AMOXICILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0010)

AMOXICILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0011)

AMOXICILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0012)

UKPAR

TABLE OF CONTENTS

Lay Summary Page 2
Scientific discussion Page 3
Steps taken for assessment Page 12
Steps taken after authorisation – summary Page 13
Summary of Product Characteristics
Product Information Leaflet
Labelling
AMOXICILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0010)

AMOXICILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0011)

AMOXICILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0012)

LAY SUMMARY

On 26th March 2009, the MHRA granted Bowmed Limited Marketing Authorisations (licences) for the medicinal products Amoxicillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 24610/0010-12). These are prescription-only medicines (POM) used to treat a wide range of bacterial infections, which may include those affecting the:

- Chest (bronchitis or pneumonia)
- Tonsils (tonsillitis)
- Ears (otitis media)
- Sinuses (sinusitis)
- Kidneys, bladder or the urethra (the tube which carries urine from the bladder)
- Female reproductive system, including infections caused by difficulties during childbirth (puerperal sepsis and septic abortion)
- Abdomen (intra-abdominal sepsis and peritonitis)
- Heart (endocarditis)
- Blood (septicaemia)
- Teeth and gums
- Skin (including animal bites)

Amoxicillin injection can also be used to treat gonorrhoea (a sexually transmitted infection), infections associated with pregnancy and typhoid and paratyphoid (fevers caused by a group of bacteria called Salmonella).

Amoxicillin Powder for Solution for Injection or Infusion contains the active substance amoxicillin (as amoxicillin sodium), which is one of a group of medicines called “penicillins”. These medicines are also known as “antibiotics” and they work by killing the bacteria that cause infections.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Amoxicillin Powder for Solution for Injection or Infusion outweigh the risks, hence Marketing Authorisations have been granted.
AMOXICILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0010)

AMOXICILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0011)

AMOXICILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0012)

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Pharmaceutical assessment</td>
<td>5</td>
</tr>
<tr>
<td>Preclinical assessment</td>
<td>7</td>
</tr>
<tr>
<td>Clinical assessment (including statistical assessment)</td>
<td>8</td>
</tr>
<tr>
<td>Overall conclusions and risk benefit assessment</td>
<td>11</td>
</tr>
</tbody>
</table>
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal products Amoxicillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion (PL 24610/0010-12) on 26th March 2009 to Bowmed Limited.

These are applications for three strengths of Amoxicillin Powder for Solution for Injection or Infusion, submitted as generic applications according to Article 10(1) of Directive 2001/83/EC, cross-referring to Amoxil Vials for Injection 250mg, 500mg and 1g (PL 00038/0221, 222 and 225, respectively), which were originally granted licences to Beecham Group Plc over 10 years ago.

The products contain the active ingredient amoxicillin, an aminopenicillin that is used principally for the treatment of infections caused by susceptible gram-negative bacteria (e.g., *Haemophilus influenzae*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella*). Amoxicillin is also used for the treatment of infections caused by susceptible gram-positive bacteria (e.g., *Streptococcus pneumoniae*, enterococci, nonpenicillinase-producing staphylococci, *Listeria*). However, like other aminopenicillins, amoxicillin generally should not be used for the treatment of streptococcal or staphylococcal infections (when a natural penicillin would be effective).

Amoxicillin Powder for Solution for Injection or Infusion is 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

In children with urinary tract infection, the need for investigation should be considered. Amoxicillin may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE
Amoxicillin sodium
INN: Amoxicillin sodium
Chemical Name: Sodium(2S,5R,6R)-6-[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate
Molecular Formula: C_{16}H_{18}N_{3}NaO_{5}S
Structure:

Molecular Weight: 387.38
Appearance: White or almost white powder, very hygroscopic, very soluble in water, sparingly soluble in ethanol, very slightly soluble in acetone.

Amoxicillin sodium is the subject of a European Pharmacopoeia monograph.

The manufacture and control of active amoxicillin sodium is covered by a European Directorate for the Quality of Medicines Certificate of Suitability.

Satisfactory specifications have been provided for all packaging components. The primary packaging has been shown to comply with current legislation concerning the use of materials in contact with foodstuff.

An appropriate retest period has been stated for the active, based on stability data submitted.

DRUG PRODUCT
Other ingredients
There are no excipients used in the manufacture of the finished products.

Pharmaceutical development
A satisfactory development rationale has been provided for these products.

Manufacture
A description and flow-chart of the manufacturing method has been provided.

