NEW ZEALAND DATA SHEET
AMOXYCILLIN SANDOZ® (AMOXICILLIN THIHYDRATE)

1. PRODUCT NAME

Amoxicillin trihydrate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient: Amoxicillin trihydrate

Each Amoxycillin Sandoz® Capsules contains 250 mg or 500 mg amoxicillin (as trihydrate).

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

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Amoxycillin Sandoz® Capsules are white to cream powder in an opaque yellow hard gelatin capsule.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Treatment of infection

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

Amoxycillin Sandoz 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

Amoxycillin Sandoz 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

Normal Renal Function

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

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

Lower respiratory tract infections

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): 40 mg/kg/day in equally divided doses every 8 hours.

Urethritis, gonococcal

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.

Acute, uncomplicated lower urinary tract infections in non—pregnant adult female

Adults: 3 g as a single dose.

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.

Paediatric use

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

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.

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.

Renal impairment

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

Prophylaxis of endocarditis

Consideration should be given to local clinical guidelines for prevention of infective endocarditis associated with dental procedures and other medical interventions where necessary.

Based on the recommendations of the British Society for Antimicrobial Chemotherapy

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

4.3. CONTRAINDICATIONS

Hypersensitivity to the active substance, beta lactam antibiotics (e.g penicillin's, cephalosporins) or to any of the excipients listed in section 6.1.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Warnings

Hypersensitivity reactions

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

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

Drug-induced enterocolitis syndrome (DIES)

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

Pseudomembranous colitis

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

Crystalluria

Adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Anticoagulants

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulation treatment is prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Prolonged therapy

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

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

As with other beta-lactams, the blood formula should be checked regularly during high-dose therapy.

Seizures

High dose therapy with beta-lactams for patients with renal insufficiency or seizures history, treated epilepsy and meningeal affection, could exceptionally lead to seizures.

Skin reactions

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.

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

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.

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

Paediatric use

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

Precautions

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.

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

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

Use in renal impairment

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

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.

Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

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

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

4.5. INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Medicines and other pharmacologically active substances

Allopurinol

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

Anticoagulants

Concomitant administration of amoxicillin and anticoagulants, such as coumarin, may increase the incidence of bleeding due to prolongation of prothrombin time. Appropriate monitoring should be undertaken when anticoagulation treatment is prescribed concurrently and the dose of the anticoagulant adjusted as necessary. 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. If coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. However, some classes of antibiotics are more involved, notably fluoroquinolones, macrolides, cyclines, cotrimoxazole and some cephalosporins

Other antibiotics

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.

Digoxin

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

Methotrexate

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.

Probenecid

Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with amoxicillin may result in increased and prolonged blood levels of amoxicillin.

Oral contraceptives

In common with other antibiotics, amoxicillin may affect the gut flora. 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.

Other

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 glycemia levels

Amoxicillin may interfere with protein testing when colormetric methods are used

4.6. FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Reproduction studies have been performed in mice and rats at doses up to ten times the human dose and these studies have revealed no evidence of impaired fertility or harm to the foetus due to amoxicillin.

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. The safety of amoxicillin for use in human pregnancy has not been established by well controlled studies in pregnant women.

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

Use in labour and delivery

Oral ampicillin class antibiotics are generally poorly absorbed during labour. Studies in guinea pigs have shown that intravenous administration of ampicillin decreased the uterine tone, frequency of contractions, height of contractions and duration of contractions. However, it is not known whether the use of amoxicillin in humans during labour or delivery has immediate or delayed 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

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

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8. UNDESIRABLE EFFECTS

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

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.

General disorders and administration site conditions

Drug fever has been reported rarely.

Cardiac disorders

Kounis syndrome: not known.

Infections and infestations

Mucocutaneous candidiasis have been reported very rarely.

Gastrointestinal

Nausea, vomiting, diarrhoea, loss of appetite, flatulence, 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. Intestinal candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis) have been reported rarely. Black hairy tongue has been reported very rarely. Drug-induced enterocolitis syndrome: not known. (see section 4.4 Special warnings and precautions for use).

Skin and subcutaneous tissue disorders

Linear IgA disease: not known.

Hypersensitivity reactions

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

Whenever such reactions occur, amoxicillin should be discontinued. (Note: Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids.) Anaphylaxis is the most serious reaction experienced (see section 4.4 Special warnings and precautions for use).

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.

Liver

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

Haemic and Lymphatic systems

Reactions such as anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia and leucopenia (including severe neutropenia or agranulocytosis) have been reported during therapy with other penicillins. These reactions are usually reversible on discontinuation of

therapy and are believed to be hypersensitivity phenomena. Prolongation of bleeding time and prothrombin time have also been reported rarely.

Renal and urinary tract disorders

Interstitial nephritis. Crystalluria (including acute renal injury): not known (see section 4.9 Overdose).

CNS effects

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

Miscellaneous

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

Reporting suspected adverse effects

Reporting suspected adverse reactions after 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

Signs and symptoms

Cases of overdosage with amoxicillin are usually asymptomatic. Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water/electrolyte imbalance should be treated symptomatically. During the administration of high doses of amoxicillin, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see Section 4.4 Special warnings and precautions for use).

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 risk assessment and 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.

Pharmacodynamic effects

Inhibition of bacterial cell wall synthesis.

Antibiotic class

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

Mechanism of action

Beta-lactam antibiotic.

Amoxicillin is an aminobenzyl penicillin that has a bactericidal action due to its inhibition of the synthesis of the bacterial cell wall. It exerts a bactericidal effect against many Gram-positive and Gram-negative microorganisms. Amoxicillin is not effective against beta-lactamase producing organisms.

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 influenza. 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*.

Clinical trials

No data available.

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.

Metabolism

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.

Excretion

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

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Gelatin, microcrystalline cellulose, magnesium stearate, titanium dioxide, iron oxide yellow.

6.2. INCOMPATIBILITIES

None known.

6.3. SHELF LIFE

24 months. Store below 25°C. The expiry date can be found on the packaging

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Amoxycillin Sandoz capsules

Store below 25°C. Protect from moisture.

6.5. NATURE AND CONTENTS OF CONTAINER

Amoxycillin Sandoz® Capsules are available in a PVC/PVDC/Al blister pack. Amoxycillin Sandoz® 250 mg and 500 mg are available in packs of 12, 20, 100 and 500 capsules.

Not all presentations may be marketed.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

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

7. MEDICINE SCHEDULE

Prescription Only Medicine

8. SPONSOR

Sandoz New Zealand Limited
12 Madden Street
Auckland 1010
New Zealand
Telephone: 0800 726 369

9. DATE OF FIRST APPROVAL

30 September 2015

10. DATE OF REVISION OF THE TEXT

24 March 2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2	Revised and restructured dosing instructions
4.3	Revised contraindications wording
4.4	Revised hypersensitivity reaction warning to include Kounis syndrome Added information regarding drug-induced enterocolitis syndrome (DIES) Minor editorial changes
4.5	Minor editorial changes
4.8	Revised and restructured safety information Added Kounis syndrome and symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome)
4.9	Added risk assessment wording Minor editorial changes
6.1	Correction to registered excipients
6.5	Correction of registered pack sizes
6.6	Revised special precautions for disposal wording