, vedetön; Anhydrous Ampicillin; AY-6108; BRL-1341; NSC-528986; P-50; Vízmentes ampicillin. (6R)-6-( $\alpha$ -D-Phenylglycylamino)penicillanic acid.

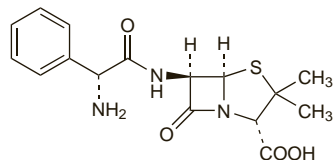
### АМПИЦИЛИН

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

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)—flucoxacillin 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, rINNM)

Aminobenzylpenicillin Sodium; Ampicilin sodná sůl; Ampicilina sodíca; Ampicilino natrio druska; Ampicilline sodique; Ampicillin-natrium; Ampicillin-nátrium; Ampicillinum natrium; Ampicilina sodowa; Ampisillinatrium; Natrii Ampicillinum; Sodyum Ampicillin.

### 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 penicilins. *Br J Intraven Ther* 1981; 2(Mar): 22–39.

## Ampicillin Trihydrate (BANM, rINNM)

Ampicilin trihidrát; Ampicilina trihidrato; Ampicilinas trihidratas; Ampicillin; Ampicilline trihydraté; Ampicillin-trihidrát; Ampicillin-trihidrat; Ampicillinum trihydricum; Ampicilina trójwodna; Ampisilliintrihydraatti.

### АМПИЦИЛИН ТРИГИДРАТ

$C_{16}H_{19}N_3O_4S \cdot 3H_2O = 403.5$ .

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.<sup>1</sup>

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,<sup>1</sup> but this could not be confirmed in a subsequent study.<sup>2</sup>

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 aminopenicillin preparations and allopurinol. *N Engl J Med* 1987; 316: 1217.

**Chloroquine.** The absorption of ampicillin has been reduced in healthy subjects taking chloroquine.<sup>1</sup>

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-