In-process controls are satisfactory based on process validation data and controls on the finished product. Validation data have been provided from batches of each strength of the finished product and the results appear satisfactory.
Finished product specification
The finished product specifications are satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container closure system
The finished product is packaged in clear Type III glass vials with chlorobutyl rubber closure, in cartons of 1, 5, 10, 20 or 50 vials. Not all pack sizes may be marketed, however, the marketing authorisation holder has committed to submitting the relevant mock-ups to the regulatory authorities before marketing any new pack size.

Satisfactory specifications and certificates of analysis have been provided for the packaging components. The applicant has confirmed that the packaging requirements comply with EU requirements for contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 36 months has been set when the product is unopened, with the storage conditions “Store below 25°C”. The product is to be used immediately upon opening.

Suitable post approval stability commitments have been provided to continue the stability studies for the current batches and to add batches from commercial-scale batches as they become available.

PRODUCT LITERATURE

Summary of Product Characteristics (SPC)
The proposed SPCs are satisfactory and in-line with that for the reference product.

Patient Information Leaflet (PIL)
The PIL is satisfactory and is consistent with the PIL for the originator products. The applicant submitted results of PIL user testing. The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

Labels
These are satisfactory.

CONCLUSION
It is recommended that Marketing Authorisations are granted for these applications.
PRECLINICAL ASSESSMENT

These applications for products claiming to be generic medicinal products of Amoxil Vials for Injection 250mg, 500mg and 1g (Beecham Group Plc, UK), which have been licensed within the EEA for over 10 years.

No new preclinical data have been supplied with these applications and none are required for applications of this type.
CLINICAL ASSESSMENT

TOXICOLOGY
A Preclinical Expert Report has been written by an appropriately qualified person. This is a suitable summary of the preclinical aspects of the dossier.

No new toxicology data have been provided and none are required for applications of this type.

CLINICAL PHARMACOLOGY
A Clinical Expert Report has been written by an appropriately qualified person. This is a suitable summary of the clinical aspects of the dossier.

No new clinical pharmacology data have been provided and none are required for applications of this type. As these products are intended for injection or infusion, no bioequivalence studies were required.

EFFICACY
A Clinical Expert Report has been written by an appropriately qualified person. This is a suitable summary of the clinical aspects of the dossier.

No new efficacy data have been provided and none are required for applications of this type.

SAFETY
The Clinical Expert Report provides an adequate review of the clinical safety of amoxicillin. No new safety data have been provided and none are required for applications of this type.

EXPERT REPORTS
The expert reports have been written by appropriately qualified persons.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
These are consistent with the reference products, where appropriate, and are medically satisfactory.

PATIENT INFORMATION LEAFLET (PIL)
This is consistent with the reference product, where appropriate, and is satisfactory.

LABELLING
These are medically satisfactory.

APPLICATION FORMS (MAA)
These are clinically satisfactory.

MEDICAL CONCLUSION
It is recommended that Marketing Authorisations are granted for these products.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Amoxicillin 250mg, 500mg and 1g Powder for Solution for Injection or Infusion are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
As the products are simple powders for solution for injection/infusion, no bioequivalence data were required and the proposed products are considered essentially identical to the brand leader products based on their quantitative and qualitative composition.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory.

RISK-BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with amoxicillin is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
AMOXICILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0010)

AMOXICILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0011)

AMOXICILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0012)

STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 10th February 2007</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 13th March 2007</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 8th April 2008, 19th August 2008, 5th December 2008 and 2nd March 2009. No requests for further information were made for the clinical dossiers.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 9th July 2008, 12th November 2008, 13th February 2009 and 6th March 2009 for the quality sections.</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 26th March 2009</td>
</tr>
</tbody>
</table>
AMOXICILLIN 250MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0010)

AMOXICILLIN 500MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0011)

AMOXICILLIN 1G POWDER FOR SOLUTION FOR INJECTION OR INFUSION (PL 24610/0012)

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11
Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Amoxicillin 250 mg, Powder for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 10ml vial contains 250 mg Amoxicillin as Amoxicillin Sodium.

Each vial contains approximately 19 mg sodium.

3 PHARMACEUTICAL FORM
Powder for Solution for Injection or Infusion.
Glass vial containing white or almost white powder.

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 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

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.

4.2 Posology and method of administration
Treatment of infection:

Adult dosage (including elderly patients):
Moderate infections: 500 mg via intramuscular injection every 8 hours (or more frequently if necessary). This dose may be given by slow intravenous injection if more convenient.

Severe infections: 1 g via intravenous injection every 6 hours.

Children's dosage (up to 10 years of age):
50-100 mg/kg body weight a day, in divided doses.

