NEW ZEALAND DATA SHEET

ALPHAMOX 125 AND 250

1. Product Name

Alphamox, 125 mg/5 mL & 250 mg/5 mL, powder for oral suspension

2. Qualitative and Quantitative Composition

Each powder for oral suspension contains 125 mg or 250 mg of amoxicillin (as trihydrate) per 5 mL when reconstituted.

Excipients with known effect:
Contains aspartame, benzoates, and sorbitol.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

ALPHAMOX 125 powder for suspension: White to off-white free-flowing powder with odour of raspberry. When reconstituted it readily produces a white to cream coloured completely homogeneous suspension. Each bottle of ALPHAMOX 125 powder for suspension contains 125 mg/5 mL of amoxicillin when reconstituted.

ALPHAMOX 250 powder for suspension: White to off-white free-flowing powder with odour of raspberry. When reconstituted it readily produces a white to cream coloured completely homogeneous suspension. Each bottle of ALPHAMOX 250 powder for suspension contains 250 mg/5 mL of amoxicillin when reconstituted.

For reconstitution instructions please refer to the Pharmaceutical Precautions section of this data sheet.

4. Clinical Particulars

4.1 Therapeutic indications

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

Treatment of Infection: ALPHAMOX is indicated in the treatment of infections due to susceptible organisms.

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

Prophylaxis for endocarditis: ALPHAMOX may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.

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).

4.2 Dose and method of administration

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 (under 20 kg): 25 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 50 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): 50 mg/kg/day in equally divided doses every 8 hours.

High dosage therapy (maximum recommended oral dosage 6 g daily in divided doses). An adult dosage of 3 g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Prophylaxis of endocarditis - dental procedures

Prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues who have not received a penicillin in the previous month:

NOTE: Patients with prosthetic heart valves should be referred to hospital (see below).

1. Patient not having a general anaesthetic:
   Adults: 3 g ALPHAMOX orally, 1 hour before procedure. A second dose may be given 6 hours later if considered necessary.
   Children under 10: half adult dose.
   Children under 5: quarter adult dose.

2. Patients having a general anaesthetic, oral antibiotics considered to be appropriate:
   Adults: 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.
   Children under 10: half adult dose.
   Children under 5: quarter adult dose.

3. Patient having general anaesthesia, oral antibiotics not appropriate:
   Adults: 1 g amoxicillin IM immediately before induction with 500 mg orally 6 hours later.
   Children under 10: half adult dose.

NOTE: 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.

Patients for whom referral to hospital is recommended:

- Patients to be given a general anaesthetic who have been given a penicillin in the previous month.
- Patients to be given a general anaesthetic who have a prosthetic heart valve.
- Patients who have had one or more attacks of endocarditis.

Adults: Initially 1 g amoxicillin/ampicillin with 120 mg gentamicin IM immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure, followed by 500 mg ALPHAMOX orally, 6 hours later.

Children under 10: the dose of amoxicillin should be half the adult dose. The dose of gentamicin should be 2 mg/kg.

NOTE: Amoxicillin and gentamicin should not be mixed in the same syringe. Please consult the appropriate Data Sheet for parenteral amoxicillin and gentamicin.

Urethritis (due to Neisseria gonorrhoeae):

Adults: 3 g as a single dose. Cases of gonorrhoea with a suspected lesion of syphilis should have dark field examinations before receiving ALPHAMOX 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):

Adults: 3 g as a single dose.

NOTE: 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.

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.

Impaired renal function

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.

Patients receiving haemodialysis

Amoxicillin may be removed from the circulation by haemodialysis.

For adults and children over 40 kg, the dose is 500 mg every 24 hours. Prior to haemodialysis, one additional dose of 500 mg should be administered. In order to restore circulating drug levels, another dose of 500 mg should be administered after haemodialysis.

For children under 40 kg, the dose is 15 mg/kg/day given as single daily dose (maximum 500 mg). Prior to haemodialysis one additional dose of 15 mg/kg should be administered. In order to restore circulating drug levels, another dose of 15 mg/kg should be administered after haemodialysis.

Patients receiving peritoneal dialysis

The maximum recommended dose 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 a day).
- 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.

4.3 Contraindications

Amoxicillin is contraindicated in patients who have had previous experience of a severe immediate anaphylaxis to a cephalosporin, penicillin or another beta-lactam agent (e.g. a carbopenem or monobactam).

Hypersensitivity to the active substance, to any of the penicillin or to any of the excipients in ALPHAMOX (see section 6.1).

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Amoxicillin should be given with caution to patients who have experienced symptoms of allergy associated with a cephalosporin or penicillin.

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphaloctoid and severe cutaneous reactions) have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic patients. If an allergic reaction occurs, amoxicillin therapy must be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation, may also be required. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8).

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin (see section 5.1). This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

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).

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.

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.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).

Overgrowth of non-susceptible microorganisms

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

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life-threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or, subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a physician consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation.

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.

Anticoagulants

Prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain desired level of anticoagulation (see section 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 4.5, 4.8 and 4.9).

