NEW ZEALAND DATA SHEET

ALPHAMOX

1. Product Name

Alphamox, 250 mg and 500 mg, capsules.

2. Qualitative and Quantitative Composition

Each Alphamox 250 mg capsule contains 250 mg of amoxicillin (as trihydrate)

Each Alphamox 500 mg capsule contains 500 mg of amoxicillin (as trihydrate)

Excipient(s) with known effect:

Microcrystalline cellulose and gelatin

Allergen Declaration:

Contains sulfites.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

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

ALPHAMOX 500 mg Capsules: Size 0 l hard gelatin capsule with ivory body and green cap, filled with almost white granular powder.

4. Clinical Particulars

4.1 Therapeutic indications

Amoxicillin should be used in accordance with local antibiotic-prescribing information guidelines and local susceptibility data.

Amoxicillin may be useful in instituting therapy prior to bacteriology; however bacteriological studies to determine the causative organisms and their sensitivity to Amoxicillin should be performed.

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 (see section 5.1).

Treatment of Infection:

Amoxicillin is indicated in the treatment of infections due to susceptible organisms.

Skin and skin structure:

Staphylococcus, non-penicillinase producing; Streptococcus; E. coli (see section 5.1 – Microbiology).

Respiratory (Acute and Chronic):

H. influenzae; Streptococcus; S. pneumoniae; staphylococcus, non-penicillinase-producing; E.coli (see section 5.1 – Microbiology).

Genitourinary Tract (complicated and uncomplicated, Acute and Chronic):

E.coli (see section 5.1 – Microbiology), P. mirabilis and S. faecalis.

Gonorrhoea:

N. gonorrhoeae (non-penicillinase producing).

Prophylaxis for endocarditis:

Amoxicillin may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis, such as those with a prosthetic heart valve or those who have previously had endocarditis.

4.2 Dose and method of administration

This product is not able to deliver all approved dose regimens.

Normal Renal Function

Upper respiratory tract infections (due to streptococci, pneumococci, non-penicillinase-producing staphylococci and H. influenzae);

Genito-urinary tract infections (due to Escherichia coli, Proteus mirabilis and Strep. faecalis);

Skin and soft tissue infections (due to streptococci, sensitive staphylococci and Escherichia coli):

Adults:

250 mg every 8 hours.

Children

The children's dose 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.

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 (due to streptococci, pneumococci, non-penicillinase producing staphylococci and Haemophilus influenzae):

Adults: 500 mg every 8 hours.

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

Urethritis (due to *Neisseria gonorrhoea*):

Adults: 3 g as a single dose. Cases of gonorrhoea with a suspected lesion of syphilis should have dark field examinations before receiving amoxicillin and monthly serological tests for a minimum of four months.

Acute, uncomplicated lower urinary tract infections (due to *Escherichia coli*, *Proteus mirabilis*, *Strep. Faecalis*, non-penicillinase producing staphylococci) in non-pregnant adult females:

Adults: 3 g as a single dose.

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

Renal impairment:

In renal impairment the excretion of amoxicillin will be delayed. Depending on the degree of impairment, it may be necessary to reduce the total daily dosage. No dosage adjustment is required in patients with a creatinine clearance > 30 mL/min. The maximum recommended dose in patients with creatinine clearance between 10 and 30 mL/min is 500 mg twice a day. The maximum recommended dose in patients with a creatinine clearance < 10 mL/min is 500 mg/day.

Renal impairment in children under 40 kg

- Creatinine clearance > 30 mL/min: No adjustment necessary
- Creatinine clearance 10 – 30 mL/min: 15 mg/kg given twice a day (maximum 500 mg/twice daily)
- Creatinine clearance < 10 mL/min: 15 mg/kg given as a single daily dose (maximum 500 mg)

In the majority of cases, parenteral therapy will be preferred.

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 rheumatic fever or glomerulonephritis.

Prophylaxis of endocarditis:

Based on the recommendations of the British Society for Antimicrobial Chemotherapy.

Conditions		**Adult Dosage (including elderly)**	**Children's Dosage**	**Notes**
Dental Procedures: Prophylaxis for patients undergoing extraction, scaling or surgery involving	Patients not having a general anaesthetic:	3 g amoxicillin 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 penicillin within