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

In renal impairment the excretion of the antibiotic will be delayed and, depending on the degree of impairment, it may be necessary to reduce the total daily dosage.
### Prophylaxis of endocarditis:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults’ dosage including elderly</th>
<th>Children’s dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dental procedures:</strong> 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).</td>
<td>Patient not having general anaesthetic</td>
<td>3 g Amoxicillin orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.</td>
<td>Under: 10: half adult dose. Under: 5: quarter adult dose.</td>
</tr>
<tr>
<td></td>
<td>Patient having general anaesthetic: if oral antibiotics considered to be appropriate</td>
<td>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. 1 g Amoxicillin IV or IM immediately before induction; with 500 mg orally, 6 hours later.</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Patient having general anaesthetic: if oral antibiotics not appropriate.</td>
<td></td>
<td>Note 2. To minimise pain on injection, Amoxicillin may be given as two injections of 500 mg dissolved in sterile 1% lidocaine solution (see Administration).</td>
</tr>
<tr>
<td><strong>Dental procedures:</strong> 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.</td>
<td>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</td>
<td>Under: 10: the doses of Amoxicillin should be half the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
<td>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.</td>
</tr>
<tr>
<td><strong>Genitourinary Surgery or Instrumentation:</strong> 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 Gastrointestinal Procedures—routine prophylaxis is recommended only for patients with prosthetic heart valves.</td>
<td>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.</td>
<td>Under: 5: the doses of Amoxicillin should be quarter the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
<td>See Notes 2, 3 and 4 above.</td>
</tr>
</tbody>
</table>
### Condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults’ dosage including elderly</th>
<th>Children’s dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery or Instrumentation of the Upper Respiratory Tract</td>
<td>Patients other than those with prosthetic heart valves.</td>
<td>1 g Amoxicillin IV or IM immediately before induction; 500 mg Amoxicillin IV or IM 6 hours later.</td>
<td>Under 10: half adult dose. Under 5: quarter adult dose. See Note 2 above. Note 5. The second dose of Amoxicillin may be administered orally.</td>
</tr>
<tr>
<td></td>
<td>Patients with prosthetic heart valves.</td>
<td>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.</td>
<td>Under 10: the dose of Amoxicillin should be half the adult dose; the gentamicin dose should be 2 mg/kg. Under 5: the dose of Amoxicillin should be quarter the adult dose; the dose of gentamicin should be 2 mg/kg. See Notes 2, 3, 4 and 5 above.</td>
</tr>
</tbody>
</table>

### Administration:

Intravenous injection, intravenous infusion, intramuscular injection:
See Section 6.6, Instructions for use and handling.

### 4.3 Contraindications

Amoxicillin is a penicillin and should not be given to patients with a history of hypersensitivity to penicillins or other beta-lactam antibiotics e.g. cephalosporins.

### 4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to beta-lactam antibiotics (see Section 4.3).

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). Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of large doses. A regular check of patency should be maintained.

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

Amoxicillin injection contains approximately 3.3 mmol sodium per gram. This should be taken into consideration by patients on a sodium controlled diet.
4.5 Interaction with other medicinal products and other forms of interaction
In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

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.

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 Pregnancy and lactation

Pregnancy
Animal studies with amoxicillin have shown no teratogenic effects. It has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies. When antibiotic therapy is required during pregnancy, amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.

Lactation
Amoxicillin may be given during 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) and very rare (<1/10,000).

The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.

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 (see Section 4.5)

Immune system disorders

Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis (see Section 4.4), serum sickness and hypersensitivity vasculitis. If a hypersensitivity reaction is reported, 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.

Gastrointestinal disorders

Common: Diarrhoea and nausea.

Uncommon: Vomiting.

Very rare: Mucocutaneous candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis).
Hepato-biliary 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: Urticaria and pruritus
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 disorders
Very rare: Interstitial nephritis, crystalluria (See Section 4.9).

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 special precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
ATC code: J01CF05
Pharmacotherapeutic group: Beta-lactamase resistant penicillins

Amoxicillin is a broad spectrum antibiotic. 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:

<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus faecalis</td>
<td>Haemophilus influenzae</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
<td>Salmonella species</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Shigella species</td>
</tr>
<tr>
<td>(penicillin-sensitive)</td>
<td>Bordetella pertussis</td>
</tr>
<tr>
<td>Clostridium species</td>
<td>Brucella species</td>
</tr>
<tr>
<td>Corynebacterium species</td>
<td>Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td>Neisseria meningitidis</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>Vibrio cholera</td>
</tr>
<tr>
<td></td>
<td>Pasteurella septica</td>
</tr>
</tbody>
</table>

5.2 Pharmacokinetic properties
Amoxicillin is well absorbed by the oral and parenteral routes. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

5.3 Preclinical safety data
No further information of relevance.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None

6.2 Incompatibilities
Amoxicillin should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates, or with intravenous lipid emulsions.

