

APO-AMOXI

1. PRODUCT NAME

Apo-Amoxi (250mg, 500mg capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains amoxicillin trihydrate equivalent to 250mg of amoxicillin, and typically weighs 376mg.

Each capsule contains amoxicillin trihydrate equivalent to 500mg of amoxicillin, and typically weighs 735mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

APO-AMOXI 250mg capsules are red and gold (size 2 capsules), imprinted 'APO 250'.

APO-AMOXI 500mg capsules are red and gold (size 0 capsules), imprinted 'APO 500'.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of infection

APO-AMOXI is indicated in the treatment of infections due to susceptible organisms.

APO-AMOXI 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

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

4.2 Dose and method of administration

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

Upper respiratory tract infections, Genito-urinary tract infections, skin and soft tissue infections

For upper respiratory tract infections due to streptococci, pneumococci, non-penicillinase-producing staphylococci and *H. influenzae*) or Genito-Urinary Tract Infections (due to *Escherichia coli*, *Proteus mirabilis* and *Streptococcus faecalis* or 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.

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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

For lower respiratory tract infections (due to streptococci, pneumococci, non-penicillinase producing staphylococci and *H. 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

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

Patient not having a general anaesthetic

Adults – 3 g orally, 1 hour before procedure. A second dose may be given 6 hours later if considered necessary. Children under 10 - half the adult dose. Children under 5 - quarter adult dose.

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.

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 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 gonorrhoeae*)

Adults: 3 g as 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.

Lower urinary tract infections

For acute, uncomplicated lower urinary tract infections (due to *Escherichia coli*, *Proteus mirabilis*, *Streptococcus 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 duration

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 daily. 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 to 30 ml/min: 15 mg/kg give twice daily (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.

Administration

Amoxicillin capsules should be taken with a glass of water.

4.3 Contraindications

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients.

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

Warnings

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented. Patients should be told about the potential occurrence of allergic reactions and instructed to report them. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate alternative therapy instituted.

If allergic reactions occur, the drug should be discontinued and the usual treatment with adrenaline, antihistamines and corticosteroids should be instituted, as necessary.

Oxygen, intravenous steroids and airway management, including intubation, may also be required.

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. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Amoxicillin should be given with caution to patients with lymphatic leukaemia as they are susceptible to amoxicillin induced skin rashes. Amoxicillin should not be used for the treatment of bacterial infections in patients with viral infections, presenting with sore throat, pharyngitis or infectious mononucleosis, as a high incidence of amoxicillin induced erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.

As with any potent drug, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. The possibility of superinfection with mycotic or bacterial pathogens should be particularly considered. If superinfection occurs (usually involving *Aerobacter*, *Pseudomonas* or *Candida*) discontinue amoxicillin and/or initiate appropriate therapy.

Pseudomembranous colitis should be borne in mind if severe persistent diarrhoea occurs (in most cases caused by *Clostridium difficile*). If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further. Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis eg. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the conditions and should not be used.

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Abnormal prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulation treatment is prescribed concurrently and the dose of the anticoagulant adjusted as necessary.

At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Precaution should be taken in premature children and during neonatal period: renal, hepatic and haematological functions should be monitored.

As with other beta-lactams, the blood formula should be checked regularly during high-dose therapy. Elevated liver enzymes and changes in blood counts have been reported.

High dose therapy with beta-lactams for patients with renal insufficiency or seizures history, treated epilepsy and meningeal affection, could exceptionally lead to seizures. Dosage should be adjusted in patient with renal impairments (see section 4.2).

The occurrence of a generalized erythema with fever and pustules at the beginning of treatment should make suspect a generalized acute exanthematic pustulosis; this necessitates the interruption of therapy and contraindicated any further administration of amoxicillin.

Precautions

Dosage should be adjusted in patients with renal impairment (refer to section 4.2 Dose and method of administration).

