

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

Amoxicillin 250mg/5ml Oral Suspension Sugar Free BP
and Respillin 250mg/5ml Oral Suspension Sugar Free BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxicillin Sugar Free Suspension B.P. 250mg/5ml contains amoxicillin trihydrate B.P. equivalent to amoxicillin 250mg

3. PHARMACEUTICAL FORM

Pale yellow powder for reconstitution as suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin is a broad spectrum antibiotic indicated for the treatment of commonly- occurring bacterial infections including:

Acute and chronic bronchitis

Pneumonia

Ear, nose and throat infections

Otitis media

Urinary tract infection

Gonorrhoea

Invasive salmonellosis,

Gynaecological infections

Peritonitis

Osteomyelitis

Meningitis

Endocarditis

Typhoid fever

Prophylaxis of endocarditis in patients at risk from such procedures as dental extractions.

In some of these infections initiation of treatment or indeed the whole course of treatment may need to be by the parenteral route.

In children with urinary tract infection, the need for further clinical investigation should be considered.

4.2 Posology and method of administration **Adult Dosage (including elderly patients)**

Standard Adult Dosage:

5ml of 250mg/5ml suspension three times daily, increasing to 10ml of 250mg/5ml suspension three times daily for more severe infections.

High dose and short course therapies, requiring doses of up to 6gm, daily, a more appropriate dosage form is recommended.

Children

Children weighing more than 40 kg should be given the usual adult dosage.

Children weighing < 40 kg

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations below and sections 4.4, 5.1 and 5.2).

*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

Special dosage recommendation

Tonsillitis: 50 mg/kg/day in two divided doses.

Acute otitis media: In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations.

Prophylaxis for endocarditis: 50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure.

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Dosage in impaired renal function:

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4 and 5.2).

Renal impairment in adults

Glomerular filtration rate >30ml/min: No adjustment necessary

Glomerular filtration rate 10-30ml/min: Amoxicillin max. 500mg BID

Glomerular filtration rate <10ml/min: Amoxicillin max. 500mg/day

Renal impairment in children under 40 kg:

Creatinine clearance ml/min	Dose	Interval between administration
> 30	Usual dose	No adjustment necessary
10 – 30	Usual dose	12 h (corresponding to 2/3 of the dose)
< 10	Usual dose	24 h (corresponding to 1/3 of the dose)

Route of administration

Oral.

4.3 Contra-indications

Use in patients with hypersensitivity to penicillins, including ampicillin or cephalosporins or to any of the other excipients.

4.4 Special warnings and special precautions for use.

Prolonged use of anti-infective agent may result in superinfection by organisms resistant to that anti-infective.

In patients with renal impairment, the rate of excretion of amoxicillin will be reduced depending on the degree of impairment and it may be necessary to reduce the total daily unit amoxicillin dosage accordingly.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These

reactions are more likely to occur in persons with a history of penicillin hypersensitivity and/ or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of severe reactions when treated with cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

Erythematous (mornilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.

If allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy should be instituted and discontinuance of amoxicillin therapy considered.

Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

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

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

This medicinal product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicaments and other forms of interaction

When administered concurrently, the following drugs may interact with amoxicillin:

Oral Contraceptives:

In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Bacteriostatic antibiotics:

Chloramphenicol, erythromycins, sulfonamides or tetracyclines may interfere with the bactericidal effects of penicillins. This has been demonstrated in vitro; however, the clinical significance of this interaction is not well documented.

Probenecid:

Probenecid may decrease renal tubular secretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.

Drug/Laboratory Test Interactions:

After treatment with amoxicillin, a false-positive reaction for glucose in the urine may occur with copper sulphate tests (Benedict's solution, fehling's solution, or Clinitest tablets) but not with enzyme based tests..

Allopurinol

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

Methotrexate

Excretion of methotrexate is reduced by penicillins; increased risk of toxicity.

Oral typhoid vaccine

The oral typhoid vaccine is inactivated by antibacterials

Sulfinpyrazone

Excretion of penicillins is reduced by sulfinpyrazone.

Anticoagulants

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

Muscle relaxants: Piperacillin (and possibly other penicillins) enhance the effects of non-depolarising muscle relaxants and suxamethonium.

Antibacterials: Absorption of phenoxymethylpenicillin (and possibly other penicillins) reduced by neomycin.

Guar Gum: Reduced absorption of penicillins.

Digoxin: An increase in the absorption of digoxin is possible on concurrent administration with amoxicillin.