If Amoxicillin is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life
Unopened vial: 36 months.
After opening: To be used immediately.

6.4 Special precautions for storage
Store below 25°C

6.5 Nature and contents of container
Clear Type III glass vials with chlorobutyl rubber closure, in cartons of 1, 5, 10, 20 or 50 vials. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Intravenous Injection:
Dissolve 250mg in 5 ml Water for Injections BP (final volume 5.2 ml).

Amoxicillin injection, suitably diluted, may be injected directly into a vein or the infusion line over a period of three to four minutes.

Intravenous Infusion:
Solutions may be prepared as described for intravenous injections and then added to an intravenous solution in a minibag or in-line burette and administered over a period of half to one hour. Alternatively, using a suitable reconstitution device, the appropriate volume of intravenous fluid may be transferred from the infusion bag into the vial and then drawn back into the bag after dissolution.

Intramuscular injection:
Add 1.5 ml Water for Injections BP and shake vigorously (final volume 1.7 ml).

A transient pink colouration or slight opalescence may appear during reconstitution. Reconstituted solutions are normally a pale straw colour.

Amoxicillin injection may be added to the following intravenous fluids and used immediately.

• Water for Injections BP
• Sodium Chloride Intravenous Infusion (0.9%)
• Potassium Chloride (0.3%) and Sodium Chloride (0.9%) Intravenous Infusion
• Glucose Intravenous Infusion
• Sodium Chloride (0.18%) and Glucose (4%) Intravenous Infusion
• Dextran 40 Intravenous Infusion (10%) in Sodium Chloride Intravenous Infusion (0.9%)
• Dextran 40 Intravenous Infusion (10%) in Glucose Intravenous Infusion (5%)
• Sodium Lactate Intravenous Infusion (M/6)
• Compound Sodium Lactate Intravenous Infusions (Ringer-Lactate: Hartmann’s Solution)
MARKETING AUTHORISATION HOLDER
Bowmed Limited
113 Promenade
Cheltenham GL50 1NW

MARKETING AUTHORISATION NUMBER(S)
PL 24610/0010

DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
26/03/2009

DATE OF REVISION OF THE TEXT
26/03/2009
1 NAME OF THE MEDICINAL PRODUCT
Amoxicillin 500 mg, Powder for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 10ml vial contains 500 mg Amoxicillin as Amoxicillin Sodium.

Each vial contains approximately 38 mg sodium.

3 PHARMACEUTICAL FORM
Powder for Solution for Injection or Infusion.
Glass vial containing white or almost white powder.

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 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

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.

4.2 Posology and method of administration
Treatment of infection:
Adult dosage (including elderly patients):
Moderate infections: 500 mg via intramuscular injection every 8 hours (or more frequently if necessary). This dose may be given by slow intravenous injection if more convenient.

Severe infections: 1 g via intravenous injection every 6 hours.

Children's dosage (up to 10 years of age):
50-100 mg/kg body weight a day, in divided doses.

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

In renal impairment the excretion of the antibiotic will be delayed and, depending on the degree of impairment, it may be necessary to reduce the total daily dosage.
**Prophylaxis of endocarditis:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults’ dosage including elderly</th>
<th>Children’s dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dental procedures:</strong> 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).</td>
<td>Patient not having general anaesthetic</td>
<td>Patient having general anaesthetic: if oral antibiotics considered to be appropriate</td>
<td>Patient having general anaesthetic: if oral antibiotics not appropriate.</td>
</tr>
<tr>
<td></td>
<td>3 g Amoxicillin orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.</td>
<td>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. 1 g Amoxicillin IV or IM immediately before induction; with 500 mg orally, 6 hours later.</td>
<td>Under 10: half adult dose. Under 5: quarter adult dose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Note 2 To minimise pain on injection, Amoxicillin may be given as two injections of 500 mg dissolved in sterile 1% lidocaine solution (see Administration).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>See Notes 2, 3 and 4 above.</td>
</tr>
<tr>
<td><strong>Dental procedures:</strong> 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.</td>
<td>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</td>
<td>Under 10: the doses of Amoxicillin should be half the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Genitourinary Surgery or Instrumentation:</strong> prophylaxis for patients who have no urinary tract infection and who are to have genitourinary surgery or instrumentation under general anaesthesia.</td>
<td>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.</td>
<td>Initially: 1 g Amoxicillin IV or IM with 120 mg gentamicin IV or IM immediately prior to induction. Followed by (6 hours later): 500 mg Amoxicillin orally or IV or IM according to clinical condition.</td>
<td>See Notes 2, 3 and 4 above.</td>
</tr>
<tr>
<td>Condition</td>
<td>Adults’ dosage including elderly</td>
<td>Children’s dosage</td>
<td>Notes</td>
</tr>
<tr>
<td>-----------</td>
<td>----------------------------------</td>
<td>-------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Surgery or Instrumentation of the Upper Respiratory Tract</td>
<td>Patients other than those with prosthetic heart valves.</td>
<td>1 g Amoxicillin IV or IM immediately before induction; 500 mg Amoxicillin IV or IM 6 hours later.</td>
<td>Under 10: half adult dose. Under 5: quarter adult dose.</td>
</tr>
<tr>
<td></td>
<td>Patients with prosthetic heart valves.</td>
<td>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.</td>
<td>Under 10: the dose of Amoxicillin should be half the adult dose; the gentamicin dose should be 2 mg/kg. Under 5: the dose of Amoxicillin should be quarter the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
</tr>
</tbody>
</table>

