SUMMARY OF PRODUCT CHARACTERISTICS

1 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 250 mg.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Pale yellow powder for reconstitution as suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of infection

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

Upper respiratory infections

Otitis media

Acute and chronic bronchitis

Chronic bronchial sepsis

Lobar and bronchopneumonia

Cystitis, urethritis, pyelonephritis

Bacteriuria in pregnancy

Gynaecological infections including puerperal sepsis and septic abortion

Gonorrhoea

Peritonitis

Intra-abdominal sepsis

Septicaemia

Bacterial endocarditis

Typhoid and paratyphoid fever

Skin and soft tissue infections

Osteomyelitis

Dental abscess (as an adjunct to surgical management)

Helicobacter pylori eradication in peptic (duodenal and gastric) ulcer disease

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 clinical investigation should be considered.

Prophylaxis of 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.

Consideration should be given to official local guidance (e.g. national requirements) on the appropriate use of antibacterial agents. Susceptibility of the causative organisms to the treatment should be tested (if possible), although the therapy may be initiated before the results are available (see section 5.1).

4.2 Posology and method of administration

Posology

Treatment of infection

Adults (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-dosage therapy

(Maximum recommended oral dosage 6 g daily in divided doses):

A dosage of 3 g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short-course therapy

Simple acute urinary tract infection: two 3 g doses with 10-12 hours between the doses.

Dental abscess: two 3 g doses with 8 hours between the doses.

Gonorrhoea: single 3 g dose.

Paediatric population

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. In severe or recurrent acute otitis media, especially where compliance may be a problem, 750 mg twice a day for two days may be used as an alternative course of treatment in children aged 3 to 10 years.

Early Lyme disease (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.

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).

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

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

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

Helicobacter *eradication in peptic (duodenal and gastric) ulcer disease:*

Amoxicillin is recommended twice daily in association with a proton pump inhibitor and antimicrobial agents as detailed below:

[Omeprazole 40 mg daily, Amoxicillin 1 g BID, Clarithromycin 500 mg BID] x 7 days

or

[Omeprazole 40 mg daily, Amoxicillin 750 mg–1 g BID, Metronidazole 400 mg TID] x 7 days

Treatment should be continued for 2 to 3 days following the disappearance of symptoms. It is recommended that at least 10 days' treatment be given for any infection caused by beta-haemolytic streptococci in order to achieve eradication of the organism.

Prophylaxis of endocarditis

Condition		Adult's dosage (including elderly)	Children's dosage (<40kg)	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 amoxicillin orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	Note 1. If prophylaxis with amoxicillin is given twice within one month, emergence of resistant streptococci is unlikely to be a problem. Alternative antibiotics are recommended if more frequent prophylaxis is required, or if the patient has received a course of treatment with a penicillin during the previous month. Note 2. To minimise pain on injection, amoxicillin may be given as two injections of 500 mg dissolved in sterile 1% lidocaine
	Patient having general anaesthetic: if oral antibiotics considered to be appropriate.	Initially 3 g amoxicillin orally 4 hours prior to anaesthesia, followed by 3 g orally (or 1 g IV or IM if oral dose not tolerated) as soon as possible after the operation.		
	Patient having general anaesthetic: if oral antibiotics not appropriate.	1 g amoxicillin IV or IM immediately before induction; with 500 mg orally, 6 hours later.		

Condition		Adult's dosage (including elderly)	Children's dosage (<40kg)	Notes
				solution (See Method of administration)
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 IV or IM with 120 mg gentamicin IV or IM immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure. Followed by (6 hours later): 500 mg amoxicillin orally.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	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.
Genitourinary 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. In the case of *obstetric and gynaecological procedures* and g*astrointestinal procedures*– routine prophylaxis is recommended only for patients with prosthetic heart valves.		Initially: 1 g amoxicillin IV or IM with 120 mg gentamicin IV or IM, immediately before induction. Followed by (6 hours later): 500 mg amoxicillin orally or IV or IM according to clinical condition.		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 IV or IM immediately before induction; 500 mg amoxicillin IV or IM 6 hours later.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	See Note 2 above. Note 5. The second dose of amoxicillin may be administered orally as amoxicillin

Condition		Adult's dosage (including elderly)	Children's dosage (<40kg)	Notes
				suspension.
	Patients with prosthetic heart valves.	Initially: 1 g amoxicillin IV or IM with 120 mg gentamicin IV or IM, immediately before induction; followed by (6 hours later) 500 mg amoxicillin IV or IM.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	See Notes 2, 3, 4 and 5 above.