4.6 Pregnancy and Lactation

Animal studies with amoxicillin have shown no teratogenic effects. Amoxicillin has been in extensive clinical use and its suitability in human pregnancy has been well documented in clinical studies. The product should only be used during pregnancy where potential benefits outweigh the potential risks associated with treatment.

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 breast-fed infant.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

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

Very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000)

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

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

Infections and Infestations

Very rare: Mucocutaneous candidiasis

Blood and lymphatic system disorders:

Very rare: As with other beta-lactam antibiotics, reversible leucopenia (including severe neutropenia and agranulocytosis), reversible thrombocytopenia and haemolytic anaemia have been reported.

Prolongation of bleeding time and prothrombin time have also been reported (see section 4.5 Interaction with other medicinal products and other forms of interaction).

Immune System disorders

Hypersensitivity reactions:

As with other antibiotics, severe allergic reactions including angioneurotic oedema, and anaphylaxis (see section 4.4 Special Warnings and Precautions for Use) serum sickness and hypersensitivity vasculitis have been reported rarely.

If hypersensitivity reaction occurs, the treatment should 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.

Gastrointestinal disorders:

Clinical Trial Data

*Common: Diarrhoea and nausea

*Uncommon: Vomiting

Post-marketing data

Very rare Antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis have been reported

Black hairy tongue.

Superficial tooth discolouration has been reported in children. This may respond to brushing.

Hepato-biliary disorders:

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT, but the significance of this is unclear.

Skin and subcutaneous tissue disorders

Clinical Trial Data

*Common: Skin rash,
*Uncommon: Pruritus and urticaria.

Post Marketing Data

Very rare: Skin reactions such as erythema multiforme and 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
Very rare: Crystalluria (See section 4.9 Overdose) can occur

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

4.9 Overdose

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. Amoxicillin crystalluria, in some cases leading to renal failure has been observed (see section 4.4 Special warnings and precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is a broad spectrum antibiotic which is bactericidal for both gram positive and gram negative bacteria.

Amoxicillin is well absorbed by the oral route. Oral administration, usually at convenient t.d.s. dosage, produces high serum levels independent of the time at which the food is taken. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic. It is rapidly bactericidal and possesses the safety profile of a penicillin.

5.2 Pharmacokinetic properties

Amoxicillin is rapidly absorbed from the gastro-intestinal tract; it is not converted to ampicillin. It is widely distributed and is reported to produce peak antibiotic plasma concentrations that are up to twice as high as those from the same dose of ampicillin. Peak plasma-amoxicillin concentrations of about 5 mcg/ml have been observed 2 hours after a dose of 250mg, with detectable amounts present for up to 8 hours. Doubling the dose can produce

double the concentration. The presence of food in the stomach does not appear to diminish absorption significantly.

Up to 20% is bound to plasma proteins in the circulation and plasma half-lives of about one hour have been reported. Amoxicillin diffuses across the placenta: little appears to be excreted in breast milk. It penetrates well into purulent and mucoid sputum and low concentrations have been found in ocular fluid. About 60% of an oral dose is excreted in the urine in six hours.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/min, very similar to the inulin clearance (GFR) in this population.

Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate B.P.
Disodium Edetate B.P.
Sodium Citrate B.P.
Citric Acid B.P.
Colloidal Anhydrous Silica B.P.
Sorbitol B.P.
Saccharin Sodium B.P.
Orange Bramble Flavour
Quinoline Yellow, E104
Xanthan Gum USNF

6.2 Incompatibilities

None Known

6.3 Shelf- life

Unopened container: 3 years
Reconstituted Suspension: 14 days.

6.4 Special precautions for storage

Dry powder: Store in a dry place below 25°C.

Reconstituted suspension: Store up to 14 days at 2°C-8°C in a refrigerator.

6.5 Nature and contents of container

High density polyethylene bottles with tamper-evident and child-resistant cap of the appropriate size to accommodate 100ml.

May also contain

Hugo Meding – polypropylene spoon – Article number 7208

Or

Hugo Meding – polypropylene spoon – Article number 7229

Or

5ml Medispoon

Or

A dosing syringe with bottle neck adaptor

6.6 Instructions for use/handling

To prepare add 82ml of potable water and shake until all contents are dispersed.

7. MARKETING AUTHORIZATION HOLDER

Athlone Laboratories Limited,
Ballymurray,
Co. Roscommon,
Ireland.

8 MARKETING AUTHORIZATION NUMBER

P.L. 06453/0050 250mg/5ml

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

21 July 1997

10 DATE OF (PARTIAL) REVISION OF THE TEXT

26/03/2012