**Administration:**
Intravenous injection, intravenous infusion, intramuscular injection:
See Section 6.6, Instructions for use and handling.

4.3 **Contraindications**
Amoxicillin is a penicillin and should not be given to patients with a history of hypersensitivity to penicillins or other beta-lactam antibiotics e.g. cephalosporins.

4.4 **Special warnings and precautions for use**
Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to beta-lactam antibiotics (see Section 4.3).

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 Overdose). Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of large doses. A regular check of patency should be maintained.

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

Amoxicillin injection contains approximately 3.3 mmol sodium per gram. This should be taken into consideration by patients on a sodium controlled diet.
4.5 Interaction with other medicinal products and other forms of interaction
In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

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.

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 Pregnancy and lactation
Pregnancy
Animal studies with amoxicillin have shown no teratogenic effects. It has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies. When antibiotic therapy is required during pregnancy, amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.

Lactation
Amoxicillin may be given during 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) and very rare (<1/10,000).

The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.

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 (see Section 4.5 – Interaction with other medicaments and other forms of action)

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 and hypersensitivity vasculitis.
If a hypersensitivity reaction is reported, 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.

Gastrointestinal disorders
Common: Diarrhoea and nausea.
Uncommon: Vomiting.
Very rare: Mucocutaneous candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis).

Hepato-biliary 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: Urticaria and pruritus
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 disorders
Very rare: Interstitial nephritis, crystalluria (See Section 4.9 Overdose).

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 special precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
ATC code:  J01CF05
Pharmacotherapeutic group: Beta-lactamase resistant penicillins

Amoxicillin is a broad spectrum antibiotic. 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:

Gram-positive
- Streptococcus faecalis
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Streptococcus viridans
- Staphylococcus aureus
- (penicillin-sensitive)
- Clostridium species
- Corynebacterium species
- Bacillus anthracis
- Listeria monocytogenes

Gram-negative
- Haemophilus influenzae
- Escherichia coli
- Proteus mirabilis
- Salmonella species
- Shigella species
- Bordetella pertussis
- Brucella species
- Neisseria gonorrhoeae
- Neisseria meningitidis
- Vibrio cholerae
- Pasteurella septica

5.2 Pharmacokinetic properties
Amoxicillin is well absorbed by the oral and parenteral routes. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

5.3 Preclinical safety data
No further information of relevance.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None

6.2 Incompatibilities
Amoxicillin should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates, or with intravenous lipid emulsions.

If Amoxicillin is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.

6.3 Shelf life
Unopened vial: 36 months.
After opening: To be used immediately.

6.4 Special precautions for storage
Store below 25°C

6.5 Nature and contents of container
Clear Type III glass vials with chlorobutyl rubber closure, in cartons of 1, 5, 10, 20 or 50 vials. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Intravenous Injection:
Dissolve 500mg in 10ml Water for Injections BP (final volume 10.4 ml).

Amoxicillin injection, suitably diluted, may be injected directly into a vein or the infusion line over a period of three to four minutes.

Intravenous Infusion:
Solutions may be prepared as described for intravenous injections and then added to an intravenous solution in a minibag or in-line burette and administered over a period of half to one hour. Alternatively, using a suitable reconstitution device, the appropriate volume of intravenous fluid may be transferred from the infusion bag into the vial and then drawn back into the bag after dissolution.

Intramuscular injection:
Add 2.5 ml Water for Injections BP and shake vigorously (final volume 2.9 ml).