Method of administration

Oral route

4.3 Contraindications

Hypersensitivity to the active substance, other penicillins or to any of the excipients in section 6.1. Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics e.g. ampicillin or cephalosporins. .

4.4 Special warnings and precautions for use

Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

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 (see section 4.2).

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in persons with a history of hypersensitivity to beta-lactam antibiotics (see section 4.3) and/ or a history of sensitivity to multiple allergens.

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

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

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 section 4.9).

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. 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 (see sections 4.5 and 4.8).

Paediatric population

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 medicinal products and other forms of interaction

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

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 the renal tubular secretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.

Allopurinol

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

Methotrexate

The excretion of methotrexate is reduced by penicillins; increased risk of toxicity.

Oral typhoid vaccine

The oral typhoid vaccine is inactivated by antibacterials.

Sulfinpyrazone

The excretion of penicillins is reduced by sulfinpyrazone.

AnticoagulantsIn the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin (see sections 4.4 and 4.8).

Muscle relaxants

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

Antibacterials

The 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.

Drug/laboratory test interactions

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies with amoxicillin have shown no teratogenic effects. Amoxicillin has been in extensive clinical use since 1972 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.

Breastfeeding

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

Amoxicillin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

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

Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

The majority of adverse events 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: Reversible leucopenia (including severe neutropenia and agranulocytosis), reversible thrombocytopenia and haemolytic anaemia have been reported.
Prolongation of bleeding time and prothrombin time (see also sections 4.4 and 4.5).

Immune system disorders

Very rare: Hypersensitivity reactions:
Severe allergic reactions including angioneurotic oedema, anaphylaxis (see section 4.4), serum sickness and hypersensitivity vasculitis.
If a hypersensitivity reaction occurs, 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.

Post-marketing data

Not known: Aseptic meningitis

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 can usually be removed by brushing.

Hepatobiliary disorders

Very rare: Hepatitis and cholestatic jaundice.
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
Crystalluria (see section 4.9) 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card scheme at www.mhra.gov.uk/yellowcard.

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).

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is a semi-synthetic, broad-spectrum penicillin, which is acid-resistant and has a similar antibacterial spectrum to ampicillin. It 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. It is rapidly bactericidal and possesses the safety profile of a penicillin.

The wide range of organisms sensitive to the bactericidal action of amoxicillin include:

Aerobes:

GRAM-POSITIVE	**GRAM-NEGATIVE**
Streptococcus faecalis	*Haemophilus influenzae*
Streptococcus pneumoniae	*Escherichia coli*
Streptococcus pyogenes	*Proteus mirabilis*
Streptococcus viridans	*Salmonella* species
Staphylococcus aureus	*Shigella* species
(penicillin-sensitive)	*Bordetella pertussis*
Corynebacterium species	*Brucella* species
Bacillus anthracis	*Neisseria gonorrhoeae*
Listeria monocytogenes	*Neisseria meningitidis*
	Vibrio cholerae
	Pasteurella septica

Anaerobes:

Clostridium species

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 250 mg, 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. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

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 from that of adults. Consequently, due to the deceased 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

Disodium edetate

Sodium citrate

Citric acid monohydrate

Colloidal anhydrous silica

Sorbitol

Saccharin sodium

Orange bramble flavour

Quinoline yYellow E104

Xanthan gum

6.2 Incompatibilities

Not applicable

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 7229

Or

5ml Medispoon

Or

A dosing syringe with bottle neck adaptor

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited

Ballymurray

Co. Roscommon

Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 06453/0050

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21 July 1997

10 DATE OF REVISION OF THE TEXT

3rd December 2015