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

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

Hypokalemia and hypernatremia

Massive doses of amoxicillin can cause hypokalaemia and sometimes hypernatraemia. Use of a potassium-sparing diuretic may be helpful. In patients undergoing high-dose treatment for more than 5 days, electrolyte balance, blood counts and renal functions should be monitored.

Important information about excipients

ALPHAMOX suspension contains aspartame, which is a source of phenylalanine, and should be used with caution in patients with phenylketonuria, a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

ALPHAMOX suspensions contain sodium benzoate (E211) which is a mild irritant to the eyes, skin and mucous membrane. May increase the risk of jaundice in newborn babies (up to 4 weeks old).

ALPHAMOX suspension contains maltodextrin (glucose). Patients with rare glucose-galactose malabsorption should not take this medicine.

ALPHAMOX suspension contains sorbitol. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

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

Allopurinol

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Tetracyclines

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

Laboratory and diagnostic tests

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

Penicillins may interfere with:

- Urinary glucose test
- Coomb’s test
- Tests for urinary or serum proteins
- Tests which use bacteria e.g. Guthrie test.

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.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, 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).

Methotrexate

Penicillins reduce the excretion of methotrexate thereby increasing the risk of methotrexate toxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Limited data on the use of amoxicillin during pregnancy in humans do not indicate an increased risk of congenital malformations. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Breast-feeding

Trace quantities of amoxicillin can be detected in breast milk with the potential for hypersensitivity reactions (e.g. drug rashes) or gastrointestinal disorders (e.g. diarrhoea) or fungal mucous membrane infections (candidosis) in the breast-fed infant. Consequently, breast-feeding might have to be discontinued. Amoxicillin should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

Fertility

There are no 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

During treatment with amoxicillin, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions) which may influence the ability to drive and use machines (see section 4.8). Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

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 to classify the occurrence of undesirable effects:

Very common (≥ 1/10),

Common (≥ 1/100 to ≤ 1/10)

Uncommon (≥ 1/1000 to ≤ 1/100)

Rare (≥ 1/10,000 to ≤ 1/1000)

Very rare (< 1/10,000)

Not known (cannot be estimated from the available data).

The majority of the side-effects listed below are not unique to amoxicillin and may occur when using other penicillins.

Unless otherwise stated, the frequency of adverse events (AE's) has been derived from more than 30 years of post-marketing reports.

Blood and lymphatic system disorders

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.
Prolongation of bleeding time and prothrombin time (see section 4.4).

Cardiac disorders

Not known: Kounis syndrome

Immune system disorders

Very rare: Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4).

Not known Jarish-Herxheimer reaction (see section 4.4)

Nervous system disorders

Very rare: Hyperkinesia, dizziness and convulsions (see section 4.4).

Not known: Aseptic meningitis

Infections and Infestations

Very rare: Mucocutaneous candidiasis

Gastrointestinal disorders

Clinical trial data

*Common: Diarrhoea and nausea

*Uncommon: Vomiting

Post-marketing data

Very rare: Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis (see section 4.4).

Black hairy tongue.

Superficial tooth discolouration#

Not known: Drug-induced enterocolitis syndrome

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT.

Skin and subcutaneous tissue disorders

Clinical Trial data

*Common: Skin rash.

*Uncommon: Urticaria and pruritus.

Post marketing data

Very 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, Symmetrical Drug Related Intertriginous and Flexural Exanthema (SDRIFE) (baboon syndrome).

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 AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

Superficial tooth discolouration has been reported in children. Good oral hygiene may help to 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 and signs of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses (see sections 4.4 and 4.8).

Treatment of intoxication

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 a semi-synthetic 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 susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Pharmacokinetic/pharmacodynamic effects

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

• Inactivation by bacterial beta-lactamases.

• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 5.0.

Organism	**MIC breakpoint (mg/L)**	
	Susceptible ≤	**Resistant >**
Enterobacteriaceae	8[1]	8
Staphylococcus spp.	Note[2]	Note[2]
Enterococcus spp.[3]	4	8
Streptococcus groups A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	Note[5]	Note[5]
Viridans group steprococci	0.5	2
Haemophilus influenzae	2[6]	2[6]
Moraxella catarrhalis	Note[7]	Note[7]
Neisseria meningitidis	0.125	1
Gram positive anaerobes except *Clostridium difficile*[8]	4	8
Gram negative anaerobes[8]	0.5	2
Helicobacter pylori	0.125[9]	0.125[9]
Pasteurella multocida	1	1
Non- species related breakpoints[10]	2	8
[1]Wild type Enterobacteriaceae are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild type isolates of *E. coli* and *P. mirabilis* as intermediate. When this is the case, use the MIC breakpoint S ≤ 0.5 mg/L		

[2]Most staphylococci are penicillinase producers, which are resistant to amoxicillin. Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.

[3]Susceptibility to amoxicillin can be inferred from ampicillin

[4]The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility.

