**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)

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.

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

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.

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.

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*

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

**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. Patients not having a general anaesthetic:***

Adults: 3 g amoxicillin 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. Patients 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 amoxicillin 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 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):

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.

#### *Special populations*

**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.

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

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.

## *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 initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins. (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse 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 individuals. If an allergic reaction occurs, amoxicillin must be discontinued and appropriate alternative therapy instituted.

### 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.

### 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.

### 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).

### Anticoagulants

Prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin. 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 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).

### 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.

## *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 of probenecid 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..

### 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 may reduce the excretion of methotrexate causing a potential increase in 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

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 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*

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*

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 ( ≥ 1/1000 to < 1/100)
Rare ( ≥ 1/10,000 to < 1/1000)
Very rare ( < 1/10,000).

Not known (cannot be estimated from the available data)

### Infections and Infestations

Very rare: Mucocutaneous candidiasis.

### 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).

### 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

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

### 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.

### 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).

### Renal and urinary tract disorders

Very rare: Interstitial nephritis, crystalluria (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.

#### 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://nzphvc.otago.ac.nz/reporting/.

## *4.9 Overdose*

### Symptoms and signs of overdosage

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of fluid and electrolyte balance 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 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 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 relationship

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 streptococci | 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 3or 4 doses daily (1.5 to 2 g/day).

The prevalence of resistance may vary geographically and with time 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*<br>Beta-hemolytic streptococci (Groups A, B, C and G)<br>*Listeria monocytogenes* |
| **Species for which acquired resistance may be a problem** |
| ***Gram-negative aerobes:*** |

| |
|---|
| *Escherichia coli*<br>*Haemophilus influenzae*<br>*Helicobacter pylori*<br>*Proteus mirabilis*<br>*Salmonella* typhi<br>*Salmonella* paratyphi.<br>*Pasteurella multocida* |
| ***Gram-positive aerobes:***<br>Coagulase negative staphylococcus<br>*Staphylococcus aureus* [£]<br>*Streptococcus pneumoniae*<br>Viridans group streptococcus |
| ***Gram-positive anaerobes:***<br>*Clostridium* spp. |
| ***Gram-negative anaerobes:***<br>*Fusobacterium* spp. |
| ***Other:***<br>*Borrelia burgdorferi* |
| **Inherently resistant organisms[†]** |
| ***Gram-positive aerobes:***<br>*Enterococcus faecium* [†] |
| ***Gram-negative aerobes:***<br>*Acinetobacter* spp.<br>*Enterobacter* spp.<br>*Klebsiella* spp.<br>*Pseudomonas* spp. |
| ***Gram-negative anaerobes:***<br>*Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant). |
| ***Others:***<br>*Chlamydia* spp.<br>*Mycoplasma* spp.<br>*Legionella* spp. |
| [†] Natural intermediate susceptibility in the absence of acquired mechanism of resistance.<br><br>[£] Almost all *S.aureus* are resistant to amoxicillin 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) | (h) | (microgram.h/mL) | (h) |
| 3.3 ± 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 0.4L/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 25L/hour in healthy subjects. Approximately 60 to 70% of the 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.

Concurrent 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 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)
- Collodial anhydrous silica (500 mg capsule only)

Alphamox 250 and 500 capsules are lactose and gluten free

## *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*

Alphamox 250 and 500 are available in Al/PVC/PVdC blister packs of 30 and 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

Mylan New Zealand Ltd
PO Box 11183
Ellerslie
AUCKLAND
Telephone 09-579-2792

# 9. Date of First Approval

23 May 1985

# 10. Date of Revision of the Text

27 June 2019

**Summary table of changes**

| Section | Summary of new information |
|---|---|
| All | Revise to SPC format |
| 4.3 | Expansion of hypersensitivity details |
| 4.4 | Added warnings on non-susceptible microorganisms, convulsions, renal impairment, skin reactions, Jaresch-Herxheimer reaction, overgrowth of non-susceptible organisms, prolonged therapy and interference with diagnostic tests |
| 4.5 | Expanded current interaction information and added methotrexate |
| 4.6 | Revised wording |
| 4.7 | Revised wording |
| 4.8 | Added Jaresch-Herxheimer reaction and DRESS |
| 4.9 | Revised wording |
| 5.1 | Additional pharmacodynamic information provided |
| 5.2 | Additional pharmacokinetic information provided |