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AMOXICILLIN 250MG CAPSULES
AMOXICILLIN 500MG CAPSULES

PL 19348/0053-4

LAY SUMMARY

The MHRA granted LPC Medical (UK) Limited Marketing Authorisations (licences) for the medicinal products Amoxicillin 250mg and 500mg Capsules on 09 March 2011. These are prescription only medicines (POM).

Amoxicillin 250mg and 500mg Capsules are used to treat a range of bacterial infections including those of the

- chest (bronchitis or pneumonia)
- ears
- sinuses
- throat
- kidneys and bladder
- gut and areas around the gut

They may also be used to help prevent infections of the heart valves that may follow some surgical and dental operations in patients who have a particular risk of developing such infections.

Amoxicillin 250mg and 500mg Capsules contain the active ingredient amoxicillin which belongs to a group of antibiotics known as penicillins.

These applications are duplicates of previously granted applications for Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3), which were granted to the Marketing Authorisation Holder Karib Kemi-Pharm Limited.

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of taking Amoxicillin 250mg and 500mg Capsules outweigh the risks; hence Marketing Authorisations have been granted.
AMOXICILLIN 250MG CAPSULES
AMOXICILLIN 500MG CAPSULES

PL 19348/0053-4

SCIENTIFIC DISCUSSION

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Preclinical assessment Page 7
Clinical assessment (including statistical assessment) Page 8
Overall conclusions and risk benefit assessment Page 9
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Marketing Authorisations for the medicinal products Amoxicillin 250mg and 500mg Capsules (PL 19348/0053-4) to LPC Medical (UK) Limited on 09 March 2011. These are prescription only medicines (POM) indicated for the treatment of the following bacterial infections caused by amoxicillin-sensitive gram-positive and gram-negative pathogens (refer to section 5.1 of the SmPC also):

- Infections of the upper respiratory tract, including infections of the ears, nose and throat: Acute otitis media, acute sinusitis and bacterial pharyngitis
- Infections of the kidneys and the genito-urinary tract: Cystitis, pyelonephritis.
- Infections associated with the gastrointestinal tract. It may be necessary to use combination therapy when treating infections caused by anaerobic organisms.
- Endocarditis: Amoxicillin 250mg and 500mg Capsules may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis. Amoxicillin 250mg and 500mg Capsules may also be used for the treatment of endocarditis as an extension of parenteral therapy.

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

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

The products contain the active ingredient amoxicillin, which is an aminopenicillin and belongs to a group of medicines called Beta-lactam antibiotics. Amoxicillin has bacterial action due to its inhibition of the synthesis of the bacterial cell wall.

These applications were submitted as simple abridged applications according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3) approved on 27 August 2003 to the Marketing Authorisation Holder Karib Kemi-Pharm Limited.

No new data were submitted nor were they necessary for these simple applications, as the data are identical to that of the previously granted cross-reference products.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 19348/0053-54
PROPRIETARY NAME: Amoxicillin 250mg and 500mg Capsules
COMPANY NAME: LPC Medical (UK) Limited
E.C. ARTICLE: Article 10(c) of Directive 2001/83/EC
LEGAL STATUS: POM

1 INTRODUCTION
These are simple, informed consent applications for Amoxicillin 250mg and 500mg Capsules submitted under Article 10(c) of Directive 2001/83/EC. The applications cross-refer to Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3), approved on 27 August 2003 to Karib Kemi-Pharm Limited

The current applications are considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)

2.1 Name(s)
The proposed names of the products are Amoxicillin 250mg and 500mg Capsules. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The products contain 250mg or 500mg amoxicillin. They are to be stored in polypropylene containers with pilfer proof polyethylene closures containing 100, 500 and 1000 capsules:

The proposed shelf life is 36 months. The storage conditions are ‘Do not store above 25°C. Store in the original container.’

The proposed shelf-life and storage conditions are consistent with the details registered for the cross-referenced products.

2.3 Legal status
On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
The proposed Marketing Authorisation Holder is LPC Medical (UK) Limited, 30 Chaul End Lane, Luton, Bedfordshire LU4 8EZ, UK

The Qualified Person (QP) responsible for pharmacovigilance is stated and their CV is included.

