AUSTRALIAN PRODUCT INFORMATION

ALPHAMOX®

(amoxicillin (as trihydrate)) capsules

1 NAME OF THE MEDICINE

Amoxicillin (as trihydrate).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ALPHAMOX capsule contains amoxicillin trihydrate equivalent to 250 mg or 500 mg of amoxicillin.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

ALPHAMOX 250: hard gelatin capsule with ivory body and green cap Size "2" filled with almost white granular powder.

ALPHAMOX 500: hard gelatin capsule of size "0el" having FEA ivory opaque body and FEG green opaque cap filled with white/almost white granular powder.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Treatment of the following infections due to susceptible strains of sensitive organisms.

Note: therapy should be guided by bacteriological studies, including sensitivity tests, and by clinical response. However, in emergency cases where the causative organism has not been identified, therapy with amoxicillin may be useful. Clinical judgement will decide whether combination with another antibiotic would provide a sufficiently broad spectrum of activity pending sensitivity test results.

Skin and Skin Structure

Staphylococcus, non-penicillinase producing; Streptococcus*; E. coli* (see Section 5.1 PHARMACODYNAMIC PROPERTIES - Microbiology).

Respiratory (Acute and Chronic)

H. influenzae; Streptococcus; *S. pneumoniae*; staphylococcus, non-penicillinase producing*; E. coli* (see Section 5.1 PHARMACODYNAMIC PROPERTIES - Microbiology).

Genitourinary Tract (complicated and uncomplicated, Acute and Chronic)

P. mirabilis; S. faecalis; *E. coli* (see Section 5.1 PHARMACODYNAMIC PROPERTIES - Microbiology).

Gonorrhoea

N. gonorrhoeae (non-penicillinase producing).

Prophylaxis of Endocarditis

Amoxicillin may be used for the prophylaxis of bacterial endocarditis in individuals at particular risk, such as those with a prosthetic heart valve or those who have previously had endocarditis.

4.2 DOSE AND METHOD OF ADMINISTRATION

The following recommended doses are for patients with normal renal function.

Upper Respiratory Tract Infections, Genitourinary Tract Infections, Skin and Soft Tissue Infections

Adults: 250 mg every 8 hours.

Children (under 20 kg): 20 mg/kg/day in equally divided doses every 8 hours.

In severe infections or those caused by less susceptible organisms, 500 mg every 8 hours for adults and 40 mg/kg/day in equally divided doses every 8 hours for children may be needed.

Lower Respiratory Tract Infections

Adults: 500 mg every 8 hours.

Children (under 20 kg): 40 mg/kg/day in equally divided doses every 8 hours.

Urethritis, Gonococcal

Adults: 3 grams as a single dose.

Cases of gonorrhoea with a suspected lesion of syphilis should have darkfield examinations before receiving ALPHAMOX and monthly serological tests for a minimum of four months.

Acute, Uncomplicated Lower Urinary Tract Infections in non-pregnant adult females

Adults: 3 grams as a single dose.

Note: Experience in neonates is too limited to make any recommendations regarding dosage or the appropriateness of the oral route.

The children's dosage is intended for individuals whose weight will not cause dosage to be calculated greater than that recommended for adults. Children weighing more than 20 kg should be dosed according to the adult recommendations.

Renal Impairment

In renal impairment, the excretion of the antibiotic will be delayed, and depending on the degree of impairment, it may be necessary to reduce the total daily dosage.

In patients receiving peritoneal dialysis, the maximum recommended dose is 500 mg/day. Amoxicillin may be removed from the circulation by haemodialysis.

It should be recognised that in the treatment of chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller doses than those recommended above should not be used. In stubborn infections, therapy may be required for several weeks. It may be necessary to continue clinical and/or bacteriological follow-up for several months after cessation of therapy.

Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. It is recommended that there be at least 10 days treatment for any infection caused by haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

Prophylaxis of Endocarditis

Prophylaxis of Endocarditis

Based on the recommendations of the British Society for Antimicrobial Chemotherapy

Condition		Adults' Dosage (including elderly)	Children's Dosage	Notes
Dental Procedures. Prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues and who have not received a penicillin in the previous month. (N.B. Patients with prosthetic heart valves should be referred to hospital- see below).	Patient not having general anaesthetic.	Amoxicillin 3 grams orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.	Under 10 years: Half adult dose. Under 5 years: Quarter adult dose.	*Note 1.* Prophylaxis with alternative antibiotics should be considered if the patient has received a penicillin within the previous month, or is allergic to penicillin. *Note 2:* To minimise pain on injection, amoxicillin should be dissolved in sterile lidocaine 1% solution (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).
	Patient having general anaesthetic: oral antibiotics not appropriate.	Amoxicillin 1 gram IM immediately before induction; with 500 mg orally, 6 hours later.	Under 10 years: Half adult dose.	
Dental Procedures. Patients for whom referral to hospital is recommended: (a) patients to be given a general anaesthetic who have been given a penicillin in the previous month. (b) patients to be given a general anaesthetic who have a prosthetic heart valve. (c) patients who have had one or more attacks of endocarditis.		Initially: Amoxicillin 1 gram IM with 120mg gentamicin IM, immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure. Followed by (6 hours later): amoxicillin 500 mg orally.	Under 10 years: The doses of amoxicillin should be half the adult dose. The dose of gentamicin should be 2mg/kg.	See *Note 2.* *Note 3.* Amoxicillin and gentamicin should not be mixed in the same syringe. *Note 4.* Please consult the appropriate data sheet for full prescribing information on gentamicin
Genito-urinary Surgery or Instrumentation. Prophylaxis for patients who have no urinary tract infection and who are to have genito-urinary surgery or instrumentation under general anaesthesia. *Obstetric and Gynaecological Procedures and Gastro-intestinal Procedures.* Routine prophylaxis is recommended only for patients with prosthetic heart valves.		Initially: Amoxicillin 1 gram IM with 120mg gentamicin IM, immediately before induction. Followed by (6 hours later): amoxicillin 500 mg orally or IM according to clinical condition.	Under 10 years: The doses of amoxicillin should be half the adult dose. The dose of gentamicin should be 2mg/kg.	See *Notes 2, 3* and *4* above.
Surgery or Instrumentation of the Upper Respiratory Tract	Patients other than those with prosthetic heart valves.	Amoxicillin 1 gram IM immediately before induction. Followed by (6 hours later): amoxicillin 500 mg IM.	Under 10 years: Half adult dose.	See *Note 2* above. *Note 5.* The second dose of amoxicillin may be administered orally as syrup.

	Patients with prosthetic heart valves.	Initially: Amoxicillin 1 gram IM with 120mg gentamicin IM, immediately before induction. Followed by (6 hours later): amoxicillin 500 mg IM.	Under 10 years: The dose of amoxicillin should be half the adult dose. The gentamicin dose should be 2mg/kg.	See Notes 2, 3, 4 and 5 above.

4.3 CONTRAINDICATIONS

Amoxicillin is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g. penicillins, cephalosporins).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypersensitivity (anaphylactic) Reactions

Serious, and occasionally fatal, hypersensitivity reactions (including anaphylaxis, anaphylactoid, and severe cutaneous reactions) have been reported in patients receiving beta-lactam antibiotics. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. Before commencing therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, appropriate therapy should be instituted and ALPHAMOX therapy discontinued.

Serious anaphylactic reactions require immediate emergency treatment with adrenaline (epinephrine). Oxygen, intravenous steroids and airway management, including intubation, should also be administered as indicated.

Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)). DIES is an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after administration of amoxicillin) in the absence of allergic skin or respiratory symptoms. Further symptoms could comprise abdominal pain, diarrhoea, hypotension or leucocytosis with neutrophilia. There have been severe cases including progression to shock.

Clostridium difficile Associated Diarrhoea

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including amoxicillin. A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. *Clostridium difficile* associated diarrhoea (CDAD) has been reported with the use of nearly all antibacterial agents and may range in severity from mild diarrhoea to fatal colitis. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately, and the patient investigated further. Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases, appropriate therapy with a suitable oral antibiotic agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

Adequate fluid intake and urinary output must be maintained in patients receiving high doses of amoxicillin.

Oral Anticoagulants

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are

prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Potential for Microbial Overgrowth or Bacterial Resistance

Prolonged use of amoxicillin may occasionally result in overgrowth of non-susceptible organisms.

