PRODUCT INFORMATION
AMOXYCILLIN SANDOZ® 1000 mg TABLETS

NAME OF THE MEDICINE

Active Ingredient: Amoxycillin trihydrate

Inactive Ingredients: Magnesium stearate, povidone, sodium starch glycollate, cellulose-microcrystalline, titanium dioxide, talc-purified and hypromellose.

DESCRIPTION

Amoxycillin 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.

Structural Formula:

\[
\begin{align*}
&\text{HO} \\
&\text{CH}_3 \\
&\text{CH}_3 \\
&\text{COOH}
\end{align*}
\]

Chemical Name: \((2S,5R,6R)-6-[(R)-2-\text{amino}-2-(4-\text{hydroxyphenyl})\text{acetamido}]3,3\text{-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic\ acid trihydrate.}

Molecular Formula: \(\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_5\text{S.3H}_2\text{O}\)

Molecular Weight: 419.4

CAS Number: 61336-70-7

PHARMACOLOGY

Microbiology
Amoxycillin trihydrate is a broad-spectrum penicillin similar to ampicillin in its bactericidal action. It is believed to act through the inhibition of biosynthesis of cell wall mucopeptide. It is active against both gram-positive and gram-negative micro-organisms. Amoxycillin is active \textit{in vitro} against beta-lactamase negative strains of \textit{Proteus mirabilis}, and \textit{Haemophilus influenzae}. \textit{In vitro} studies have also demonstrated activity against most strains of alpha- and beta-haemolytic streptococci, \textit{Streptococcus pneumoniae}, and beta-lactamase negative strains of staphylococci, \textit{Neisseria gonorrhoeae}, \textit{Neisseria meningitidis} and \textit{Enterococcus faecalis}. However, some of the organisms are sensitive to amoxycillin only at concentrations achieved in the urine. Strains of gonococci which are relatively resistant to benzyl penicillin may also be
resistant to amoxycillin. Amoxycillin is not effective against penicillinase producing bacteria, particularly resistant staphylococci which now have a high prevalence. All strains of Pseudomonas, Klebsiella, 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 amoxycillin in vitro due to the presence of penicillinase-producing strains.

<table>
<thead>
<tr>
<th>ORGANISM</th>
<th>% RESISTANT STRAINS</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em></td>
<td>16.8% intermediate resistance; 8.6% resistant</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>20.3%</td>
</tr>
<tr>
<td><em>M catarrhalis</em></td>
<td>94.0%</td>
</tr>
<tr>
<td><em>B. fragilis</em></td>
<td>100%</td>
</tr>
<tr>
<td>Enterobacter <em>spp.</em></td>
<td>96%</td>
</tr>
<tr>
<td>Klebsiella <em>spp.</em></td>
<td>98%</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>100%</td>
</tr>
<tr>
<td><em>S. aureus</em> (methicillin-susceptible)</td>
<td>85%</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>0.2%</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>80%</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>45.4%</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>14%</td>
</tr>
</tbody>
</table>

*Therapeutic Guidelines Antibiotic 2000 Edition*

**Disc Susceptibility Testing**

*Dilution of diffusion techniques.* Either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation. A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy may be selected.

**Note:** The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

**Pharmacokinetics**

Amoxycillin is stable in the presence of gastric acid and is rapidly and well absorbed after oral administration, even in the presence of food. Peak serum levels are reached within 1 to two
hours after ingestion. Amoxycillin readily distributes in most body tissues and fluids with the exception of brain and spinal fluid except when the meninges are inflamed. Amoxycillin has been shown to diffuse into sputum and saliva and is excreted mainly via the urine where it exists in a high concentration. Concentrations in the bile vary and are dependant upon normal biliary function. Amoxycillin is eliminated with a half-life of 61.3 minutes with normal renal function and up to 16-20 hours in the absence of renal function. Amoxycillin is excreted in the urine as unchanged drug and as penicilloic acid. Approximately 75% of a 1g dose is excreted in the urine within six hours with normal renal function. However, there is a proportional difference in the amount excreted following different doses, due to lack of linearity in the rate of absorption with higher doses. Elimination of amoxycillin can be delayed by concurrent administration of probenecid. Amoxycillin is only 17% protein bound in serum.

