SUMMARY OF PRODUCT CHARACTERISTICS:

1. NAME OF THE MEDICINAL PRODUCT

Amoxicillin 3 g Sachet Sugar Free **and**
Respillin 3g Sachet Sugar Free.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 3g Amoxicillin as Amoxicillin Trihydrate B.P./ Ph.Eur

Contains sodium and sorbitol.

For the full list of excipients, See Section 6.1

3. PHARMACEUTICAL FORM

Powder for oral suspension

A lemon coloured, dry, free flowing powder with a characteristic lemon flavour.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

Amoxicillin 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
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)

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 organism to the treatment should be tested (if possible), although the therapy may be initiated before the results are available.

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

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*
Clostridium species	*Brucella* species
Corynebacterium species	*Neisseria gonorrhoeae*
Bacillus anthracis	*Neisseria meningitidis*
Listeria monocytogenes	*Vibrio cholerae*
	Pasteurella septica

4.2. Posology and method of administration

Administration: Oral

Adults (including the elderly)

For severe infection of the respiratory tract:

3 g twice daily

For simple acute urinary tract infection:

Two 3 g doses with 10-12 hours between doses

For dental abscess:

Two 3 g doses with 8 hours between doses

For gonorrhoea:

Single 3g dose

Prophylaxis of endocarditis in dental procedures:

For patients undergoing extraction, scaling or surgery involving gingival tissues and who have not received penicillin in the previous month:

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

b) Patients having general anaesthetic and oral antibiotic considered appropriate:
3g orally 4 hours prior to anaesthetic followed by 3g orally as soon as possible after the operation

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 30ml/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

Children
Not
recommended

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

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.

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

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

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

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

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).

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.

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).

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

The maximum single dose of 6g of Amoxicillin contains 11g of sorbitol. May have a mild laxative effect. Calorific value 2.6 kcal/g sorbitol.

Patients with rare hereditary problems of fructose intolerance should not take this medicine**.**

The maximum single dose of 6g of Amoxicillin contains 149mg of sodium. To be taken into consideration by patients on a 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:

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
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).

4.6. 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.

Lactation
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

Adverse effects on the ability to drive or operate machinery have not been observed.

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.

Unknown: 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. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by 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, 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)

*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 Special warnings and precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5.0 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibiotic, penicillins ATC-Code: J01CA04.

5.1. Pharmacodynamic properties

General Properties:
Amoxicillin is an aminopenicillin that has a bactericidal action due to its inhibition of the synthesis of the bacterial cell wall.

Breakpoints
The MIC breakpoints for susceptible organisms vary according to species.
Enterobacteriaceae are considered susceptible when inhibited at ≤8mg/L amoxicillin.
From NCCLS recommendations and using NCCLS specified methods:
M.catarrhalis (∃-lactamase negative) is considered susceptible at ≤0.25 µg/ml and resistant at ≥0.5 µg/ml.

H. Influenzae (β-lactamase negative) is considered susceptible at ≤1 µg/ml and resistant at ≥4 µg/ml.:
S. pneumoniae is considered susceptible to amoxicillin at MIC ≥0.5 µg/ml resistant at ≥2 µg/ml.

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. This information gives only approximate guidance on the probability as to whether microorganisms will be susceptible to amoxicillin or not.

SUSCEPTIBLE:

Gram-positive aerobes	**Frequency of resistance ranges in EU (extreme values)**
Bacillus anthracis	
Corynebacterium spp [§]	
Enterococcus faecalis [§]	
Listeria monocytogenes	
Streptococcus agalactiae	
Streptococcus bovis	
Streptococcus pneumoniae #	*4.6 - 51.4%*
Streptococcus pyogenes #	
Streptococcus viridans [§]	
Gram-negative aerobes:	
Brucella spp#	
Escherichia coli	*46.7%*
Haemophilus influenzae	*2-31.7%* [Ψ]
Haemophilus parainfluenzae	*15.3%*
Neisseria gonorrhoeae [§]	*12-80%* [b]
Neisseria meningitidis#	
Proteus mirabilis	*28%*
Salmonella spp [§]	
Shigella spp [§]	
Vibrio cholerae	

Anaerobes
Bacteroides melaninogenicus [§]
Clostridium spp
Fusobacterium ssp.[§]
Peptostreptococci

RESISTANT
Gram-positive aerobes
Staphylococci (β-lactamase producing strains)
Gram-negative aerobes
Acinetobacter spp

Citrobacter spp
Enterobacter spp
Klebsiella spp
Moraxella catarrhalis
Proteus vulgaris
Providencia spp
Pseudomonas spp

Anaerobes
Bacteroides fragilis

Others
Chlamydia
Mycoplasma
Rickettsia
a) % of beta-lactamase production
b)% of penicillin-resistance (including intermediate resistance)
No β-lactamase producers have as yet been reported for these bacterial species
§ variably susceptible; susceptibility is therefore unpredictable in the absence of susceptibility testing
Bacteria may be resistance to amoxicillin (and, thus, ampicillin) due to production of beta-lactamases which hydrolyse aminopenicillins, due to alteration in penicillin-binding proteins, due to impermeability to the drug, or due to drug efflux pumps. One or more of these mechanisms may co-exist in the same organism, leading to variable and unpredictable cross-resistance to other beta-lactams and to antibacterial drugs of other classes.

5.2 Pharmacokinetic properties

Absorption:
The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 250mg and 750mg the bioavailability (parameters: AUC and/or recovery in urine) is linearly proportional to the dose. At higher doses the extent of absorption decreases. Absorption is not affected by concomitant food intake. Oral administration of a single dose of 500mg amoxicillin results in plasma concentrations of 6-11mg/l. After administration of a single dose of 3g amoxicillin, the plasma concentrations reach 27mg/l. Peak plasma concentrations are present about 1-2 hours after administration.

Distribution:
Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. Amoxicillin can penetrate inflamed meninges and enter the cerebrospinal fluid. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.

Biotransformation and elimination:
The main route of excretion of amoxicillin is the kidney. About 60-80% of an oral dose of amoxicillin is excreted in unchanged active form in the urine within 6 hours of administration, and a small fraction is excreted in the bile. Approximately 7-25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1-1.5 hour. In patients with end-stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

5.3. Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and reprotoxicity.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium edetate.
Colloidal Anhydrous Silica
Sodium citrate.
Lemon flavour.
Quinoline yellow.
Xanthan gum.
Sorbitol.

6.2. Incompatibilities

Not Applicable

6.3. Shelf life

Product in an unopened sachet: 36 Months

6.4. Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5. Nature and contents of container

Unit Dose foils laminate sachet made from Gloss Coated Paper, Polyethylene and Aluminum layers. Each outer cardboard carton contains 2 or 14 foil lined sachets.

6.6. Special precautions for disposal and other handling

Each sachet carries instructions for preparation and each pack contains a patient information leaflet. To be taken immediately following reconstitution.

7. MARKETING AUTHORISATION HOLDER

Athlone Laboratories, Ballymurray, Co. Roscommon, Ireland.

8. MARKETING AUTHORISATION NUMBER

PL 6453/0054

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20 March 2003

10. DATE OF REVISION OF THE TEXT

3rd December 2015