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 higher dose or prolonged course of treatment may be appropriate.

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

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 (refer to section 4.9 Overdose). The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals.

Patients suffering from severe gastrointestinal disturbances with diarrhoea and vomiting should not be treated with amoxicillin, due to the risk of reduced absorption. In these cases a parenteral treatment with amoxicillin is advisable.

Jarisch-Herxheimer reaction: The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease. 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.

Amoxicillin should be used with caution in patients with allergic diathesis and asthma.

Precautions should be taken for children, premature infants and during the neonatal period, renal, hepatic and haematological functions should be monitored.

4.5 Interaction with other medicines and other forms of interaction

Medicines and other pharmacologically active substances

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

Concomitant administration of amoxicillin and anticoagulants, such as coumarin, may increase the incidence of bleeding due to prolongation of prothrombin time.

If coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with addition or withdrawal of amoxicillin. A large number of cases showing an increase of oral anticoagulant activity has been reported in patients receiving antibiotics. The infectious and inflammatory context, age and the general status of the patient appear as risk factors. In these circumstances, it is difficult to know the part of the responsibility between the infectious disease and its treatment in the occurrence of INR disorders. However, some classes of antibiotics are more involved, notably fluoroquinolones, macrolides, cyclines, cotrimoxazole and some cephalosporins

There is a possibility that the bactericidal action of amoxicillin could be antagonised on co-administration with bacteriostatic agents such as macrolides, tetracyclines, sulphonamides or chloramphenicol.

An increase in the absorption of digoxin is possible on concurrent administration with amoxicillin. A dose adjustment of digoxin may be necessary.

Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

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.

Administration of amoxicillin can transiently decrease the plasma level of estrogens and progesterone, and may reduce the efficacy of oral contraceptives. It is therefore recommended to take supplemental non-hormonal contraceptive measures.

Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxicillin.

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.

The occurrence of diarrhoea may impair the absorption of other medicines consequently limiting their efficacy.

Amoxicillin may decrease the amount of urinary estriol in pregnant women.

At high concentrations, amoxicillin may diminish the results of serum glycaemia levels

Amoxicillin may interfere with protein testing when colorimetric methods are used

Abnormal laboratory test results

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

Amoxicillin may interfere with protein testing when colorimetric methods are used.

4.6 Fertility, pregnancy and lactation

Fertility

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

Use in Pregnancy

Category A

Assigned Category A by the Australian Drug Evaluation Committee. This category includes medicines which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

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 and duration of contractions. However, it is not known whether the use of amoxicillin in humans during labour or delivery has immediate or delayed adverse effects on the 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.

Use in lactation

Residual amoxicillin may be present in breast milk at levels corresponding to approximately 0.7% of the maternal dose. Penicillins are considered to be compatible with breastfeeding although there are theoretical risks of alterations to infant bowel flora and allergic sensitisation. So far no detrimental effects for the breast-fed infant have been reported after taking amoxicillin. Amoxicillin can be used during breast-feeding. However, breast-feeding must be stopped if gastrointestinal disorders (diarrhoea, candidosis or skin rash) occur in the new born.

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

Side-effects, as with other penicillins, are uncommon and mainly of a mild and transitory nature. The majority of the side-effects listed below are not unique to amoxicillin and may occur when using other penicillins.

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

Undesirable effects are classified systematically and by frequency according to the following convention: very common (above 1 in 10); common (from 1 in 100 to 1 in 10); uncommon (from 1 in 1000 to 1 in 100); rare (from 1 in 10,000 to 1 in 1,000); very rare (below 1 in 10,000).

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

Haemic and the lymphatic system disorders

Very rare

Reactions such as anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia and leucopenia (including severe neutropenia or agranulocytosis), have been reported during therapy with other penicillins. All were reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Prolongation of bleeding time and prothrombin time have also been reported rarely (refer to section 4.4 Special warnings and precautions for use).

