SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 250mg Capsules BP

Respillin 250mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250 mg of amoxicillin as amoxicillin trihydrate Ph.Eur.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules size 2 for the 250 mg capsules, with a scarlet/ivory opaque hard gelatin capsule with 'AMOX 250' printed on the capsule shell.

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 such as:

Upper respiratory tract infection

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 children with urinary tract infection the need for 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

250 mg three times daily, increasing to 500 mg 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.

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

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

Paediatric population

The capsule formulation of amoxicillin may not be suitable for children. In such cases a suspension formulation should be used.

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

Children weighing < 40kg

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.

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)

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.

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 solution (See Method of
	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
				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 syrup SF/DF.

Condition		Adult's dosage (including elderly)	Children's dosage (<40kg)	Notes
	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.

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).

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).

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.

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

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

In 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

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

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, however, better absorbed after oral administration, yielding blood levels approximately twice as high as those obtained with similar doses of ampicillin.

Amoxicillin is used for the same purposes as ampicillin and is especially suitable for the treatment of infections of the urinary and respiratory tracts by ampicillin-sensitive organisms. 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 trihydrate is rapidly absorbed when given by mouth. 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 per ml have been observed 2 hours after a dose of 250 mg. 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.

Amoxicillin is mainly excreted in the urine, about 60% being excreted in 6 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 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

Magnesium stearate Ph. Eur.

Maize starch Ph. Eur.

Capsule shell

Erythrosin E127

Quinoline yellow E104

Titanium dioxide E171

Red iron oxide E172

Gelatin NF

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 25^{o}C. Protect from light and moisture.

6.5 Nature and contents of container

An opaque white polypropylene securitainer with a polyethylene air proof security cap.

15, 18, 20, 21, 28, 30, 50, 100 or 500 capsule pack sizes contain a polyethylene jayfilla

The 1,000 capsule pack size contains a polyethylene bag.

Or an opaque PVDC/PVC blister 250/40 with an aluminium lidding foil 20 micron containing 15, 18, 20, 21, 28, 30, 50, 100, 500 or 1,000 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited

Ballymurray

Co. Roscommon

Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 6453/0017

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First granted 4/11/1988; Renewal granted 7/4/1995.

10 DATE OF REVISION OF THE TEXT

30th November 2015

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pinamox 250mg hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains Amoxicillin Trihydrate equivalent to 250mg of anhydrous amoxicillin.

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.

Size 2 hard gelatin capsules with scarlet caps and ivory bodies, printed in black with a 'P' logo and 'Pinamox 250' and containing an off-white granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Pinamox is a broad spectrum antibiotic, indicated for the treatment of commonly occurring bacterial infections such as:

- Upper respiratory tract infections
- Otitis media
- Acute and chronic bronchitis
- 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 (see also Oral prophylaxis of endocarditis)
- Typhoid and paratyphoid fever
- Skin and soft tissue infections
- Dental abscess (as adjunct to surgical management)

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

Parenteral therapy is indicated if the oral route is considered impracticable or unsuitable and particularly for the urgent treatment of severe episodes of the above conditions.

In children: urinary tract infection (the need for investigation should be considered).

4.2 Posology and method of administration

Pinamox Capsules are for oral use.

The absorption of Pinamox is virtually unimpaired by the presence of food.

Adults and children weighing over 40kg

Standard adult dosage: The usual daily dosage is 750mg in divided doses (i.e. 250mg three times daily by the oral route).

In cases of severe infection the dosage may be doubled, or amoxicillin given by injection.

High dosage therapy: (maximum recommended oral dosage of 6g daily in divided doses): A dosage of 3g 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 3g doses with 10-12 hours between the doses.
Gonorrhoea: 3g as a single dose.
Dental Abscess: two 3g doses with 8 hours between the doses.

Prophylaxis of endocarditis:

For dental procedures where an oral dose is appropriate:
Adults and children weighing over 40kg:
3g dose followed by (6 hours later) a further 3g dose (or a 1g IM if oral dose not tolerated) if necessary.

Paediatric population

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.

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

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

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

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 and children weighing over 40kg:

Glomerular filtration rate	Oral treatment
> 30 ml/min	No adjustment necessary
10-30 ml/min	Pinamox Max 500mg b.d.
< 10ml/min	Pinamox 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)

For small children (younger than 6 years of age) appropriate paediatric formulation should be used.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

Use in patients with a history of hypersensitivity to beta-lactam antibiotics including penicillins, ampicillin or cephalosporins.

4.4 Special warnings and precautions for use

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. 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. Attention should also be paid to possible cross-reactivity with other beta-lactam antibiotics e.g. cephalosporins (see section 4.3)

If an allergic reaction occurs, amoxicillin should be discontinued and appropriate alternative therapy instituted.

