

DATA SHEET

AMOXIL®

amoxicillin trihydrate

Presentation

AMOXIL Paediatric Drops: Fruit flavoured suspension providing 125mg amoxicillin per 1.25mL (measured by the pipette supplied). Presented as powder in bottles for preparing 20mL.

AMOXIL Syrups: Fruit flavoured sugar free syrup providing 125mg or 250mg amoxicillin per 5mL. Presented as powder in bottles for preparing 100mL.

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: AMOXIL is indicated in the treatment of infections due to susceptible organisms.

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

Prophylaxis for endocarditis: AMOXIL 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 *in vitro*:

Gram-positive

Streptococcus faecalis

Gram-negative

Haemophilus influenzae

Other

Borrelia burgdorferi

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| <i>Streptococcus pneumoniae</i> | <i>Escherichia coli</i> |
| <i>Streptococcus pyogenes</i> | <i>Proteus mirabilis</i> |
| <i>Streptococcus viridans</i> | <i>Salmonella</i> species |
| <i>Staphylococcus aureus</i> (penicillin sensitive) | <i>Shigella</i> species |
| <i>Clostridium</i> species | <i>Bordetella pertussis</i> |
| <i>Corynebacterium</i> species | <i>Brucella</i> species |
| <i>Bacillus anthracis</i> | <i>Neisseria gonorrhoeae</i> |
| <i>Listeria monocytogenes</i> | <i>Neisseria meningitidis</i> |
| | <i>Pasteurella septica</i> |
| | <i>Helicobacter pylori</i> |
| | <i>Leptospira spp</i> |
| | <i>Fusobacterium spp</i> |
| | <i>Vibrio Cholerae</i> |

Pharmacokinetic properties

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

Preclinical safety data

No further information of relevance to add.

Dosage and Administration

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

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

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

Adults: 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 influenzae*):

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 AMOXIL 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 AMOXIL 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 amoxycillin/ampicillin with 120mg gentamicin IM immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure, followed by 500mg AMOXIL orally, 6 hours later.

Children under 10 - the dose of amoxycillin should be half the adult dose. The dose of gentamicin should be 2mg/kg.

Note: Amoxycillin and gentamicin should not be mixed in the same syringe. Please consult the appropriate Data Sheet for parenteral amoxycillin 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 AMOXIL 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.

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 follow-up for several months after cessation of therapy.

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

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

Impaired renal function

In renal impairment the excretion of amoxycillin 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 is 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.

Contraindications

Amoxicillin is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (eg. penicillins, cephalosporins).

Warnings and Precautions

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.

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.

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 Posology 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 (see Overdosage).

Amoxil paediatric drops and sugar free syrups contain sodium benzoate.

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: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.
Prolongation of bleeding time and prothrombin time
(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 hypersensitivity vasculitis.

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

Nervous system disorders

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

Infections and Infestations

Very rare: Mucocutaneous candidiasis

Gastrointestinal disorders

Common: Diarrhoea and nausea.

Uncommon: Vomiting.

Very rare: Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis).

Black hairy tongue

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

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT.

The significance of a rise in AST and/or ALT is unclear.

Skin and subcutaneous tissue disorders

Common: Skin rash.

Uncommon: Urticaria and pruritus.

Very rare: Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP).
(See also *Immune system disorders*).

Renal and Urinary tract disorders

Very rare: Interstitial nephritis, crystalluria (*see Overdosage*)

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

Interactions

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.

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.

Pregnancy and lactation

Use in pregnancy:

The safety of this medicinal product 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 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.

Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed.

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.

Pharmaceutical Precautions

AMOXIL syrups and paediatric drops should be stored at the temperature, and used within the periods stated on the labels. Any remaining syrup or suspension should be discarded. All presentations should be kept out of reach of children.

Medicine Classification

Prescription Only Medicine.

Package Quantities

AMOXIL Syrups: 125mg and 250mg per 5mL: 100mL bottles.

AMOXIL Paediatric Drops: 125mg per 1.25mL: 20mL bottles with graduated dropper.

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