2.5 Manufacturers
The proposed manufacturing site is consistent with that registered for the reference products and evidence of compliance with current Good Manufacturing Practice has been provided.

2.6 Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the reference products.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the reference products and the maximum batch size is stated.
2.8 Finished product/shelf-life specification
The proposed finished product specifications are in line with the details registered for the reference products.

2.9 Drug substance specification
The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

A European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability for the drug substance manufacturer has been provided to support the manufacturing and control of the active substance. These details are in line with those of the reference products.

2.10 TSE Compliance
With the exception of gelatin, none of the excipients are of animal or human origin. The supplier of gelatin has provided European Directorate for the Quality of Medicines (EDQM) Certificates of Suitability, which covers all aspects of the manufacture and control of the excipient. No genetically modified organisms (GMO) have been used in the preparation of these excipients. This is consistent with the reference product.

2.11 Bioequivalence
No bioequivalence data are required to support these informed consent applications, as the proposed products are manufactured to the same formula utilising the same process as the reference products Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3).

3 EXPERT REPORT
The applicant has included detailed pharmaceutical expert report, written by an appropriately qualified person.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The appearance of the products is identical to that of the reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPCs are consistent with the details registered for the reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING
PIL
The patient information leaflet has been prepared in line with the details registered for the reference products.

Container
The proposed artwork complies with the relevant statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with these applications is acceptable. The grant of Marketing Authorisations is recommended.
PRECLINICAL ASSESSMENT

As these applications are identical to the reference products Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3), no new preclinical data have been supplied with these applications and none are required. A preclinical expert report has been written by a suitably qualified person and is satisfactory.
CLINICAL ASSESSMENT

As these applications are identical to the reference products Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3), no new clinical data have been supplied with these applications and none are required. A clinical expert report has been written by a suitably qualified person and is satisfactory.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the reference products and as such have been judged to be satisfactory.

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

EFFICACY
The applications are identical to the previously granted applications for Amoxicillin 250mg and 500mg Capsules (PL 18224/0052-3), granted to Karib Kemi-Pharm Limited on 27 August 2003.

SAFETY
No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with those of the reference products.

Colour mock-ups of the labelling have been provided and are satisfactory. The approved labelling artwork complies with statutory requirements. The name of the product in Braille appears on the outer packaging.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s products are identical to the reference products. Extensive clinical experience with amoxicillin is considered to have demonstrated the therapeutic values of the compound. The benefit/risk is therefore considered to be positive.
AMOXICILLIN 250MG CAPSULES
AMOXICILLIN 500MG CAPSULES

PL 19348/0053-4

STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation Applications on 27 April 2005</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 04 July 2006</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 08 November 2006.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 03 March 2010</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 09 March 2011</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Amoxicillin 250mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains:
Amoxicillin Trihydrate 294mg equivalent to Amoxicillin 250mg.
For excipients, see 6.1.

3 PHARMACEUTICAL FORM
Size ‘2’ scarlet/ivory hard gelatin capsules.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Amoxicillin 250mg Capsules is indicated for the oral treatment of the following bacterial infections caused by amoxicillin-sensitive gram-positive and gram-negative pathogens (see section 5.1):

- Infections of the upper respiratory tract, including infections of the ears, nose and throat:
  - Acute otitis media, acute sinusitis and bacterial pharyngitis
- Infections of the kidneys and the genito-urinary tract: Cystitis, pyelonephritis
- Infections associated with the gastrointestinal tract. It may be necessary to use combination therapy when treating infections caused by anaerobic organisms.
- Endocarditis: Amoxicillin 250mg Capsules may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis. Amoxicillin 250mg Capsules may also be used for the treatment of endocarditis as an extension of parenteral therapy.

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

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

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
The dosage depends on the susceptibility of the pathogens and the severity of the disease.

Standard dosage:

Adults and adolescents (> 40 kg body weight):
The usual dosage covers a range from 750 mg to 3g amoxicillin daily in three divided doses. In some areas 1500 mg amoxicillin daily in three divided doses is recommended as the upper usual dose.