Immune system disorders

Very rare

As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis (refer to section 4.4 Special warnings and precautions for use), serum sickness and allergic vasculitis. If a hypersensitivity reaction is reported, the treatment must be discontinued. (see also Skin and subcutaneous tissue disorders).

Infections and infestations

Uncommon

Prolonged and repeated use of the preparation can result in superinfections and colonisation with resistant organisms or yeasts such as oral and vaginal candidiasis.

Gastrointestinal disorders

Common

Gastric complaints, nausea, loss of appetite, flatulence, soft stools, diarrhoea, enanthemas (particularly in the region of the mouth), dry mouth, taste disturbances. These effects on the gastrointestinal system are mostly mild and frequently disappear either during the treatment or very soon after completion of therapy. The occurrence of these side effects can generally be reduced by taking amoxicillin during meals.

Uncommon

Vomiting.

Rare

Superficial discoloration of the teeth (especially if an oral suspension is used). Usually the discoloration can be removed by teeth brushing.

Very rare

Mucocutaneous candidiasis. Antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis. If severe and persistent diarrhoea occurs, the very rare possibility of pseudomembranous colitis should be considered. The administration of anti-peristaltic agents is contraindicated.

Development of a black hairy tongue.

General disorders and administration site conditions**Rare**

Drug fever

Hepatobiliary disorders**Rare**

Hepatitis and cholestatic jaundice.

Uncommon

Moderate and transient increase of liver enzymes. The significance of a rise in liver enzymes is unclear

Nervous system disorders**Rare**

Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function, epilepsy meningitis, or in those receiving high doses.

Skin and subcutaneous tissue disorders**Common**

Cutaneous reactions such as exanthema, pruritus, urticaria, erythematous maculopapular rash; the typical morbilliform exanthema occurs 5 to 11 days after commencement of therapy. The immediate appearance of urticaria indicates an allergic reaction to amoxicillin and therapy should therefore be discontinued.

Rare

Skin reactions such as Angioneurotic oedema (Quincke's oedema), erythema multiforme exudativum, exsudativum, acute generalized pustulosis, Lyell's syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP) and Jarisch-Herxheimer reaction (see also Immune system disorders).

Renal and urinary tract disorders**Rare**

Interstitial nephritis, crystalluria (refer to section 4.9 Overdose)

The incidence of these adverse events was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

Miscellaneous

Very rare

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

Reporting 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

Signs and symptoms

Cases of overdose with amoxicillin are usually asymptomatic. Gastrointestinal disturbances such as nausea, vomiting and diarrhoea and symptoms of fluid-electrolyte imbalance may be evident. In patients with severely impaired renal function, large overdoses can result in signs of renal toxicity and crystalluria is possible. During the administration of high doses of amoxicillin, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Management

There is no specific antidote for an overdose of amoxicillin. Treatment consists primarily of administration of activated charcoal (a gastric lavage is usually not necessary), or symptomatic and supportive measures. Particular attention should be directed to the water and electrolyte balance of the patient. Amoxicillin can be removed from the circulation by haemodialysis.

For advice on the management of overdose, please contact the National Poisons Centre on 0800 POISON (0800 764766).

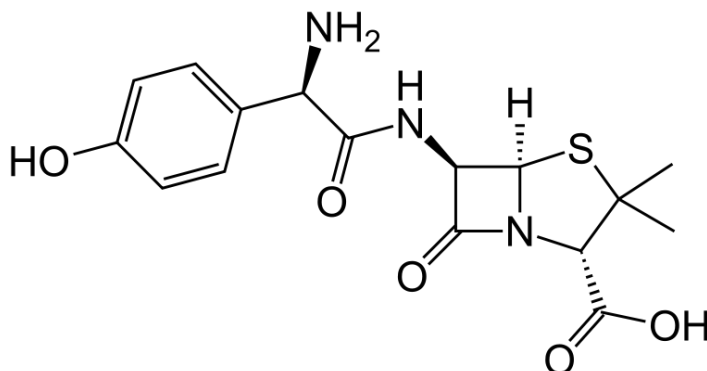
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

J01CA04 – Penicillins with extended spectrum, amoxicillin.