As with any potent drug, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving Aerobacter, Pseudomonas or Candida), the drug should be discontinued and/or appropriate therapy instituted.

Use in Patients with Mononucleosis

Amoxicillin, an aminopenicillin, is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of which there is a high incidence of rash if amoxicillin is used.

Amoxicillin should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Patients with Lymphatic Leukaemia

Amoxicillin should be given with caution to patients with lymphatic leukaemia, since they are especially susceptible to ampicillin-induced skin rashes.

Patients with Acute Lower Urinary Tract Infection

Following single dose therapy of acute lower urinary tract infections, the urine should be cultured. A positive culture may be evidence of a complicated or upper urinary tract infection and call for a longer or larger course of therapy.

Adequate fluid intake and urinary output must be maintained in patients receiving high doses of amoxicillin.

Use in Renal Impairment

Dosage should be adjusted in patients with renal impairment (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

In patients with reduced urine output, crystalluria (including acute renal injury) has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and Section 4.9 OVERDOSE).

Use in the Elderly

No data available.

Paediatric Use

No data available (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Effects on Laboratory Tests

Oral administration of amoxicillin will result in high urine concentrations of amoxicillin. Since high urine concentrations of amoxicillin may result in false positive reactions when testing for the presence of glucose in urine using Clinitest, Benedict's Solution or Fehling's Solution, it is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix or Testape) be used.

Following administration of ampicillin to pregnant women, a transient decrease in plasma concentration of total conjugated estriol, estriol-glucuronide, conjugated oestrone and estradiol has been noted. This effect may also occur with amoxicillin.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with ALPHAMOX may result in increased and prolonged blood levels of amoxicillin.

The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. Similar reactions can be expected with amoxicillin.

In common with other broad-spectrum antibiotics, amoxicillin may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives.

In the literature, there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin.

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of amoxicillin.

Methotrexate: Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy

Pregnancy category: A

Animal studies with amoxicillin have shown no teratogenic effects. Amoxicillin has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies.

Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Labour and Delivery

Oral ampicillin class antibiotics are generally poorly absorbed during labour. Studies in guinea pigs have shown that intravenous administration of ampicillin decreased the uterine tone, frequency of contractions, height of contractions and duration of contractions. However, it is not known whether the use of amoxicillin in humans during labour or delivery has immediate or delayed adverse effects on the fetus, prolongs the duration of labour or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Use in Lactation

Ampicillin class antibiotics are excreted in the milk; therefore, caution should be exercised when amoxicillin is administered to breastfeeding women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins.

The following adverse reactions have been reported as associated with the use of amoxicillin:

Cardiac disorders

Kounis syndrome: not known.

Infections and infestations

Mucocutaneous candidiasis have been reported very rarely.

Gastrointestinal

Nausea, vomiting, diarrhoea. Intestinal candidiasis and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) have been reported rarely. Black hairy tongue has been reported very rarely (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Drug-induced enterocolitis syndrome: not known (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Skin and subcutaneous tissue disorders

Linear IgA disease: not known.

Hypersensitivity Reactions

Erythematous maculopapular rashes, pruritus and urticaria have been reported occasionally. Rarely, skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and bullous, exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), and symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome) have been reported. As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness, hypersensitivity vasculitis and interstitial nephritis have been reported rarely.

Whenever such reactions occur, ALPHAMOX should be discontinued. (Note: urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids). Anaphylaxis is the most serious reaction experienced (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Hepatic

A moderate rise in AST and/or ALT has occasionally been noted, but the significance of this finding is unknown. As with other beta-lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely.

Haemic and Lymphatic Systems

Reactions such as anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia and leucopenia (including severe neutropenia or agranulocytosis) have been reported during therapy with other penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Prolongation of bleeding time and prothrombin time have also been rarely reported.

Renal and Urinary Tract Disorders

Interstitial nephritis. Crystalluria (including acute renal injury): not known (see Section 4.9 OVERDOSE).

Central Nervous System Effects

CNS effects have been seen rarely. They include aseptic meningitis, hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Miscellaneous

Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident, and symptoms of water/ electrolyte imbalance should be treated symptomatically. During the administration of high doses of amoxicillin, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Amoxicillin can be removed from the circulation by haemodialysis.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Microbiology

Amoxicillin is similar to ampicillin in its bactericidal action against Gram-positive and Gram-negative susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of the cell wall mucopeptide.