Efficacy of β-lactam antibiotic is related to the time in which the concentration of antibiotic at the site of infection exceeds the minimal inhibitory concentration (MIC) of that antibiotic for the pathogen. Analysis of pharmacokinetic data from a single dose study of the amoxycillin 500 mg capsule and a single dose study of the amoxycillin 1 g film-coated tablet showed that the mean amoxycillin plasma concentrations were above the (MIC) for similar proportions of the dose interval for the MIC levels of 0.5, 1.0 and 2.0 μg/mL. The time above the MIC for other MIC levels and the time above MIC at steady state were not assessed for either formulation and/or dose regimen of amoxycillin.

Data to establish the bioequivalence of the 1 x 1000 mg tablet with 2 x 500 mg capsules have not been submitted and as such, the products should not be directly substituted.

**Clinical Trials**

Amoxycillin Sandoz (1000 mg tablets bid) and amoxycillin (500 mg capsules tds) were compared in a multi-centre, double-blind, randomised study of 395 adult patients with acute exacerbations of chronic bronchitis. Patients were treated for 10 days and were assessed during therapy (days 3 – 5), after the end of therapy (days 12 – 15) and at follow-up (days 28 – 35).

The statistical analysis for each clinical efficacy parameter during therapy (pooling moderate/severe severity and mucopurulent/purulent sputum appearance) is shown below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Amoxycillin Sandoz 1000 mg bid</th>
<th>Amoxycillin 500 mg tds</th>
<th>95% CI</th>
<th>Comparison X²-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment of subjective general state (moderate or severe)</td>
<td>24.6%</td>
<td>31.5%</td>
<td>-16.5%, 2.7%</td>
<td>p=0.15</td>
</tr>
<tr>
<td>Severity of cough (moderate or severe)</td>
<td>26.3%</td>
<td>40.7%</td>
<td>-24.4, -4.5%</td>
<td>p=0.005</td>
</tr>
<tr>
<td>Severity of dyspnoea (moderate or severe)</td>
<td>16.0%</td>
<td>22.2%</td>
<td>-14.6%, 2.2%</td>
<td>p=0.15</td>
</tr>
<tr>
<td>Severity of rales/rhonchi (moderate or severe)</td>
<td>11.5%</td>
<td>13.5%</td>
<td>-9.2%, 4.9%</td>
<td>p=0.55</td>
</tr>
<tr>
<td>Sputum appearance (mucopurulent or purulent)</td>
<td>32.5%</td>
<td>35.9%</td>
<td>-13.4%, 6.9%</td>
<td>p=0.53</td>
</tr>
</tbody>
</table>
The primary endpoint of this study was the clinical success at the end of therapy. For clinically evaluable patients, the clinical success rate at the end of therapy was 156/175 (89.1%) in the Amoxycillin Sandoz 1000 mg bid group and 150/162 (92.6%) in the amoxicillin 500 mg tds group. The results (p-value=0.27; CI 95%=-0.96%, 2.7%) confirm the equivalence in clinical efficacy between the two treatment groups. Bacteriological success was a secondary endpoint in this study. A total of 219 patients were eligible for assessment of bacteriological success at the end of treatment. Bacteriological success was achieved for 85/109 (78%) of patients given Amoxycillin Sandoz and 83/110 (75.5%) of patients given amoxicillin 500 mg tds.

Assessment at follow-up yielded a clinical recurrence rate of 13.4% in the bid group and 13.7% in the tds group. No statistically significant differences between the two treatment groups.

**INDICATIONS**

Amoxycillin Sandoz is indicated in the treatment of acute exacerbation of chronic bronchitis.

**Notes:**
Therapy should be guided by bacteriologic studies including sensitivity tests and by clinical response. Amoxycillin alone or in combination with another antibiotic, may be used in an emergency where the causative agent has yet to be identified.

Amoxycillin Sandoz 1000 mg tablets have not been shown to be bioequivalent to the 500 mg and 250 mg capsule formulations given in equivalent doses. Therefore, Amoxycillin Sandoz 1000 mg tablets and other forms of amoxycillin are not considered interchangeable.

Infections caused by pathogens with established penicillin G susceptibility should preferentially be treated with penicillin G.

