SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 250mg/5ml Oral Suspension BP **And**
Respillin 250mg/5ml Oral Suspension BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of suspension contains 250mg of amoxicillin as amoxicillin trihydrate Ph.Eur

3 PHARMACEUTICAL FORM

Powder for oral suspension

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Amoxicillin is a broad-spectrum anti-bacterial agent recommended for the treatment
In Children of -
Upper respiratory infections
Otitis media
Acute and chronic bronchitis
Lobar and bronchopneumonia
Cystitis, urethritis pyelonephritis
Peritonitis
Intra-abdominal sepsis
Septicaemia
Bacterial endocarditis
Typhoid and paratyphoid fever
Skin and soft tissue infections
Osteomyelitis

In Adults in addition to the above
Bacteriuria in pregnancy
Gynaecological infections including puerperal sepsis and septic abortion
Gonorrhoea.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults: 250mg three times daily by the oral route. In cases of severe infection the dosage may be doubled.

In simple, acute urinary tract infection in adults: two 3g doses with 10 - 12 hours between the doses.

A single dose of 3g is recommended for the treatment of gonorrhoea.

Oral prophylaxis of endocarditis: A single 3g dose about one hour before the procedure from which bacteraemia may arise (N.B Oral dosage is generally inappropriate for patients who require a general anaesthetic).

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.

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 CONTRAINDICATIONS

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

4.4 SPECIAL WARNINGS AND 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 (morbilliform) rashes have been associated with glandular fever, cytomegalovirus infection and lymphocytic leukaemia (acute or chronic) 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 product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucosegalactose malabsorption or sucrase-isomaltase insufficiency 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:

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.

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

Guar Gum: Reduced absorption of penicillins.

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

Amoxicillin has no effect on ability to drive

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 pencillins.

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 semisynthetic 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.

5.2 PHARMACOKINETIC PROPERTIES

Absorption: Amoxicillin is stable to gastric acid and 50 to 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 500 mg, peak serum concentration of 3 to 20 ug/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 fluids 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 to 25 % bound to plasma protein.

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

Excretion: 35 to 45 % is excreted in the urine after an oral dose; urinary excretion is delayed by probenecid and it also occurs more slowly in the new born; 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 – 2 ml/min, very similar to the inuline 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
Disodium edetate
Sodium citrate anhydrous
Lemon flavour powder
Quinoline yellow
Sucrose

6.2 INCOMPATIBILITIES

None stated

6.3 SHELF LIFE

Unopened container: a shelf life of 3 years
Reconstituted suspension: a shelf life of 7 days

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Protect from light.
Dry powder: Store in a dry place below 25°C.
Reconstituted suspension: Store for 7 days at 2°C-8°C in a refrigerator.

6.5 NATURE AND CONTENTS OF CONTAINER

Natural high density polyethylene bottle 150ml with white cap with a blue TE band containing 100ml of suspension on reconstitution
Natural high density polyethylene bottle 150ml with a child resistant /tamper evident cap containing 100 ml of suspension on reconstitution

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORIZATION HOLDER

Athlone laboratories limited,
Ballymurray,
Co. Roscommon,
Ireland.

8 MARKETING AUTHORISATION NUMBER

PL 6453/0022

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

17/10/1990

10 DATE OF REVISION OF TEXT

25/01/2012

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pinamox (Amoxicillin Oral Suspension BP) 250mg / 5ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted as directed the powder yields a mixture containing amoxicillin trihydrate B.P. equivalent to 250mg of amoxicillin per 5 ml.

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Powder for oral suspension.
A pale yellow crystalline powder for oral suspension with the odour and flavour of lemon.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

(a) Properties
A broad spectrum antibiotic well absorbed after oral administration, reaching peak levels 1-2 hours later, and excreted in urine.

(b) Indications for use
In the treatment of infections due to organisms sensitive to amoxicillin and in the oral prophylaxis of endocarditis related to dental procedures, and acute uncomplicated gonorrhoea.

4.2 Posology and method of administration

Adults and children over 10 years of age:
The usual total daily dosage is 750 mg in three divided doses.

In the treatment of uncomplicated gonorrhoea a single dose of 3g may be used.

Children

6 - 10 years: The usual total daily dosage is 375 - 750 mg in divided doses.

2 - 5 years: 375mg daily in divided doses.

Under 2 years: 100 - 300mg daily in divided doses.

Dosage may be doubled in cases of severe infections

Prophylaxis:

Adults: A single dose of 3g prior to dental procedure.

Children: A single dose of 1 to 1.5g prior to the procedure.
In patients with renal insufficiency, total daily dosage may need reduction if excretion of drug is delayed.

For oral administration only.

4.3 Contraindications

Use in patients with hypersensitivity to penicillins, including ampicillin or cephalosporins.

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.

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

If an 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 also be administered as indicated.

Amoxicillin Oral Suspension BP 250mg/5ml contains 2.98g of sucrose per dose. This should be taken into account in patients with diabetes mellitus.

This medicinal product contains 3.372mmol sodium per 3g dose. To be taken into consideration by patients on controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

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

<u>Bacteriostatic antibiotics</u>
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.

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

<u>Drug/Laborotory Test Interactions</u>

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.

4.6 Pregnancy and lactation

The product should not be used during pregnancy unless considered essential by the physician. Amoxicillin is excreted in breast milk, presenting the risk of candidiasis and also of central nervous system toxicity due to prematurity of the blood brain barrier. There is a theoretical possibility of later sensitisation.

4.7 Effects on ability to drive and use machines

Amoxicillin has no effect on the ability to drive.

4.8 Undesirable effects

Side effects include gastrointestinal upset, including nausea, vomiting and diarrhoea. Macular, maculopapular rashes and urticaria may occur.

Patients with infectious mononucleosis frequently develop rashes with ampicillin therapy. A similar tendency may be apparent with amoxicillin.

4.9 Overdose

Since amoxicillin is a penicillin, problems of overdosage are unlikely to be encountered.

In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures as required. Amoxicillin can be removed from the circulation 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 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 Pharmacokeinetic properties

<u>Absorption</u>
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 hour, 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 probenicide and it also occurs more slowly in the new born; small amounts are excreted in the bile.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate (E211)
Disodium Edetate
Sodium Citrate Anhydrous
Lemon Flavour powder
Quinoline Yellow (E104)
Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened container: 2 years
Reconstituted powder: 7 days

6.4 Special precautions for storage

Dry powder: Do not store above 25°C. Store in original container.
Reconstituted powder: Store in a refrigerator (2°C-8°C).

6.5 Nature and contents of container

Natural high-density polyethylene bottle with a tamper evident cap containing 100ml of suspension on reconstitution.
Natural high-density polyethylene bottle with a tamper evident/child resistant cap containing 100ml of suspension on reconstitution.

A spoon with graduations of 1.25ml, 2.5ml and 5 ml measures or a spoon with a 5ml graduation may be supplied with packs of this product.

Not all pack sizes may be marketed.

6.5 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

To prepare a 100ml solution add 61mls of water and shake well.
The reconstituted powder should be a yellow solution with a lemon odour and flavour.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA 298/10/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 18th May 1988
Date of last renewal: 18th May 2008

10 DATE OF (PARTIAL) REVISION OF THE TEXT

August 2011