Conditions		Adult Dosage (including elderly)	Children's Dosage	Notes
gingival tissues who have not received a penicillin in the previous month: (N.B. Patients with prosthetic heart valves should be referred to hospital – see below)	Patients having a general anaesthetic, oral antibiotics considered to be appropriate:	Initially 3 g orally 4 hours prior to anaesthesia followed by 3 g orally (or 1 g amoxicillin/ampicillin IM if the dose is not tolerated) 6 hours after the initial dose.	Under 10 years: half adult dose. Under 5 years: quarter adult dose.	the previous month or is allergic to penicillin. If prophylaxis with amoxicillin is given twice within one month, emergence of resistant streptococci is unlikely to be a problem. Alternatively, antibiotics are recommended if more frequent prophylaxis is required, or the patient has received a course of treatment with a penicillin during the previous month. Note 2: To minimise pain on injection, amoxicillin should be dissolved in lignocaine 1% solution (see section 4.2).
	Patients having general anaesthesia, oral antibiotics not appropriate:	1 g amoxicillin 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 1 g amoxicillin IM with 120 mg gentamicin IM immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure, followed by 500 mg amoxicillin orally, 6 hours later.	Under 10 years: the dose of amoxicillin should be half the adult dose. The dose of gentamicin should be 2 mg/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.

Conditions		Adult Dosage (including elderly)	Children's Dosage	Notes
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 values.		Initially 1 g amoxicillin IM with 120 mg gentamicin IM immediately before induction. Followed by 500 mg amoxicillin orally or IM, 6 hours later according to clinical condition.	Under 10 years: the dose of amoxicillin should be half the adult dose. The dose of gentamicin should be 2 mg/kg.	See Notes 2, 3 and 4 above.
Surgery or Instrumentation of the Upper Respiratory Tract	Patients other than those with prosthetic heart valves.	1 g amoxicillin IM immediately before induction. Followed by 500 mg IM, 6 hours later.	Under 10 years: half adult dose.	See Note 2 above. Note 5: The second dose of amoxicillin may be administered orally as a syrup.
	Patients with prosthetic heart valves.	1 g amoxicillin IM with 120 mg gentamicin IM immediately before induction. Followed by 500 mg amoxicillin IM, 6 hours later.	Under 10 years: the dose of amoxicillin should be half the adult dose. The dose of gentamicin should be 2 mg/kg.	See Notes 2, 3, 4 and 5 above.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients listed in section 6.1.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Before commencing therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactams. (See sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (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). These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin must be discontinued and appropriate alternative therapy instituted.

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

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

Drug-induced enterocolitis syndrome (DIES)

Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin (see section 4.8). DIES is an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after taking the medicine) 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.

Non-susceptible microorganisms

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.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders) (see section 4.8).

Use in renal impairment

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP, see section 4.8). This reaction requires amoxicillin discontinuation and contra-indicates any subsequent administration.

Infectious mononucleosis

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.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease (see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

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

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 (see section 4.8). *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 suitable oral antibiotic agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Anti-peristaltic medicinal products, e.g. opiates and diphenoxylate with atropine may prolong and /or worsen the condition and should not be used.

Renal, hepatic and haematopoietic function

As with any potent drug, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).The possibility of superinfections and 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.

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 desired level of anticoagulants (see sections 4.5 and 4.8).

Crystalluria

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 sections 4.8 and 4.9).

Lymphatic leukaemia

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

Urinary tract infections

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 the elderly

No data available

Paediatric use

No data available.

Effects on laboratory tests

Oral administration of amoxicillin will result in high urinary 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.

The presence of amoxicillin may distort assay results for oestriol in pregnant women

4.5 Interaction with other medicines and other forms of interaction

Methotrexate

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

Probenecid

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

Allopurinol

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

Tetracyclines

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

Oral anticoagulants (acenocoumarol or warfarin)

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. In the literature there are 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. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Oral contraceptives

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Category A

Animal studies with amoxicillin have shown no teratogenic effects. The product 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.

Use in 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 effects on the foetus, prolongs the duration of labour or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Breastfeeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitisation. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breastfeeding might have to be discontinued. Amoxicillin should only be used during breastfeeding after benefit/risk assessment by the physician in charge.

Fertility

No available data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 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 most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.

The following terminologies have been used in order to classify the occurrence of undesirable effects:
Very common (1/10)
Common (>1/100 to < 1/10)
Uncommon (>1/1,000 to < 1/100)
Rare (>1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (cannot be estimated from the available data)

Infections and Infestations	
Very rare	Mucocutaneous candidiasis
Blood and lymphatic system disorders	
Rare	Reversible thrombocytopenia, thrombocytopenic purpura, haemolytic anaemia, eosinophilia and. leucopenia (including severe neutropenia or agranulocytosis). Prolongation of bleeding time and prothrombin (see section 4.4)
Immune system disorders	
Very rare	Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4)
Not known	Jarisch-Herxheimer reaction (see section 4.4)