Short course treatment:
Uncomplicated urinary tract infections: two 3 g doses with 10-12 hours between the doses are recommended in some areas.

Children (under 12 years)
For infants and children oral suspensions containing amoxicillin are recommended.

Dosage for the prevention of endocarditis:
For the prevention of endocarditis, in patients not having a general anaesthetic, 3 g amoxicillin are given in the hour preceding the surgical procedure, followed by (6 hours later) a further 3 g dose, if considered necessary.

Dosage in impaired renal function:
The dose should be reduced in patients with severe renal impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval or a reduction in the subsequent doses is recommended (see section 4.4). Short course treatments with a single dose of 3 g cannot be given in patients with renal failure.

**Duration of therapy:**

In general the therapy should be continued for 2 to 3 days following the disappearance of symptoms. In β-haemolytic streptococcal infections the duration of therapy should be at least 10 days in order to achieve eradication of the organism.

**Method of administration:**

The preparations are administered orally.

Amoxicillin 250mg Capsules should be taken unchewed with liquid (e.g. a glass of water).

The absorption of amoxicillin is not reduced by food intake.

Children weighing < 40 kg

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations below and sections 4.4, 5.1 and 5.2).

*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

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

Special dosage recommendation

- **Tonsillitis:** 50 mg/kg/day in two divided doses.
- **Acute otitis media:** In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations.
- **Early Lyme disease** (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.
- **Prophylaxis for endocarditis:** 50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure.

**Dosage in impaired renal function:**

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4 and 5.2).

Renal impairment in children under 40 kg:

<table>
<thead>
<tr>
<th>Creatinine clearance ml/min</th>
<th>Dose</th>
<th>Interval between administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Usual dose</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>10 – 30</td>
<td>Usual dose</td>
<td>12 h (corresponding to 2/3 of the dose)</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>Usual dose</td>
<td>24 h (corresponding to 1/3 of the dose)</td>
</tr>
</tbody>
</table>

**4.3 CONTRAINDICATIONS**

Amoxicillin 250mg Capsules is contraindicated in patients with a previous history of hypersensitivity to amoxicillin or to any of the excipients.
Amoxicillin 250mg Capsules must not be administered to patients with a verified hypersensitivity to any beta-lactam drug (e.g. penicillins, cephalosporins, carbapenems, monobactams). Consequently a careful history should be taken in regard to any allergic reactions before commencing treatment.

Amoxicillin 250mg Capsules is also contraindicated in viral infections, acute lymphatic leukaemia, or infectious mononucleosis (due to an increased risk of erythematous skin rashes).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Patients suffering from severe gastrointestinal disturbances with diarrhoea and vomiting should not be treated with Amoxicillin 250mg Capsules, due to the risk of reduced absorption. In these cases parenteral treatment with amoxicillin is advisable.

Amoxicillin 250mg Capsules should be used with caution in patients with allergic diathesis and asthma.

In patients with renal impairment the excretion of amoxicillin will be delayed and, depending on the degree of the impairment, it may be necessary to reduce the total daily dosage (see section 4.2.).

The prolonged use of amoxicillin may occasionally result in an overgrowth of non-susceptible organisms or yeasts. Patients should therefore be watched carefully for superinfections.

The occurrence of anaphylactic shock and other severe allergic reactions is rare following the oral administration of amoxicillin. However, if such reactions occur, appropriate emergency treatment measures must be taken: i.v. administration of epinephrine, followed by antihistaminic drugs, volume substitution and administration of glucocorticoids. Patients should be kept under close observation, and further therapeutic measures (artificial respiration, oxygen) should be administered as required.

The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals. At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Amoxicillin 250mg Capsules contains sunset yellow. This may cause allergic reactions.

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concomitant use not recommended

**Allopurinol**
Concomitant administration of allopurinol may promote the occurrence of allergic cutaneous reactions.

**Digoxin**
An increase in the absorption of digoxin is possible on concurrent administration with Amoxicillin 250mg Capsules.

**Anticoagulants**
Concomitant administration of amoxicillin and anticoagulants, such as coumarin, may increase the incidence of bleeding.

