

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 500 mg Capsules BP  
Respillin 500mg Capsules

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 500 mg of amoxicillin as amoxicillin trihydrate Ph.Eur.

### 3 PHARMACEUTICAL FORM

Capsules, size 0 for the 500mg capsules, with a scarlet/ivory opaque hard gelatin capsule with 'AMOX 500' 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

Lobar and bronchopneumonia

Cystitis, urethritis, pyelonephritis

Bacteriuria in pregnancy

Gynaecological infections including puerperal sepsis and septic abortion

Gonorrhoea

Peritonitis

Intra-abdominal sepsis

Septicaemia

Peritonitis

Intra-abdominal sepsis

Septicaemia

Bacterial endocarditis

Typhoid and paratyphoid fever

Skin and soft tissue infections

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.

## 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

For Oral Administration Only

### **TREATMENT OF INFECTION:**

#### **Adult dosage (Including elderly patients)**

**Standard adult dosage:** 250mg three times daily, increasing to 500mg three times daily for more severe infections.

**High dosage therapy:** (Maximum recommended oral dosage 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. Dental abscess: two 3g doses with 8 hours between the doses. Gonorrhoea: Single 3g 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).

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

#### **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 40mg daily, Amoxicillin 1g BID, Clarithromycin 500mg BID]  
x 7 days

or

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

#### **Children's dosage**

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

#### **Children weighing < 40 kg**

The capsule formulation of Amoxicillin Capsules BP 250mg may not be suitable for children. In such cases a suspension formulation should be used.

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.

### **Dental procedures (prophylaxis for endocarditis):**

#### **Adult:**

Patients not having general anaesthetic: 3g 1 hour before procedure, a second dose may be given 6 hours later if considered necessary.

Patients having general anaesthetic (where oral antibiotics are considered appropriate) 3g 4 hours prior to anaesthesia followed by 3g 6 hours after the initial dose.

#### **Children weighing < 40 kg**

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

The capsule formulation of Amoxicillin Capsules BP 250mg may not be suitable for children. In such cases a suspension formulation should be used.

NOTE: 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.

#### 4.3 CONTRA-INDICATIONS

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

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.

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.

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

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).

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 Overdose).

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 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.

#### 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 OVERDOSAGE

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 PARTICULARS

### 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.

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

**Aerobes:**

**GRAM-POSITIVE**

Streptococcus faecalis  
Streptococcus pneumoniae  
Streptococcus pyogenes  
Streptococcus viridans  
Staphylococcus aureus  
(penicillin sensitive)

Corynebacterium species  
Bacillus anthracis  
Listeria monocytogenes

**GRAM-NEGATIVE**

Haemophilus influenzae  
Escherichia coli  
Protease mirabilis  
Salmonella species  
Shigella species  
Bordetella pertussis  
Brucella species  
Neisseria gonorrhoeae  
Neisseria meningitidis  
Vibrio cholera  
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 5ug per ml have been observed 2 hours after a dose of 250mg. The presence of food in the stomach does not appear to diminish absorption significantly.

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 0.75-2ml/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**

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

**6.2 INCOMPATIBILITIES**

None stated

**6.3 SHELF LIFE**

48 months

**6.4 SPECIAL PRECAUTIONS FOR STORAGE**

Store below 25°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 or 100 capsule pack sizes contain a polyethylene jayfilla  
500 capsule pack size contain 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 and 500 capsules.

**6.6 INSTRUCTIONS FOR USE/HANDLING**

No special instructions

**7 MARKETING AUTHORIZATION HOLDER**

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

**8 MARKETING AUTHORIZATION NUMBER**

PL 6453/0018

**9 DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION**

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

**10      DATE OF PARTIAL REVISION OF TEXT**

21<sup>st</sup> Mar 2012

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Pinamox 500mg hard Capsules

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each hard capsule contains Amoxicillin Trihydrate equivalent to 500mg of anhydrous amoxicillin.

For a full list of excipients see section 6.1

### **3 PHARMACEUTICAL FORM**

Capsule, hard.

Size zero elongated hard gelatin capsules with scarlet caps and ivory bodies, printed in black with a 'P' logo and 'Pinamox 500' and containing an off-white granular powder.

### **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 3 g 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 3 g prior to dental procedure.

*Children:*

A single dose of 1 to 1.5 g 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 Contra-indications**

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.

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.

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.

#### **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 such as Clinistix and Tes-Tape.

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

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

#### **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**

None.

#### **4.8 Undesirable effects**

*Hypersensitivity reactions:*

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

Skin rash, pruritis and urticaria have been reported occasionally. Rarely, skin reactions such as erythema multiforme and Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP), serum sickness like syndrome and hypersensitivity vasculitis have been reported.

If hypersensitivity reaction occurs, the treatment should be discontinued.

As with other antibiotics, severe allergic reactions including angioneurotic oedema and anaphylaxis (see section 4.4) have been reported rarely.

*Renal and Urinary Tract disorders :*

Interstitial nephritis and crystalluria can occur rarely.

*Gastrointestinal reactions:*

Side effects include gastrointestinal upset, including nausea, vomiting, indigestion and diarrhoea. Mucocutaneous candidiasis and antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis have been reported rarely.

Nausea although uncommon is more often associated with higher oral doses.

As with other antibiotics the incidence of gastrointestinal side effects may be raised in children under 2 years.

*Hepatic effects :*

A moderate rise in AST and/or ALT and alkaline phosphatases have occasionally been noted but the significance of this is unclear. As with other beta-lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely.

Hepatic reactions have been reported more frequently in males and elderly patients, particularly those over 65 years. The risk increases with duration of treatment longer than 14 days. These reactions have been very rarely reported in children. In some cases signs and symptoms of hepatic reactions may not occur until several weeks after treatment has ended. These reactions are usually reversible, but may be severe and very rarely deaths have been reported.

*Haematological effects :*

As with other beta-lactam antibiotics, reversible leucopenia (including severe neutropenia and agranulocytosis), reversible thrombocytopenia and haemolytic anaemia have been reported rarely. Prolongation of bleeding time and prothrombin time have also been reported rarely (refer to section 4).

*CNS effects :*

CNS effects have been seen rarely. They include hyperactivity, dizziness, headache and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

#### **4.9 Overdose**

Since amoxicillin is a penicillin, problems of overdosage are unlikely to be encountered. Gastrointestinal symptoms and disturbance of fluid and electrolyte balance may occur.

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.

### **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 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 probenecide and it also occurs more slowly in the newborn; small amounts are excreted in the bile.

**5.3 Preclinical safety data**

Not applicable.

**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 °C.

**6.5 Nature and contents of container**

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

30 or 100 capsule pack sizes contain a polyethylene jayfilla.

500 capsule pack size contain a polyethylene bag.

Not all pack sizes may be marketed.

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

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

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

**8 MARKETING AUTHORISATION NUMBER**

PA 298/10/4

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**

Date of first authorisation: 29<sup>th</sup> June 1988

Date of last renewal: 29<sup>th</sup> June 2008

**10 DATE OF (PARTIAL) REVISION OF THE TEXT**

18/05/2011