A transient pink colouration or slight opalescence may appear during reconstitution. Reconstituted solutions are normally a pale straw colour.

Amoxicillin injection may be added to the following intravenous fluids and used immediately.

- Water for Injections BP
- Sodium Chloride Intravenous Infusion (0.9%)
- Potassium Chloride (0.3%) and Sodium Chloride (0.9%) Intravenous Infusion
- Glucose Intravenous Infusion
- Sodium Chloride (0.18%) and Glucose (4%) Intravenous Infusion
- Dextran 40 Intravenous Infusion (10%) in Sodium Chloride Intravenous Infusion (0.9%)
- Dextran 40 Intravenous Infusion (10%) in Glucose Intravenous Infusion (5%)
- Sodium Lactate Intravenous Infusion (M/6)
- Compound Sodium Lactate Intravenous Infusions (Ringer-Lactate: Hartmann’s Solution)

7 MARKETING AUTHORISATION HOLDER
Bowmed Limited
113 Promenade
Cheltenham GL50 1NW
8 MARKETING AUTHORISATION NUMBER(S)
PL 24610/0010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
26/03/2009

10 DATE OF REVISION OF THE TEXT
26/03/2009
1 NAME OF THE MEDICINAL PRODUCT
Amoxicillin 1g, Powder for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 20ml vial contains 1g Amoxicillin as Amoxicillin Sodium.

Each vial contains approximately 76mg sodium.

3 PHARMACEUTICAL FORM
Powder for Solution for Injection or Infusion.
Glass vial containing white or almost white powder.

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 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

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.

4.2 Posology and method of administration
_Treatment of infection:_

**Adult dosage (including elderly patients):**
Moderate infections: 500 mg via intramuscular injection every 8 hours (or more frequently if necessary). This dose may be given by slow intravenous injection if more convenient.

Severe infections: 1 g via intravenous injection every 6 hours.

**Children's dosage (up to 10 years of age):**
50-100 mg/kg body weight a day, in divided doses.

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

In renal impairment the excretion of the antibiotic will be delayed and, depending on the degree of impairment, it may be necessary to reduce the total daily dosage.
**Prophylaxis of endocarditis:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults’ dosage including elderly</th>
<th>Children’s dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dental procedures:</strong> 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).</td>
<td>Patient not having general anaesthetic</td>
<td>3 g Amoxicillin orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.</td>
<td>Under 10: half adult dose. Under 5: quarter adult dose.</td>
</tr>
<tr>
<td></td>
<td>Patient having general anaesthetic: if oral antibiotics considered to be appropriate</td>
<td>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. 1 g Amoxicillin IV or IM immediately before induction; with 500 mg orally, 6 hours later.</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Patient having general anaesthetic: if oral antibiotics not appropriate.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dental procedures:</strong> 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.</td>
<td>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.</td>
<td>Under 10: the doses of Amoxicillin should be half the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
<td>See Note 2. Note 3. Amoxicillin and gentamicin should not be mixed in the same syringe.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Under 5: the doses of Amoxicillin should be quarter the adult dose; the dose of gentamicin should be 2 mg/kg.</td>
<td>Note 4. Please consult the appropriate data sheet for full prescribing information on gentamicin.</td>
</tr>
<tr>
<td><strong>Genitourinary Surgery or Instrumentation:</strong> prophylaxis for patients who have no urinary tract infection and who are to have genitourinary surgery or instrumentation under general anaesthesia. In the case of Obstetric and Gynaecological Procedures and Gastrointestinal Procedures— routine prophylaxis is recommended only for patients with prosthetic heart valves.</td>
<td>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.</td>
<td></td>
<td>See Notes 2, 3 and 4 above.</td>
</tr>
</tbody>
</table>
### Administration:
Intravenous injection, intravenous infusion, intramuscular injection:  
See Section 6.6, Instructions for use and handling.

### 4.3 Contraindications
Amoxicillin is a penicillin and should not be given to patients with a history of hypersensitivity to penicillins or other beta-lactam antibiotics e.g. cephalosporins.

### 4.4 Special warnings and precautions for use
Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to beta-lactam antibiotics (see Section 4.3).

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). Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of large doses. A regular check of patency should be maintained.