Chemical structure:



Mechanism of action

Beta-lactam antibiotic.

Pharmacodynamic effects

Inhibition of bacterial cell wall synthesis.

Antibiotic class

Amoxicillin is a semi-synthetic aminopenicillin of the beta-lactam group of antibiotics.

Antibiotic nature and mode of action

Amoxicillin has a broad spectrum of antibacterial activity against many Gram-positive and Gram-negative microorganisms, acting through the inhibition of biosynthesis of cell wall mucopeptide. Amoxicillin is active *in vitro* against beta-lactamase negative strains of *Proteus mirabilis*, and *Haemophilus influenzae*. *In vitro* studies have also demonstrated activity against most strains of alpha- and beta-haemolytic streptococci. *Streptococcus pneumoniae*, and beta-lactamase negative strains of staphylococci, *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Enterococcus faecalis*. However, some of the organisms are sensitive to amoxicillin only at concentrations achieved in the urine. Strains of gonococci which are relatively resistant to benzyl penicillin may also be resistant to amoxicillin.

Amoxicillin is susceptible to degradation by beta-lactamases and therefore it is ineffective against bacteria which produce these enzymes particularly resistant staphylococci, which now have a high prevalence. All strains of *Pseudomonas*, *Klebsiella* and *Enterobacter*, indole positive *Proteus*, *Serratia marcescens*, *Citrobacter*, penicillinase producing *N. gonorrhoeae* and penicillinase producing *H. influenzae* are also resistant. *Escherichia coli* isolates are becoming increasingly resistant to amoxicillin *in vitro* due to the presence of penicillinase-producing strains.

Susceptibility

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.

Breakpoints

The MIC breakpoints for susceptible organisms vary according to species. Enterobacteriaceae are considered susceptible when inhibited at NMT 8 mcg/ml amoxicillin and resistant at NLT 32 mcg/ml.

From NCCLS recommendations and using NCCLS-specified methods, *M. catarrhalis* (beta-lactamase negative) and *H. influenzae* (beta-lactamase negative) are considered susceptible at NMT 1 mcg/ml and resistant at NLT 4 mcg/ml; *Str. pneumoniae* are considered susceptible to amoxicillin at MIC NMT 2 mcg/ml and resistant at NLT 8 mcg/ml.

Susceptibility data

Strains of the following named organisms are generally sensitive to the bactericidal action of amoxicillin *in vitro*.

Susceptible Gram-positive aerobes include: *Enterococcus faecalis* (Note 2), *Streptococcus pneumoniae* (Notes 1, 3), *Streptococcus pyogenes* (Notes 1, 3), *Streptococcus viridans* (Note 2), *Streptococcus agalactiae*, *Streptococcus bovis*, *Staphylococcus aureus* (penicillin sensitive), *Corynebacterium* species (Note 2), *Bacillus anthracis*, *Listeria monocytogenes*.

Susceptible Gram-negative aerobes include: *Haemophilus influenzae* (Note 3), *Haemophilus parainfluenzae* (Note 3), *Escherichia coli* (Note 3), *Proteus mirabilis*, *Salmonella* species (Note 2), *Shigella* species (Note 2), *Bordetella pertussis*, *Brucella* species (Note 1), *Neisseria gonorrhoeae* (Note 2), *Neisseria meningitidis* (Note 1), *Pasteurella septica*, *Helicobacter pylori*, *Leptospira* spp, *Vibrio Cholerae*

Susceptible anaerobes include: *Bacteroides melaninogenicus* (Note 2), *Clostridium* species, *Fusobacterium* spp. (Note 2), *Peptostreptococci*

Other susceptible organisms include *Borrelia burgdorferi*.