**Probenecid**
By inhibiting the renal elimination of amoxicillin the concomitant administration of probenecid leads to an increase in the concentrations of amoxicillin in serum and bile.

**Other antibiotics**
There is a possibility that the antibacterial action of amoxicillin could be antagonised on coadministration with macrolides, tetracyclines, sulphonamides or chloramphenicol.

Caution is recommended when amoxicillin is given concomitantly with:
Oral hormonal contraceptives
Administration of amoxicillin can transiently decrease the plasma level of estrogens and progesterone, and may reduce the efficacy of oral contraceptives. Patients should be advised to use supplemental non-hormonal contraceptive measures.

Other forms of interactions:
- Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxicillin.
- The occurrence of diarrhoea may impair the absorption of other medicaments and consequently adversely affect efficacy.
- Amoxicillin may produce false positive results in glucose determination tests performed with nonenzymatic methods. Likewise the urobilinogen test can be affected.
- Amoxicillin may decrease the amount of urinary estriol in pregnant women.

4.6 PREGNANCY AND LACTATION
Pregnancy
Amoxicillin crosses the placenta and foetal plasma concentrations are approximately 25-30% of the maternal plasma concentrations. However, since there is no evidence of any embryotoxic or other adverse effects of the drug, amoxicillin may be considered appropriate for use during pregnancy when the potential benefits outweigh the potential risks.

Lactation
Amoxicillin diffuses into the breast milk (approx. 10% of the corresponding serum concentration) and in rare cases this can lead to diarrhoea and/or fungal colonisation of the mucosa in the infant. The possibility of sensitisation of the infant to beta-lactam drugs should also be considered.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
No effects on the ability to drive and use machines have been observed.

4.8 UNDESIRABLE EFFECTS
The most commonly reported adverse drug reactions are hypersensitivity reactions:

Common (≥1% but <10%)
- Cutaneous reactions such as exanthema, pruritus, urticaria; the typical morbilliform exanthema occurs 5 - 11 days after start of therapy. Immediate appearance of urticaria indicates an allergic reaction to amoxicillin and therapy should therefore be discontinued.
- Angioneurotic oedema (Quincke's oedema)
- Erythema multiforme exsudativum
- Stevens-Johnson syndrome
- Eosinophilia
- Drug fever
- Laryngeal oedema
- Serum sickness
- Haemolytic anaemia
- Allergic vasculitis
- Interstitial nephritis
- Anaphylactic shock

Rare (≥0.01% but <0.1%): (see also section 4.4)
- Angioneurotic oedema (Quincke's oedema)
- Erythema multiforme exsudativum
- Stevens-Johnson syndrome
- Eosinophilia
- Drug fever
- Laryngeal oedema
- Serum sickness
- Haemolytic anaemia
- Allergic vasculitis
- Interstitial nephritis
- Anaphylactic shock

Blood disorders:
There have been isolated reports of leucopenia, granulocytopenia, thrombocytopenia, pancytopenia, anaemia, myelosuppression, agranulocytosis, prolongation of bleeding time, and prolongation of prothrombin time. However, these changes were reversible on discontinuation of therapy.

Gastrointestinal disorders:
Common (≥1% but <10%):
- Gastric complaints, nausea, loss of appetite, vomiting, flatulence, soft stools, diarrhoea, enanthemas (particularly in the region of the mouth), dry mouth, taste disturbances. These effects on the gastrointestinal system are mostly mild and frequently disappear either during the treatment or very soon after completion of
therapy. The occurrence of these side-effects can generally be reduced by taking Amoxicillin 250mg Capsules
during meals or with some food.
If severe and persistent diarrhoea occurs, the very rare possibility of pseudomembranous colitis should be
considered. The administration of anti-peristaltic drug is contraindicated.

*Very rare (<> 0.01%):*
Development of a black tongue.

*Liver disorders:*
*Uncommon (≥ 0.1% but < 1%)*
Moderate and transient increase of liver enzymes. Rare reports of hepatitis and cholestatic jaundice.

*Renal disorders*
*Rare (≥ 0.01% but < 0.1%):*
Acute interstitial nephritis may occur in rare cases.