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

Amoxicillin injection contains approximately 3.3 mmol sodium per gram. This should be taken into consideration by patients on a sodium controlled diet.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adults’ dosage including elderly</th>
<th>Children’s dosage</th>
<th>Notes</th>
</tr>
</thead>
</table>
| 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. | Under 10: half adult dose.  
Under 5: quarter adult dose. | See Note 2 above. Note 5. The second dose of Amoxicillin may be administered orally. |
| | 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. | Under 10: the dose of Amoxicillin should be half the adult dose; the gentamicin dose should be 2 mg/kg.  
Under 5: the dose of Amoxicillin should be quarter the adult dose; the dose of gentamicin should be 2 mg/kg. | See Notes 2, 3, 4 and 5 above. |
4.5 Interaction with other medicinal products and other forms of interaction
In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

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.

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 Pregnancy and lactation
Pregnancy
Animal studies with amoxicillin have shown no teratogenic effects. It has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies. When antibiotic therapy is required during pregnancy, amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.

Lactation
Amoxicillin may be given during 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) and very rare (<1/10,000).

The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.

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 (see Section 4.5 – Interaction with other Medicaments and other Forms of Interaction)

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 and hypersensitivity vasculitis.
If a hypersensitivity reaction is reported, 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.

Gastrointestinal disorders
Common: Diarrhoea and nausea.
Uncommon: Vomiting.
Very rare: Mucocutaneous candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis).

Hepato-biliary 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: Urticaria and pruritus
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 disorders
Very rare: Interstitial nephritis, crystalluria (See Section 4.9 Overdose).

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 special precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
ATC code: J01CF05
Pharmacotherapeutic group: Beta-lactamase resistant penicillins

Amoxicillin is a broad spectrum antibiotic. 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:

<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus faecalis</td>
<td>Haemophilus influenzae</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
<td>Salmonella species</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Shigella species</td>
</tr>
<tr>
<td>(penicillin-sensitive)</td>
<td>Bordetella pertussis</td>
</tr>
<tr>
<td>Clostridium species</td>
<td>Brucella species</td>
</tr>
<tr>
<td>Corynebacterium species</td>
<td>Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td>Neisseria meningitidis</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>Vibrio cholerae</td>
</tr>
<tr>
<td></td>
<td>Pasteurella septica</td>
</tr>
</tbody>
</table>

5.2 Pharmacokinetic properties
Amoxicillin is well absorbed by the oral and parenteral routes. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

5.3 Preclinical safety data
No further information of relevance.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
None

6.2 Incompatibilities
Amoxicillin should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates, or with intravenous lipid emulsions.

If Amoxicillin is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life
Unopened vial: 36 months.
After opening: To be used immediately.

6.4 Special precautions for storage
Store below 25°C

6.5 Nature and contents of container
Clear Type III glass vials with chlorobutyl rubber closure, in cartons of 1, 5, 10, 20 or 50 vials. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Intravenous Injection:
Dissolve 1g in 20ml Water for Injections BP (final volume 20.8 ml).

Amoxicillin injection, suitably diluted, may be injected directly into a vein or the infusion line over a period of three to four minutes.

Intravenous Infusion:
Solutions may be prepared as described for intravenous injections and then added to an intravenous solution in a minibag or in-line burette and administered over a period of half to one hour. Alternatively, using a suitable reconstitution device, the appropriate volume of intravenous fluid may be transferred from the infusion bag into the vial and then drawn back into the bag after dissolution.

Intramuscular injection:
Add 2.5 ml Water for Injections BP and shake vigorously (final volume 3.3 ml).

A transient pink colouration or slight opalescence may appear during reconstitution. Reconstituted solutions are normally a pale straw colour.

Amoxicillin injection may be added to the following intravenous fluids and used immediately.
- Water for Injections BP
- Sodium Chloride Intravenous Infusion (0.9%)
- Potassium Chloride (0.3%) and Sodium Chloride (0.9%) Intravenous Infusion
- Glucose Intravenous Infusion
- Sodium Chloride (0.18%) and Glucose (4%) Intravenous Infusion
- Dextran 40 Intravenous Infusion (10%) in Sodium Chloride Intravenous Infusion (0.9%)
- Dextran 40 Intravenous Infusion (10%) in Glucose Intravenous Infusion (5%)
- Sodium Lactate Intravenous Infusion (M/6)
- Compound Sodium Lactate Intravenous Infusions (Ringer-Lactate: Hartmann’s Solution)
7 MARKETING AUTHORISATION HOLDER
Bowmed Limited
113 Promenade
Cheltenham GL50 1NW

8 MARKETING AUTHORISATION NUMBER(S)
PL 24610/0012

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
26/03/2009

10 DATE OF REVISION OF THE TEXT
26/03/2009
UKPAR Amoxicillin 250mg, 500mg and 1g Powder for Sol for Inf or Inf

PL 24610/0010-12

The following side effects may also occur. Tell your doctor if any of these become troublesome:

Common side effects (probably affecting more than 1 in 100 people given this injection)

- Feeling sick (nausea)
- Diarrhoea

Uncommon side effects (probably affecting fewer than 1 in 100 people given this injection)

- Throat is yeast infection of the mouth, gums or skin folds. You can get treatment from your doctor or pharmacist.
- Crystals forming in your urine (crystalluria) which may cause difficulty or discomfort in passing urine.
- Excessive body movements (hypokinesia)
- Dizziness
- Convulsions (fits). People who are on high doses of amoxicillin or whose kidneys do not work properly may experience convulsions.
- Reduction in blood cell counts which makes infections more liable.
- Anaemia is a reduction in the body's red blood cells or haemoglobin which may be characterised by feeling weak or light-headed
- A longer time takes for blood to clot.

Tell your doctor that you are taking amoxicillin if you are having blood tests.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

5. HOW TO STORE AMOXICILLIN INJECTION

Keep out of reach of the sight and children. Store in a cool place. Do not use this medicine after the expiry date which is printed on the label and carton, or if the powder shows signs of discolouration.

Medicines should not be disposed of via wastewaster or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What amoxicillin contains

Each vial contains 250mg, 500mg or 1g of amoxicillin (as amoxicillin sodium). There are no other ingredients.

What amoxicillin looks like and contents of the pack

Amoxicillin injection is a white or almost white powder in a glass vial.

Each carton contains 1, 5, 10, 20 or 50 glass vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Bionest Limited, 113 Promenade, Deolsarto (EMA), 16100

Manufacturer:

Istituto Bioclinica Italiano, Via Passigliere, 00155 Aprili (LT), Italy

The manufacturer has not approved this answer

Amoxicillin injection may be added to the following intravenous fluids and used immediately:

- Sodium Chloride Intravenous Infusion (0.9%)
- Sodium Chloride Intravenous Infusion (10%)
- Sodium Chloride Intravenous Infusion (3%)
- Compound Sodium Lactate Intravenous Infusion (Ringer’s Lactate: Hartmann’s Solution)

 Intravenous Infusion:

Solutions may be prepared as described for intravenous infusions and then added to an intravenous solution in a suitable container and administered over a period of half to one hour. Alternatively, using a suitable reconstruction device, the appropriate volume of intravenous fluid may be transferred from the infusion bag into the vial and then drawn back into the bag after dissolution.

Intravenous injection:

Add 3.3 ml (25mg vial) or 4 ml (50mg vial) Water for Injections BP and shake vigorously. Insert veins in the skin, or into the tissues of the body, using a needle of the correct size.
UKPAR Amoxicillin 250mg, 500mg and 1g Powder for Sol for Inj or Inf Amoxicillin as Amoxicillin Sodium

3. HOW AMOXICILLIN INJECTION IS GIVEN

Your doctor or nurse will prepare your injection in the form of a liquid. They will inject this into a muscle or as a slow injection. Your doctor will decide how much you need and how often the injections should be given.

4. SAFETY INFORMATION

Before you are given Amoxicillin Injection

- You must tell the doctor or nurse if any of the following apply to you:
  - You are on a low sodium diet (see "Important information about some of the ingredients of Amoxicillin injection")
  - You have any history of allergy to penicillins or any other penicillins
  - You have a skin rash, itching or swelling of the face, neck or tongue when taking any antibiotic.

5. POSSIBLE SIDE EFFECTS

- You should not give this medicine to:
  - You have a skin rash or itching or swelling of the face, neck or tongue when taking any antibiotic.

6. FURTHER INFORMATION

- We recommend that you consult a healthcare professional before using any Amoxicillin preparation.

The following information is intended for medical or healthcare professionals only.

Special precautions for storage

- Store below 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Instructions for use and handling Intravenous Injection:

- Dissolve 250mg in 5 ml Water for Injections BP (final volume 5.2 ml) Dissolve 500mg in 10 ml Water for Injections BP (final volume 10.4 ml). Dissolve 1g in 20ml Water for Injections BP (final volume 20.8 ml).

Amoxicillin, suitably diluted, may be injected directly into a vein or the infusion line over a period of three to four minutes.
UKPAR Amoxicillin 250mg, 500mg and 1g Powder for Sol for Inj or Inf

Amoxicillin Powder for injection or infusion

Contains 1 g Amoxicillin as Amoxicillin sodium.
For i.v. or i.m. use. To be given as directed by the physician.
Read package leaflet before use.
Bowned Limited, 113 Promenade, Cheltenham, UK. PL 24610/0012

Keep out of the reach and sight of children.