AMOXICILLIN ACTAVIS
Amoxicillin Oral Suspension BP

Presentation

**Powder for Oral Suspension 125mg/5ml**

**60ml:** Light pink coloured granular powder to prepare 60ml oral suspension. When reconstituted as directed, produces 60mL of pink coloured suspension with each 5mL containing Amoxicillin Trihydrate BP equivalent to amoxicillin 125mg.

**100ml:** Light pink coloured granular powder to prepare 100ml oral suspension. When reconstituted as directed, produces 100mL of pink coloured suspension with each 5mL containing Amoxicillin Trihydrate BP equivalent to amoxicillin 125mg.

**Powder for Oral Suspension 250mg/5ml**

**60ml:** Light pink coloured granular powder to prepare 60ml oral suspension. When reconstituted as directed, produces 60mL of pink coloured suspension with each 5mL containing Amoxicillin Trihydrate BP equivalent to amoxicillin 250mg.

**100ml:** Light pink coloured granular powder to prepare 100ml oral suspension. When reconstituted as directed, produces 100mL of pink coloured suspension with each 5mL containing Amoxicillin Trihydrate BP equivalent to amoxicillin 250mg.

Uses

**Actions**

Amoxicillin is a semi-synthetic aminopenicillin of the beta-lactam group of antibiotics which exerts a bactericidal effect against many Gram-positive and Gram-negative microorganisms. Amoxicillin is not effective against beta-lactamase producing organisms.

**Indications**

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

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

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

**Pharmacodynamic properties**

Amoxicillin is a semisynthetic aminopenicillin of the beta-lactam group of antibiotics. It 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, however, susceptible to degradation by beta-lactamases and therefore the spectrum of activity does not include organisms which produce these enzymes including resistant staphylococci, and all strains of Pseudomonas, Klebsiella and Enterobacter.

Strains of the following organisms are generally sensitive to the bactericidal action of amoxicillin \textit{in vitro}:

<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus faecalis</td>
<td>Haemophilus influenzae</td>
<td>Borrelia burgdorferi</td>
</tr>
<tr>
<td>\textit{Streptococcus pneumoniae}</td>
<td>Escherichia coli</td>
<td></td>
</tr>
<tr>
<td>\textit{Streptococcus pyogenes}</td>
<td>Proteus mirabilis</td>
<td></td>
</tr>
<tr>
<td>\textit{Streptococcus viridans}</td>
<td>Salmonella species</td>
<td></td>
</tr>
<tr>
<td>\textit{Staphylococcus aureus} (penicillin sensitive)</td>
<td>Shigella species</td>
<td></td>
</tr>
<tr>
<td>Clostridium species</td>
<td>Bordetella pertussis</td>
<td></td>
</tr>
<tr>
<td>\textit{Corynebacterium species}</td>
<td>Brucella species</td>
<td></td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td>Neisseria gonorrhoeae</td>
<td></td>
</tr>
<tr>
<td>\textit{Listeria monocytogenes}</td>
<td>Neisseria meningitidis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pasteurella septica</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Helicobacter pylori</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leptospira spp</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fusobacterium spp</td>
<td></td>
</tr>
<tr>
<td></td>
<td>\textit{Vibrio Cholerae}</td>
<td></td>
</tr>
</tbody>
</table>

\textit{Pharmacokinetic properties}

\textbf{Absorption}

Amoxicillin is rapidly absorbed from the gut to an extent of 72-93%. Absorption is independent of food intake.

\textbf{Distribution}

Peak blood levels are achieved 1-2 hours after administration. After 250 and 500mg doses of amoxicillin, average peak serum concentrations of 5.2mcg/ml and 8.3mcg/ml respectively have been reported.

Amoxicillin is not highly protein bound, approx. 18% of total plasma drug content is bound to protein. Amoxicillin diffuses readily into most body tissues and fluids, with the exception of the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to amoxicillin.
Excretion
The major route of elimination for amoxicillin is via the kidney. Approximately 60-70% 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.
Amoxicillin is also partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to 10-25% of the initial dose.
Concurrent administration of probenecid delays amoxicillin excretion.
Small amounts of the drug are also excreted in faeces and bile.

Dosage and Administration

Upper Respiratory Tract Infections (due to streptococci, pneumococci, nonpenicillinase-producing staphylococci and H. influenzae);

Genito-Urinary Tract Infections (due to Escherichia coli, Proteus mirabilis and Strep. faecalis);

Skin And Soft Tissue Infections (due to streptococci, sensitive staphylococci and Escherichia coli)

Adults: 250mg every 8 hours
Children (under 20kg): 25mg/kg/day in equally divided doses every 8 hours.
In severe infections or those caused by less susceptible organisms, 500mg every 8 hours for adults and 50mg/kg/day in equally divided doses every 8 hours for children may be needed.

Lower Respiratory Tract Infections (due to streptococci, pneumococci, non-penicillinase producing staphylococci and Haemophilus influenza)

Adults: 500mg every 8 hours.
Children (under 20kg): 50mg/kg/day in equally divided doses every 8 hours.
High Dosage Therapy (maximum recommended oral dosage 6g daily in divided doses). An adult dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Prophylaxis of Endocarditis - Dental Procedures

Prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues who have not received a penicillin in the previous month:
Note: Patients with prosthetic heart valves should be referred to hospital (see below).

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

Adults - initially 3g orally 4 hours prior to anaesthesia followed by 3g orally (or 1g amoxicillin/ampicillin IM if the dose is not tolerated) 6 hours after the initial dose. Children under 10 - half adult dose. Children under 5 - quarter adult dose.