Amoxicillin should be avoided if infectious mononucleosis (glandular fever) is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Prolonged use of anti-infective agent may occasionally result in overgrowth of non-susceptible organisms

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 concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Dosage should be adjusted in patients with renal impairment (see Section 4.2).
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.

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

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

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 penicillin's. This has been demonstrated in vitro; however, the clinical significance of this interaction is not well documented.

Probenecid:
Probenecid may decrease renal tubular excretionof amoxicillin. Concurrent use with amoxicillin may result in increased and prolonged blood levels of amoxicillin.

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, such as Clinistix and Test-Tape.

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

Methotrexate:
Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

Anticoagulants:
In 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.

4.6 Fertility, pregnancy and lactation

Pregnancy:
The product should not be used during pregnancy unless considered essential by the physician. Animal studies 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. Amoxicillin may be used during pregnancy where potential benefits outweigh the potential risks associated with treatment.
Breast-feeding:
Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation and of central nervous system toxicity (due to prematurity of the blood-brain barrier) 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 or use machines

4.8 Undesirable effects

Evaluation of undesirable effects is based on the following frequency information: 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 (frequency cannot be estimated from available data).

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 (AEs) 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 section 4.4 Special warnings and precautions for use).

Immune System disorders:
Very rare: As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis (see section 4.4 Special Warnings and precautions for use) serum sickness-like syndrome and hypersensitivity vasculitis

If 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.
Aseptic meningitis

Infections and Infestations:
Very rare: Mucocutaneous candidiasis

Gastrointestinal disorders:
*Common: Diarrhoea and nausea
*Uncommon: Vomiting
Very rare: Antibiotic associated colitis (including pseudomembranous 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 (for suspension and chewable tablet formulations only).

Hepatobiliary 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: Pruritus and urticaria
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 Overdose).

*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:

HPRA Pharmacovigilance

Earlsfort Terrace

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4.9 Overdose

Gross overdose will produce very high urinary concentrations, more so after parenteral administration. Symptoms of water/electrolyte imbalance should be treated symptomatically. Problems are unlikely to occur if adequate fluid intake and urinary output are maintained; however amoxicillin crystalluria in some cases leading to renal failure has been observed (see Section 4.4, Special Warnings and Precautions for Use). More specific measures may be necessary inpatients with impaired renal function: the antibiotic is removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is a semisynthetic penicillin, which is acid resistant and has a similar antibacterial spectrum to Ampicillin. It acts by inhibiting bacterial cell-wall synthesis.

It is, however, better absorbed after oral administration, yielding blood levels approximately twice as high as those obtained with similar doses of Ampicillin.

Amoxicillin is used for the same purposes as Ampicillin and is especially suitable for the treatment of infections of the urinary and respiratory tracts by Ampicillin sensitive organisms.

5.2 Pharmacokinetic Properties

Absorption:
Amoxicillin is stable to gastric acid and 50 - 90% of a dose is absorbed after oral administration: absorption is more complete than that of Ampicillin and it is not greatly influenced by the presence of food.

Blood Concentration:
After an oral dose of 500mg, peak serum concentration of 3 to 20ug/ml are attained in 1 to 2 hours, detectable concentrations are present after 8 hours. Peak concentrations occur earlier in children and infants, but later in neonates.

Half-life:
Serum half-life, 1 hour which may be increased to 15 hours in renal failure.

Distribution:
Enters most tissues and fluid but is not detectable in the cerebrospinal fluid even when meninges are inflamed; crosses the placenta and small amounts are secreted in the milk; volume of distribution at steady-state serum concentrations, about 0.3 litres/kilogram body weight; protein binding, 15 - 25% bound to plasma protein.

Metabolic Reactions:
Metabolised to inactive metabolites and 10 - 25% appears to be converted to penicilloic acid.

Excretion:
35 - 45% is excreted in the urine after an oral dose; urinary excretion is delayed by probenecid and it also occurs more slowly in the newborn; small amounts are excreted in the bile.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75-2ml/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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate
Maize Starch
Capsule Shell
Erythrosine E127
Quinoline Yellow E104
Titanium Dioxide E171
Red Iron Oxide E172
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25 ^{O} C.

6.5 Nature and contents of container

An opaque white polypropylene securitainer with a polyethylene air proof security cap.

30, 100 or 500 capsule pack sizes contain a polyethylene jayfilla

1000 capsule pack size contain a polyethylene bag.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited,

Ballymurray,

Co. Roscommon,

Ireland

8 MARKETING AUTHORISATION NUMBER

PA 298/10/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

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