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

*Other undesirable effects*
Prolonged and repeated use of the preparation can result in superinfections and colonization with resistant
organisms or yeasts such as oral and vaginal candidiasis.

4.9 OVERDOSE
Symptoms of overdose:
Amoxicillin is not generally associated with acute toxic effects, even when accidentally consumed in high
doses. Overdosage can lead to symptoms such as gastrointestinal disturbances and fluid and electrolyte
imbalance.

Management of overdose:
There is no specific antidote for an overdose of amoxicillin. Treatment consists primarily of administration of activated charcoal (gastric lavage is usually not necessary) or symptomatic measures. Particular attention should be paid to the water and electrolyte balance of the patients. In patients with severely impaired renal function, large overdoses can result in signs of renal toxicity; crystalluria is possible. Amoxicillin can be eliminated via haemodialysis.

5 PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Beta-lactam antibiotics, penicillins

5.1 PHARMACODYNAMIC PROPERTIES
General Properties

ATC CLASSIFICATION
ATC-Code:J01 A04

MODE OF ACTION
Amoxicillin is an aminopenicillin that has bacterial action due to its inhibition of the synthesis of the bacterial
cell wall

MECHANISM (S) OF RESISTANCE
Bacteria may be resistant to amoxicillin (and, thus, ampicillin) due to production of betalactamases 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.

Breakpoints
The MIC breakpoints for susceptible organisms vary according to species.

Enterobacteriaceae are considered susceptible when inhibited at ≤ 8 mg/L amoxicillin.
From NCCLS recommendations and using NCCLS-specified methods:

- M. catarrhalis (β-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 and 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. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

**SUSCEPTIBLE:**

<table>
<thead>
<tr>
<th>Gram-positive aerobes</th>
<th>Frequency of resistance ranges in EU (extreme values)</th>
</tr>
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<tbody>
<tr>
<td>Bacillus anthracis</td>
<td></td>
</tr>
<tr>
<td>Corynebacterium spp §</td>
<td></td>
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<tr>
<td>Enterococcus faecalis §</td>
<td></td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
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<tr>
<td>Streptococcus agalactiae</td>
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<tr>
<td>Streptococcus bovis</td>
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<tr>
<td>Streptococcus pneumonia §</td>
<td></td>
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<tr>
<td>Streptococcus pyogenes §</td>
<td></td>
</tr>
<tr>
<td>Streptococcus viridans §</td>
<td></td>
</tr>
</tbody>
</table>

| Gram-negative aerobes:        |                                                      |
| Brucella spp #                |                                                      |
| Escherichia coli              | 46.7%                                                |
| Haemophilus influenzae        | 2 – 31.7%                                            |
| Haemophilus parainfluenzae    | 15.3%                                                |
| Neisseria gonorrhoeae §       | 12 – 80%                                             |
| Neisseria meningitidis #      |                                                      |
| Proteus mirabilis             | 28%                                                  |
| Salmonella spp §              |                                                      |
| Shigella spp §                |                                                      |
| Vibrio cholerae               |                                                      |

**Anaerobes**

- Bacteroides melaninogenicus §
- Clostridium spp
- Fusobacterium spp §
- Peptostreptococci

**RESISTANT**

**Gram-positive aerobes**

- Staphylococci (β-lactamase producing strains)

**Gram-negative aerobes**

- Acinetobacter spp
- Citrobacter spp
- Enterobacter spp
- Klebsiella spp
- Moraxella catarrhalis
- Proteus spp (indole positive)
- Proteus vulgaris
- Providencia spp
- Pseudomonas spp
**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 250 mg and 750 mg 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 500 mg amoxicillin results in plasma concentrations of 6-11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/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.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/min, very similar to the inuline clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

**5.3 PRECLINICAL SAFETY DATA**

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**

**Capsule contents**

Magnesium Stearate

Gelatin

**Capsule (Body),**

Erythrosine E 127

Patent Blue E 131
Sunset Yellow E 110
Titanium Dioxide E 171

Capsule (Cap)
Yellow Iron Oxide E 172
Titanium Dioxide E 171

6.2 INCOMPATIBILITIES
Not applicable.

6.3 SHELF LIFE
36 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25°C.
Store in the original container

6.5 NATURE AND CONTENTS OF CONTAINER
Polypropylene container with pilfer proof polyethylene closure containing 100, 500 and 1000 capsules.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
None.