Note 1: No beta-lactamase producers have as yet been reported for these bacterial species.
Note 2: Inconstantly susceptible; susceptibility is therefore unpredictable in the absence of susceptibility testing.

Note 3: Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications.

Resistance

Bacteria may be resistant to amoxicillin due to production of beta-lactamases which hydrolyse aminopenicillins, due to alteration in penicillin-binding proteins, due to impermeability to the drug, or due to drug efflux pumps. One or more of these mechanisms may co-exist in the same organism, leading to a variable and unpredictable cross-resistance to other beta-lactams and to antibacterial drugs of other classes.

Resistant Gram-positive aerobes include: *Staphylococcus* (beta-lactamase producing strains).

Resistant Gram-negative aerobes include: *Acinetobacter* spp., *Citrobacter* spp., *Enterobacter* spp., *Klebsiella* spp., *Moraxella catarrhalis* (non-susceptible isolates), *Proteus* spp. (indole positive), *Proteus vulgaris*, *Providencia* spp., *Pseudomonas* spp., *Serratia* spp.

Resistant anaerobes include: *Bacteroides fragilis*.

Other resistant organisms include: *Chlamydia*, *Mycoplasma*, *Rickettsia*

5.2 Pharmacokinetic properties

Absorption

Amoxicillin is stable in the presence of gastric acid and rapidly absorbed from the gut to an extent of 72 to 93%. Absorption is independent of food intake. Peak blood levels are achieved 1 to 2 hours after administration. After 250 and 500 mg doses of amoxicillin, average peak serum concentrations of 5.2 mcg/ml and 8.3 mcg/ml respectively have been reported.

Distribution

Amoxicillin is not highly protein bound. Approximately 18% of total plasma drug content is bound to protein. Amoxicillin diffuses readily into most body tissues and fluids, including sputum and saliva but not the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to amoxicillin. Amoxicillin diffuses across the placenta and a small percentage is excreted into the breast milk.

Biotransformation

Amoxicillin is excreted mainly via the urine where it exists in a high concentration. Amoxicillin is also partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to 10 to 25% of the initial dose. Small amounts of the drug are also excreted in faeces and bile. Concentrations in the bile may vary and are dependent upon normal biliary function.

Elimination

Approximately 60 to 70% of amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a standard dose. The elimination half-life is approximately 1 hour. Concurrent administration of probenecid delays amoxicillin excretion. In patients with end-stage renal failure, the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for human based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each capsule contains the following excipients:

- Croscarmellose sodium
- Silicon dioxide
- Stearic acid
- Gelatin capsule shell

The capsule shell also contains the following colourants:

- Allura red
- Brilliant Blue
- Quinoline yellow
- Sunset yellow
- Eosine I Bluish
- Titanium dioxide

6.2 Incompatibilities

Nil.

6.3 Shelf-Life

Shelf life: 3 years from the date of manufacture.

6.4 Special Precautions for Storage

Store at or below 25°C
Protect from heat light and moisture.

6.5 Nature and contents of container

APO-AMOXI

APO-AMOXI 250 mg capsules: Bottles of 28, 100 and 500 capsules.
APO-AMOXI 500 mg capsules: Bottles of 28, 100 and 500 capsules
Not all strengths and packs sizes may be available.

6.6 Special precautions for disposal

No special requirements for disposal.

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

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR DETAILS

Apotex NZ Ltd
32 Hillside Road
Wairau Valley
Private Bag 102-995
North Shore Mail Centre
Auckland
Telephone: (09) 444 2073
Fax: (09) 444 2951

9. DATE OF FIRST APPROVAL

31 October 1996

10. DATE OF PREPARATION

12 November 2018

Summary Table of Changes

Section changed	Summary of new information
4.4, 4.5, 4.6, 4.7, 4.8 & 5.3	Sections were updated as per latest approved and registered information.
Whole data sheet	Change to new format