**CONTRAINDICATIONS**

Amoxycillin is a penicillin and should not be given to patients with a history of hypersensitivity to ß-lactam antibiotics (e.g. penicillins, cephalosporins, carbapenem or monobactam). Known and suspected hypersensitivity to penicillins. Potential cross allergy to other ß-lactams such as Cephalosporins should be taken into account

Known hypersensitivity to the active substance, to any of the penicillins or to any of the excipients.

Antibiotics have no place in trivial infections.

**PRECAUTIONS**

Serious, and occasionally fatal, hypersensitivity (anaphylactoid) reactions have been reported in patients receiving penicillin therapy. These reactions are more frequently associated with
Parenteral therapy but have been reported for patients receiving oral penicillins. Careful assessment should be made prior to administration of amoxycillin to determine any previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. Amoxycillin therapy should be immediately discontinued if hypersensitivity reactions occur. Serious anaphylactoid reactions should be treated with adrenaline. Oxygen, intravenous steroids and airways management, including intubation should be administered as necessary.

Non-susceptible microorganisms: Amoxycillin 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 amoxycillin. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including amoxycillin. A toxin produced by *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. 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 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 condition and should not be used.

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

Patients should be told about the potential occurrence of allergic reactions and instructed to report them.

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

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. If superinfection occurs (usually involving Aerobacter, Pseudomonas or Candida) discontinue the drug and/or institute appropriate therapy.

Elevated liver enzymes and changes in blood counts have been reported.

Amoxycillin should be given with caution to patients with lymphatic leukaemia as they are susceptible to amoxycillin induced skin rashes.
Jarisch-Herxheimer reaction: The Jarisch-Herxheimer reaction has been seen following amoxycillin treatment of Lyme disease. It results directly from the bactericidal activity of amoxycillin 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.

Amoxycillin 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 amoxycillin induced erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxycillin.

Special caution should be exercised in patients with allergic diatheses or bronchial asthma and hay fever.

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 amoxycillin.

The presence of high urinary concentrations of amoxycillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals. At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxycillin crystalluria.

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

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.

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 patients with renal impairments (see DOSAGE AND ADMINISTRATION).

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 amoxycillin.

**Use in Pregnancy**
**Category A**
Drugs 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 amoxycillin 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.

Amoxycillin 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 and duration of contractions. However, it is not known whether the use of amoxycillin 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 breast milk and caution should be exercised when amoxycillin is administered to nursing mothers. So far no detrimental effects for the breast-fed infant have been reported after taking amoxycillin. Amoxycillin 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.

Effects on laboratory tests

Oral administration of amoxycillin will result in high urine concentrations of amoxycillin. Since high urine concentrations of amoxycillin 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.

**INTERACTIONS WITH OTHER MEDICINES**

**Allopurinol**

Concomitant ingestion of allopurinol and ampicillin may promote the occurrence of skin rashes. The underlying mechanism is still poorly understood. Similar reactions can be expected with amoxycillin.

**Digoxin**

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

**Anticoagulants**

Concomitant administration of amoxycillin and anticoagulants from the coumarin class, may prolong the bleeding time. A dose adjustment of anticoagulants may be necessary (See Precautions). If coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxycillin.
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.

In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxycillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxycillin.

**Methotrexate**
Interaction between amoxycillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxycillin and methotrexate simultaneously (see Precautions). Amoxycillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

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

**Probenecid**
Concomitant use of probenecid is not recommended. The concomitant administration of probenecid produces sustained and higher plasma levels by reducing renal elimination of amoxycillin.

Oral administration of amoxycillin will result in high urine concentrations of amoxycillin. Since high urine concentrations of ampicillin may result in false positive reactions when testing for the presence of glucose in urine using Clinistest, 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.

**Caution is recommended when amoxycillin is given concomitantly with:**

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

**Other forms of interactions:**

- Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxycillin.
- Amoxycillin may decrease the amount of urinary estriol in pregnant women.
- At high concentrations, amoxycillin may diminish the results of serum glycemiam levels.
- Amoxycillin may interfere with protein testing when colorometric methods are used.
ADVERSE EFFECTS

Amoxycillin 1000 mg tablets twice daily and amoxycillin 500 mg capsules three times daily for ten days were compared in a study of 395 adult patients with acute exacerbations of chronic bronchitis. There were no significant differences on the incidence or severity of adverse events between the treatment groups.