7 MARKETING AUTHORISATION HOLDER
LPC Medical (UK) Limited
30 Chaul End Lane
Luton
Bedfordshire LU4 8EZ
U. K.

8 MARKETING AUTHORISATION NUMBER(S)
PL 19348/0053

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
09/03/2011

10 DATE OF REVISION OF THE TEXT
09/03/2011
NAME OF THE MEDICINAL PRODUCT
Amoxicillin 500mg Capsules

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains:
Amoxicillin Trihydrate 588mg equivalent to Amoxicillin 500mg.
For excipients, see 6.1.

PHARMACEUTICAL FORM
Size ‘0’ scarlet/ivory hard gelatin capsules.

CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Amoxicillin 500mg Capsules is indicated for the oral treatment of the following bacterial infections caused by amoxicillin-sensitive gram-positive and gram-negative pathogens (see section 5.1):

- Infections of the upper respiratory tract, including infections of the ears, nose and throat: Acute otitis media, acute sinusitis and bacterial pharyngitis
- Infections of the kidneys and the genito-urinary tract: Cystitis, pyelonephritis.
- Infections associated with the gastrointestinal tract. It may be necessary to use combination therapy when treating infections caused by anaerobic organisms.
- Endocarditis: Amoxicillin 500mg Capsules may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis. Amoxicillin 500mg Capsules may also be used for the treatment of endocarditis as an extension of parenteral therapy.

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

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

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
The dosage depends on the susceptibility of the pathogens and the severity of the disease.

Standard dosage:

Adults and adolescents (> 40 kg body weight):

The usual dosage covers a range from 750 mg to 3g amoxicillin daily in three divided doses. In some areas 1500 mg amoxicillin daily in three divided doses is recommended as the upper usual dose.

Short course treatment:
Uncomplicated urinary tract infections: two 3 g doses with 10-12 hours between the doses are recommended in some areas.

Children (under 12 years)

For infants and children oral suspensions containing amoxicillin are recommended.

Dosage for the prevention of endocarditis:

For the prevention of endocarditis, in patients not having a general anaesthetic, 3 g amoxicillin are given in the hour preceding the surgical procedure, followed by (6 hours later) a further 3 g dose, if considered necessary.

Dosage in impaired renal function:

The dose should be reduced in patients with severe renal impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval or a reduction in the subsequent doses is recommended.
(see section 4.4). Short course treatments with a single dose of 3 g cannot be given in patients with renal failure.

**Duration of therapy:**

In general the therapy should be continued for 2 to 3 days following the disappearance of symptoms. In β-haemolytic streptococcal infections the duration of therapy should be at least 10 days in order to achieve eradication of the organism.

**Method of administration:**

The preparations are administered orally.

Amoxicillin 500mg Capsules should be taken unchewed with liquid (e.g. a glass of water).

The absorption of amoxicillin is not reduced by food intake.

Children weighing < 40 kg

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations below and sections 4.4, 5.1 and 5.2).

*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

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

Special dosage recommendation

**Tonsillitis:** 50 mg/kg/day in two divided doses.

Acute otitis media: In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations.

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

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

**Dosage in impaired renal function:**

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4 and 5.2).

Renal impairment in children under 40 kg:

<table>
<thead>
<tr>
<th>Creatinine clearance ml/min</th>
<th>Dose</th>
<th>Interval between administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Usual dose</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>10 – 30</td>
<td>Usual dose</td>
<td>12 h (corresponding to 2/3 of the dose)</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>Usual dose</td>
<td>24 h (corresponding to 1/3 of the dose)</td>
</tr>
</tbody>
</table>

**CONTRAINDICATIONS**

Amoxicillin 500mg Capsules is contraindicated in patients with a previous history of hypersensitivity to amoxicillin or to any of the excipients.
Amoxicillin 500mg Capsules must not be administered to patients with a verified hypersensitivity to any beta-lactam drug (e.g. penicillins, cephalosporins, carbapenems, monobactams). Consequently a careful history should be taken in regard to any allergic reactions before commencing treatment.