Amoxicillin is active in vitro against most strains of *Haemophilus influenzae**, *Neisseria gonorrhoeae**, *Neisseria meningitidis*, *Escherichia coli**, *Proteus mirabilis** and Salmonellae. Because amoxicillin does not resist destruction by penicillinase, it is not active against penicillinase-producing organisms, particularly penicillinase-producing staphylococci.

All strains of *Pseudomonas* species, *Klebsiella* species, *Enterobacter* species, indole-positive *Proteus* species, *Serratia marcescens*, *Citrobacter* species, penicillinase-producing *N. gonorrhoeae* and penicillinase producing *H. influenzae* are resistant.

In vitro studies have demonstrated the susceptibility of most strains of the following gram-positive bacteria: alpha- and beta-haemolytic streptococci, *Diplococcus pneumoniae,* non-penicillinase producing staphylococci and *Streptococcus faecalis*. These organisms are susceptible to amoxicillin at serum concentrations, which

* Activity refers only to beta-lactamase negative strains.

may be expected following the recommended doses. However, some of the organisms were susceptible to amoxicillin only at concentrations achieved in the urine (see Section 4.1 THERAPEUTIC INDICATIONS).

Escherichia coli isolates are becoming increasingly resistant to amoxicillin *in vitro* due to the presence of penicillinase-producing strains.

Strains of gonococci which are relatively resistant to benzylpenicillin may be sensitive to amoxicillin.

The following *in vitro* data are available, but their clinical significance is unknown.

***In vitro* data for amoxicillin vs. clinical pathogens**	
Organism (n)	**MIC90 (mcg/mL)**
S. pneumoniae (3493)[1]	2
H. influenzae (3366)[1]	32
S. pyogenes (683)[1]	0.03
H. influenzae b-lac + (725)[1]	32
H. influenzae b-lac – (2587)[1]	1
Klebsiella pneumonia (1161)[1]	32
M. catarrhalis (864)[1]	16
MSSA (1232)[1]	32
Bacteroides fragilis group (80)[2]	64
Fusobacterium sp (23)[2]	8
Clostridium difficile (21)[2]	2
N. gonorrhoeae (34)[3]	128

[1] Data from the Augmentin Global Surveillance Study: June 1999- December 2000 from USA, Canada, Brazil, Mexico, Hong Kong, Australia, France, Belgium, Italy, Netherlands, Spain, Sweden and the UK.

[2] Data from 1994-1995, France (Dubreuil L et al, 1996. In vitro evaluation of nitazoxanide and tizoxanide against anaerobes and aerobic organisms. Antimicrob Agents Chemother. 40(10), 2266-2270.)

[3] Data from 1994-1995, UK (Wise R et al, 1996. In vitro activity of the tricyclic β-lactam GV104326. Antimicrob Agents Chemother. 40(5), 1248-1253.)

A positive β-lactamase test predicts resistance to penicillin, ampicillin and amoxicillin.

The following are rates of resistance to amoxicillin for common pathogens in Australia.

Rates of resistance to amoxicillin for common pathogens in Australia	
Organism	**Average Resistance (%)**
B. fragilis	100
Enterobacter spp.	96
Klebsiella spp.	98
M. catarrhalis	94
P. aeruginosa	100
S. aureus (methicillin-susceptible)	85
Enterococcus faecalis	0.2

Enterococcus faecium	80
E. coli	45.4
H. influenzae	20.3
P. mirabilis	14
S. pneumoniae	0.6 (fully resistant) 3.2(intermediate resistance)

Breakpoints

Streptococcus pneumoniae: S ≤ -2 mcg/mL; I = 4 mcg/mL; R ≥ 8 mcg/mL

Note: Because amoxicillin has greater *in vitro* activity against *S. pneumoniae* than does ampicillin, the majority of *S. pneumoniae* strains with intermediate susceptibility to ampicillin are fully susceptible to amoxicillin.

Susceptibility Tests

Dilution or Diffusion Techniques

Either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to the alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of the drug can be used. This category also provides a buffer zone, which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections. This information gives only an approximate guidance on probabilities whether organisms will be susceptible to amoxicillin.