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

The incidence of adverse events reported at a frequency of >1%, and possibly or probably drug related, is shown in the following table:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>No. of Reports (%)</th>
<th>1000 mg b.i.d. (n=197)</th>
<th>500 mg t.d.s. (n=198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>8 (4.06)</td>
<td>12 (6.06)</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (3.55)</td>
<td>4 (2.02)</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>4 (2.03)</td>
<td>1 (0.51)</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>1 (0.51)</td>
<td>3 (1.52)</td>
<td></td>
</tr>
<tr>
<td>Exanthema</td>
<td>2 (1.02)</td>
<td>1 (0.51)</td>
<td></td>
</tr>
<tr>
<td>Resistance mechanism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candidiasis</td>
<td>1 (0.51)</td>
<td>2 (1.01)</td>
<td></td>
</tr>
<tr>
<td>Fungal/mycotic infection</td>
<td>3 (1.52)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>10 (5.08)</td>
<td>11 (5.56)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36 (18.27)</td>
<td>34 (17.17)</td>
<td></td>
</tr>
</tbody>
</table>

The following adverse reactions have been reported as associated with the use of amoxycillin.

Gastrointestinal. Nausea, vomiting, diarrhoea. Intestinal candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis) superficial discoloration of the teeth (especially with the suspension) have been reported rarely (see Precautions). Usually the discoloration can be removed by teeth brushing. If severe and persistent diarrhoea occurs, the very rare possibility of pseudomembranous colitis should be considered. The administration of anti-peristaltic drug is contraindicated. Black hairy tongue and haemorrhagic colitis have been reported very rarely.

Hypersensitivity. Erythematous maculopapular rash, pruritus and urticaria have been reported occasionally. Rarely, skin reactions such as erythema multiforme exsudativum, acute generalised exanthematous pustulosis (AGEP), Lyell’s syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, Jarisch-Herxheimer reaction and bullous and exfoliative dermatitis have been reported. As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness, hypersensitivity vasculitis and interstitial nephritis (crystalluria) have been reported rarely.

Whenever such reactions occur, amoxycillin 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 Precautions).

Hepatic. 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.

Renal. Crystalluria has 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 (see Overdosage) have been reported very rarely.

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

Infections and infestations. Mucocutaneous candidiasis have been reported very rarely.

Miscellaneous. 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.

As the blood-brain barrier becomes more permeable in meningitis, toxic symptoms may be precipitated by lower levels of amoxycillin in patients with meningitis.

**DOSAGE AND ADMINISTRATION**

Amoxycillin Sandoz may be taken without regard to food.

Adults: 1000 mg twice daily.

Treatment should be continued for a minimum of 48 to 72 hours beyond the time when patients become asymptomatic or evidence of bacterial eradication has been obtained.

Bacteriological and clinical appraisals may have to be continued for several months following cessation of treatment.
Dosage in patients with renal impairment
In renal impairment the excretion of the antibiotic will be delayed, and depending on the degree of impairment, it may be necessary to reduce the total daily dose.

OVERDOSAGE

Signs of overdosage of amoxycillin would predominantly be gastrointestinal related. The symptoms may include abdominal or stomach cramps and pain, severe nausea, vomiting or diarrhoea. Treatment of penicillin overdosage should be symptomatic and supportive. Haemodialysis may aid in the removal of penicillins from the blood.

Please also refer to Precautions and Adverse Reactions.

PRESENTATION AND STORAGE CONDITIONS

Amoxycillin Sandoz tablets are oval, biconvex, white to cream-coloured, scored on both sides. Each tablet contains 1000 mg amoxycillin as the trihydrate.

Amoxycillin Sandoz are packed in blisters of 2 or 14 tablets.

Store below 25°C, protect from moisture.

NAME AND ADDRESS OF THE SPONSOR

Sandoz Pty Ltd
54 Waterloo Road
Macquarie Park, NSW 2113
Australia
Tel: 1800 634 500

DATE OF FIRST INCUSION ON THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG): 29th January 2004

DATE OF LAST AMENDMENT: 11/04/2016