3. Patient having general anaesthesia, oral antibiotics not appropriate:

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

Children under 10 - the dose of amoxicillin should be half the adult dose. The dose of gentamicin should be 2mg/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: 3g 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 (due to Escherichia coli, Proteus mirabilis, Strep. faecalis, non-penicillinase producing staphylococci)

Adults: 3g as a single dose.

General Dosing Recommendations

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 20kg 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 followup for several months after cessation of therapy.
Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained.

It is recommended that there be at least 10 days treatment for any infection caused by haemolytic streptococci to prevent the occurrence of rheumatic fever or glomerulonephritis.

**Impaired renal function**

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

In patients receiving peritoneal dialysis, the maximum recommended dose in 500mg/day.

Amoxicillin may be removed from the circulation by haemodialysis.

**Renal Impairment in Children under 40kg**

- Creatinine clearance >30mL/min: No adjustment necessary.
- Creatinine clearance 10-30mL/min: 15 mg/kg given b.i.d. (maximum 500mg/twice daily).
- Creatinine clearance <10mL/min: 15 mg/kg given as a single daily dose (maximum 500mg)

In the majority of cases, parenteral therapy will be preferred.

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**Contraindications**

AMOXICILLIN ACTAVIS is contraindicated in patients who have had previous experience of a major allergy or anaphylaxis to a cephalosporin or penicillin.

Hypersensitivity to any of the excipients.

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**Warnings and Precautions**

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

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins or cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation, may also be required.
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.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It is important to consider this diagnosis in patients who develop severe and persistent diarrhoea during or after receiving AMOXICILLIN ACTAVIS. In this situation, even if Clostridium difficile is only suspected, administration of AMOXICILLIN ACTAVIS should be discontinued and appropriate treatment given.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Dosage should be adjusted in patients with renal impairment (see Impaired renal function).

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 (see Overdosage).

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

Amoxicillin Actavis suspension contains sodium benzoate as a preservative.

**Pregnancy and lactation**

**Use in pregnancy**

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

Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the infant. Trace quantities of penicillin can be detected in breast milk with the potential for hypersensitivity
reactions (e.g. drug rashes) or gastrointestinal disorders (e.g. diarrhoea or candidosis) in the breast-fed infant. Consequently, breastfeeding might have to be discontinued.

**Effects on ability to drive and use machines**

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

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**Adverse Effects**

The following convention has been utilised for the classification of undesirable effects:

*Very common* (more than 1/10), *common* (more than 1/100, less than 1/10), *uncommon* (more than 1/1000, less than 1/100), *rare* (more than 1/10,000, less than 1/1000), *very rare* (less than 1/10,000).

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

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

**Blood and lymphatic system disorders**

Very rare: 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 (see *Warnings and Precautions*).

**Immune system disorders**

Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis (see *Warnings and Precautions*), serum sickness and allergic vasculitis.

If a hypersensitivity reaction is reported, the treatment must be discontinued. (See also *Skin and subcutaneous tissue disorders*).

**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.

**Infections and Infestations**

Uncommon: Prolonged or 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 discolouration of the teeth. Good oral hygiene may help to prevent tooth discolouration which can usually 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.

**Hepato-biliary disorders**

Rare: Hepatitis and cholestatic jaundice.

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

**Skin and subcutaneous tissue disorders**

Common: Cutaneous reactions such as exanthema, pruritus, urticarial, 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 generalised pustulosis, Lyell’s syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP). (See also Immune system disorders).

**Renal and Urinary tract disorders**

Rare: Interstitial nephritis, crystalluria (see Overdosage). The incidence of these adverse effects was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

**General disorders and administration site conditions**

Rare: Drug fever.

**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/)

**Interactions**

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

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

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

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

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

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

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.

In common with other antibiotics, amoxicillin may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

**Overdosage**

Cases of overdosage with amoxicillin are usually asymptomatic. If encountered 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 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).

**Pharmaceutical Precautions**

**Reconstitution instructions**

**Powder for Oral Suspension 125mg/5ml**

60ml bottle: Shake bottle until all powder flows freely. Add 49 ml of purified water in two portions. Add approximately $\frac{2}{3}$ of the purified water with intermittent shaking, then add remaining purified water and shake vigorously.

100ml bottle: Shake bottle until all powder flows freely. Add 86 ml of purified water in two portions. Add approximately $\frac{2}{3}$ of the purified water with intermittent shaking, then add remaining purified water and shake vigorously.
Powder for Oral Suspension 250mg/5ml

60ml bottle: Shake bottle until all powder flows freely. Add 48 ml of purified water in two portions. Add approximately \( \frac{2}{3} \) of the purified water with intermittent shaking, then add remaining purified water and shake vigorously.

100ml bottle: Shake bottle until all powder flows freely. Add 81 ml of purified water in two portions. Add approximately \( \frac{2}{3} \) of the purified water with intermittent shaking, then add remaining purified water and shake vigorously.

**Storage conditions**

Store dry powder below 25°C. Protect from light. Keep out of reach of children.

Once reconstituted, the prepared suspension should be stored at 2-8°C. Refrigerate, do not freeze.

Discard prepared suspension after 10 days.

**Medicine Classification**

Prescription Only Medicine

**Package Quantities**

**Amoxicillin Actavis Powder for Oral Suspension**

**125mg/5ml**

60ml and 100ml bottles

**250mg/5ml**

60ml and 100ml bottles

*Not all pack sizes may be marketed.*

**Further Information**

**List of excipients**

Sucrose, carmellose sodium, sodium benzoate, purified talc, anhydrous citric acid, colloidal anhydrous silica, Essence BTM Dm 7020A, Colour Erythrosine Supra.

**Name and Address**

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**Date of Preparation**

26 July 2016