Nervous system disorders	
Rare	Aseptic meningitis, hyperkinesia, dizziness and convulsions (see section 4.4).
Cardiac disorders	
Not known	Kounis syndrome
Gastrointestinal disorders	
Clinical Trial Data	
*Common	Diarrhoea and nausea
*Uncommon	Vomiting
Post-marketing data	
Rare	Intestinal candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis) (see section 4.4). Superficial tooth discolouration#
Very Rare	Black hairy tongue
Not known	Drug-induced enterocolitis syndrome
Hepato-biliary disorders	
Rare	Hepatitis and cholestatic jaundice
Very Rare	A moderate rise in AST and/or ALT
Skin and subcutaneous tissue disorders	
Clinical Trial Data	
*Common	Erythematous maculopapular rash, skin rash
*Uncommon	Urticaria and pruritus
Post-Marketing Data	
Rare	Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP) (see section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS).
Not known	Linear IgA disease
Renal and urinary tract disorders	
Very rare	Interstitial nephritis, crystalluria (including acute renal injury) (see sections 4.4 and 4.9)

*The incidence of these adverse effects was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.
#Superficial tooth discolouration in children has been reported rarely. Good oral hygiene may help prevent tooth discolouration as it can be removed by brushing.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms

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 sections 4.4). Convulsions may occur in patients with impaired renal function or in those receiving high doses (see sections 4.4 and 4.8).

Treatment

Gastrointestinal symptoms may be treated symptomatically, with attention to the water electrolyte balance.

Amoxicillin can be removed from the circulation by haemodialysis.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Penicillins with extended spectrum.

ATC code: J01CA04

Mechanism of action

Amoxicillin is similar to ampicillin in its bactericidal action against Gram-positive and Gram-negative susceptible organisms during the state of active multiplication. Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

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 no 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 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).

*Activity refers only to beta-lactamase negative strains.

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

Stains 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

Organism (n)	MIC90 (mcg/mL)
H. influenzae (3366)[1]	32
S. pyogenes (683)[1]	0.003
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 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 (Dubreuill 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.

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

Organism	Average % resistance
P. mirabilis	14
P. 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 Test

Dilution or diffusion techniques – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardisation 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 in 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 alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in the body sites where the drug is physiologically concentrated or in situations where high dosage of 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 concentration 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 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.

Elimination

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

Amoxicillin is excreted in the urine both unchanged and as penicilloic acid. About 75% of a 1g dose is excreted in the urine in 6 hours in the presence of normal renal function (60% is biologically active and 15% is penicilloic acid). However, about 32% of a 3g 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 the extent of absorption with a levelling off at higher doses or 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.

Orally administered doses of 250 mg and 500 mg amoxicillin result in average peak serum levels one to two hours after administration of 5.0 mcg/mL and 6.6-10.8 mcg/mL respectively. Detectable serum levels of amoxicillin are present 8 hours after ingestion of a single dose.

5.3 Preclinical safety data

Genotoxicity

No data available

Carcinogenicity

No data available.

6. Pharmaceutical Particulars

6.1 List of excipients

Alphamox 250 and 500 capsules also contain:

- purified talc
- magnesium stearate
- sodium starch glycollate
- gelatin
- yellow iron oxide
- titanium dioxide
- brilliant blue
- microcrystalline cellulose (250 mg capsule only)
- colloidal anhydrous silica (500 mg capsule only)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Al/PVC/PVdC blister packs. Pack sizes of 30 or 500 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

23 May 1985

10. Date of Revision of the Text

04 December 2023

Summary table of changes

Section	Summary of new information
4.1, 4.4, 4.5, 4.8, 5.2, 8	Minor Editorial Changes
2	Inclusion of information: Excipient(s) with known effect and allergen declaration
4.4	Updated information on: • hypersensitivity reactions, • overgrowth of non-susceptible microorganisms, • renal, hepatic and haematopoietic function • effects on laboratory tests
4.5	Updated information on Oral anticoagulants (acenocoumarol or warfarin)
4.6	Updated information on: • Breastfeeding • Fertility
4.8	Added information on the most commonly reported ADRs. Added some frequencies to ADRs previously reported. Added additional ADRS: • Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis. • correction of anaemia to haemolytic anaemia • addition of skin rash • removal of duplicate information already in section 4.4 on convulsions in patients with impaired renal function or in those receiving high doses • removal of duplicate information ‘Severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness, hypersensitivity vasculitis” from the Skin and subcutaneous tissue disorders SOC as these are listed in the Immune system disorders SOC. • removal of duplicate information 'interstitial nephritis' from the Skin and subcutaneous tissue disorders SOC as it is listed under the Renal and urinary tract disorders SOC. • removal of obsolete note. Updated reporting URL in section 4.8 to https://pophealth.my.site.com/carmreportnz/s/.
4.9	Added information to Overdose symptoms on convulsions in patients with impaired renal function or those receiving high doses.

10	Update date of revision of text