Susceptibility to amoxicillin will vary with geography and time and local susceptibility data should be consulted where available and microbiological sampling and susceptibility testing performed where necessary.

Cross-Resistance

Other β-lactams, β-lactam/β-lactamase inhibitor combinations and cephalosporins.

Resistance Mechanisms

Production of penicillinase, altered penicillin binding proteins.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Amoxicillin is stable in the presence of gastric acid and is rapidly and well absorbed after oral administration, even in the presence of food.

Distribution

Amoxicillin diffuses rapidly into most body tissues and fluids, with the exception of brain and spinal fluid except when meninges are inflamed.

Amoxicillin has been shown to diffuse into sputum and saliva and is excreted mainly via the urine where it exists in a high concentration.

The amount to be found in the bile is variable depending on normal biliary secretory function.

Excretion

The half-life of amoxicillin is 61.3 minutes with normal renal function, and in the absence of renal function 16 to 20 hours.

Amoxicillin is excreted in the urine both unchanged and as penicilloic acid. About 75% of a 1 g dose is excreted in the urine in 6 hours in the presence of normal renal function (60% as amoxicillin and 15% as penicilloic acid). However, only 32% of a 3 g dose is excreted via the urine as the biologically active component in 8 hours (by which time most of the urinary excretion is complete). This proportional difference in the amount excreted from the different doses reflects a lack of linearity between doses and extent of absorption with a levelling off at higher doses of oral amoxicillin.

Excretion of amoxicillin can be delayed by concurrent administration of probenecid, thus prolonging its therapeutic effect.

Amoxicillin is not highly protein-bound, being only 17% protein-bound in serum as measured by ultrafiltration or equilibrium dialysis. The average peak serum levels resulting from the oral administration of 250 mg and 500 mg amoxicillin are 5 mcg/mL and 6.6 to 10.8 mcg/mL respectively, occurring one to two hours after administration. Measurable serum levels of amoxicillin are present eight hours after ingestion of a single oral dose.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The capsules contain colloidal anhydrous silica, magnesium stearate, purified talc, sodium lauryl sulfate, and sodium starch glycollate.

ALPHAMOX 250 mg also contains microcrystalline cellulose and Empty Hard Gelatin Capsule Shell Cap - Green Opaque Body - Ivory Opaque Size 2 (ARTG PI No: 12436).

ALPHAMOX 500 mg also contains Empty Hard Gelatin Capsule Shells Cap - Green Opaque Body - Ivory Opaque Size 0el (ARTG PI No: 12361).

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25ºC.

6.5 NATURE AND CONTENTS OF CONTAINER

Container type: blister pack (PVC/PVDC/Al)

Pack sizes: blister pack – 6 (500 mg), 20, 28 (500 mg), 30 capsules

Some strengths, pack sizes and/or pack types may not be marketed.

Australian Register of Therapeutic Goods (ARTG)

AUST R 17678 – ALPHAMOX 250 amoxicillin 250mg (as trihydrate) capsule blister pack

AUST R 17679 – ALPHAMOX 500 amoxicillin 500mg (as trihydrate) capsule blister pack

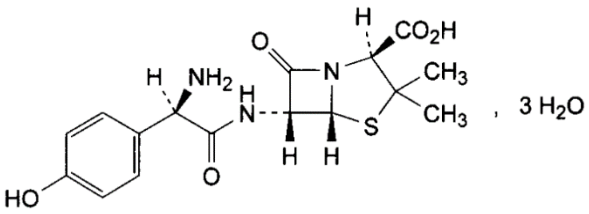
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Amoxicillin trihydrate is a white or almost white, crystalline powder, which is slightly soluble in water and in ethanol (96%) and is practically insoluble in chloroform, in ether, and in fixed oils.

Chemical Structure



Chemical name: (2*S*,5*R*,6*R*)-6-[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

Molecular formula: $C_{16}H_{19}N_3O_5S$, $3H_2O$

Molecular weight: 419.5

CAS Number

61336-70-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

Alphapharm Pty Ltd trading as Viatris

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

www.viatris.com.au

Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

20/09/1991

10 DATE OF REVISION

09/08/2024

Summary Table of Changes

Section Changed	Summary of New Information
All	Minor editorial change
4.8	Added symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome)

ALPHAMOX® is a Viatris company trade mark

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