[5]Breakpoints relate only to non-meningitis isolates. For isolates categorised as intermediate to ampicillin avoid oral treatment with amoxicillin. Susceptibility inferred from the MIC of ampicillin.

[6]Breakpoints are based on intravenous administration. Beta-lactamase positive isolates should be reported resistant.

[7]Beta lactamase producers should be reported resistant

[8]Susceptibility to amoxicillin can be inferred from benzylpenicillin.

[9]The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.

[10]The non-species related breakpoints are based on doses of at least 0.5 g x 3 or 4 doses daily (1.5 to 2 g/day).

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

In vitro susceptibility of micro-organisms to amoxicillin

Commonly susceptible species

Gram-positive aerobes:

Enterococcus faecalis
Beta-hemolytic streptococci (Groups A, B. C and G)
Listeria monocytogenes

Gram-negative aerobes:

Bordetella pertussis

Other:

Leptospira icterohaemorrhagiae
Treponema pallidum

Species for which acquired resistance may be a problem

Gram-negative aerobes:

Escherichia coli
Haemophilus influenzae
Helicobacter pylori
Proteus mirabilis
Salmonella typhi
Salmonella paratyphi
Pasteurella multocida

Gram-positive aerobes: Coagulase negative staphylococcus *Staphylococcus aureus*[#] *Streptococcus pneumoniae* Viridans group streptococcus
Gram-positive anaerobes: *Clostridium* spp.
Gram-negative anaerobes: *Fusobacterium* spp.
Other: *Borrelia burgdorferi*
Inherently resistant organisms[†]
Gram-positive aerobes: *Enterococcus faecium*[†]
Gram-negative aerobes: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp. *Pseudomonas* spp.
Gram-negative anaerobes: *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).
Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.
† Natural intermediate susceptibility in the absence of acquired mechanism of resistance. #Almost all *S.aureus* are resistant to amoxilcillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin is approximately 70% bioavailable. The time to peak plasma concentration (T_{max}) is approximately one hour.

The pharmacokinetic results for a study, in which an amoxicillin dose of 250 mg three times daily was administered in the fasting state to groups of healthy volunteers are presented below.

C_{max}	T_{max}*	$AUC_{(0-24h)}$	T½
Microgram/ml (µg/mL)	(h)	Microgram.h/ml (µg.h/mL)	(h)
33 ± 1.12	1.5 (1.0-2.0)	26.7 ± 4.56	1.36 ± 0.56
*Median (range)			

In the range 250 to 3000 mg the bioavailability is linear in proportion to dose (measured as C_{max} and AUC). The absorption is not influenced by simultaneous food intake.

Haemodialysis can be used for elimination of amoxicillin.

Distribution

About 18% of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0.3 to 0.4 l/kg.

Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle, tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is no evidence for significant tissue retention of drug-derived material. Amoxicillin, like most penicillins, can be detected in breast milk (see section 4.6).

Amoxicillin has been shown to cross the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose.

Elimination

The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70% of amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a single 250 mg or 500 mg dose of amoxicillin. Various studies have found the urinary excretion to be 50-85% for amoxicillin over a 24 hour period.

Concomitant use of probenecid delays amoxicillin excretion (see section 4.5).

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender

Following oral administration of amoxicillin/ to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of amoxicillin.

Renal impairment

The total serum clearance of amoxicillin decreases proportionately with decreasing renal function (see sections 4.2 and 4.4).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

Carcinogenicity studies have not been conducted with amoxicillin.

6. Pharmaceutical Particulars

6.1 List of excipients

ALPHAMOX suspension contains:

- Propylene glycol alginate
- Sodium benzoate
- Aspartame
- Sodium citrate dihydrate
- Disodium edetate
- Colloidal anhydrous silica
- Sorbitol
- Maltodextrin
- Propylene glycol
- Starch
- Natural flavouring

Contains aspartame, benzoates and sorbitol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

ALPHAMOX powders for suspension should be stored in a dry place below 25°C. Protect from light.

Once reconstituted, ALPHAMOX suspensions should be stored under refrigeration between 2-8°C and used within 14 days. Any remaining suspension should be discarded.

All presentations should be kept out of reach of children.

6.5 Nature and contents of container

PP bottle with child resistant closure, pack size of 100mL.

Each bottle of ALPHAMOX 125 powder for suspension contains 125 mg/5 mL of amoxicillin when reconstituted.

Each bottle of ALPHAMOX 250 powder for suspension contains 250 mg/5 mL of amoxicillin when reconstituted.

6.6 Special precautions for disposal and other handling

Reconstitution Instructions

125 mg/5 mL: Add 90 mL of purified water to make up to 100 mL
250 mg/5 mL: Add 80 mL of purified water to make up to 100 mL

Close container and shake vigorously for 15 seconds immediately to make up the suspension. Shake vigorously for 15 seconds before each use to reconstitute the suspension.

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

02 October 2014

10. Date of Revision of the Text

12 August 2024

Section	
4.8	Added ADR Symmetrical Drug Related Intertriginous and Flexural Exanthema (SDRIFE) (baboon syndrome).