Amoxicillin 500mg Capsules is also contraindicated in viral infections, acute lymphatic leukaemia, or infectious mononucleosis (due to an increased risk of erythematous skin rashes).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Patients suffering from severe gastrointestinal disturbances with diarrhoea and vomiting should not be treated with Amoxicillin 500mg Capsules, due to the risk of reduced absorption. In these cases parenteral treatment with amoxicillin is advisable.

Amoxicillin 500mg Capsules should be used with caution in patients with allergic diathesis and asthma.

In patients with renal impairment the excretion of amoxicillin will be delayed and, depending on the degree of the impairment, it may be necessary to reduce the total daily dosage (see section 4.2.).

The prolonged use of amoxicillin may occasionally result in an overgrowth of non-susceptible organisms or yeasts. Patients should therefore be watched carefully for superinfections.

The occurrence of anaphylactic shock and other severe allergic reactions is rare following the oral administration of amoxicillin. However, if such reactions occur, appropriate emergency treatment measures must be taken: I.v. administration of epinephrine, followed by antihistaminic drugs, volume substitution and administration of glucocorticoids. Patients should be kept under close observation, and further therapeutic measures (artificial respiration, oxygen) should be administered as required.

The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals. At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Amoxicillin 500mg Capsules contains sunset yellow. This may cause allergic reactions.

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concomitant use not recommended

Allopurinol
Concomitant administration of allopurinol may promote the occurrence of allergic cutaneous reactions.

Digoxin
An increase in the absorption of digoxin is possible on concurrent administration with Amoxicillin 500mg Capsules.

Anticoagulants
Concomitant administration of amoxicillin and anticoagulants, such as coumarin, may increase the incidence of bleeding.

Probenecid
By inhibiting the renal elimination of amoxicillin the concomitant administration of probenecid leads to an increase in the concentrations of amoxicillin in serum and bile.

Other antibiotics
There is a possibility that the antibacterial action of amoxicillin could be antagonised on coadministration with macrolides, tetracyclines, sulphonamides or chloramphenicol.

Caution is recommended when amoxicillin is given concomitantly with:
**Oral hormonal contraceptives**
Administration of amoxicillin can transiently decrease the plasma level of estrogens and progesterone, and may reduce the efficacy of oral contraceptives. Patients should be advised to use supplemental non-hormonal contraceptive measures.

**Other forms of interactions:**

- Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxicillin.
- The occurrence of diarrhoea may impair the absorption of other medicaments and consequently adversely affect efficacy.
- Amoxicillin may produce false positive results in glucose determination tests performed with nonenzymatic methods. Likewise the urobilinogen test can be affected.
- Amoxicillin may decrease the amount of urinary estriol in pregnant women.

### 4.6 PREGNANCY AND LACTATION

**Pregnancy**
Amoxicillin crosses the placenta and foetal plasma concentrations are approximately 25-30% of the maternal plasma concentrations. However, since there is no evidence of any embryotoxic or other adverse effects of the drug, amoxicillin may be considered appropriate for use during pregnancy when the potential benefits outweigh the potential risks.

**Lactation**
Amoxicillin diffuses into the breast milk (approx. 10% of the corresponding serum concentration) and in rare cases this can lead to diarrhoea and/or fungal colonisation of the mucosa in the infant. The possibility of sensitisation of the infant to beta-lactam drugs should also be considered.

### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No effects on the ability to drive and use machines have been observed.

### 4.8 UNDESIRABLE EFFECTS

The most commonly reported adverse drug reactions are hypersensitivity reactions:

**Common** $(\geq 1\% \text{ but } < 10\%)$
Cutaneous reactions such as exanthema, pruritus, urticaria; the typical morbilliform exanthema occurs 5 - 11 days after start of therapy. Immediate appearance of urticaria indicates an allergic reaction to amoxicillin and therapy should therefore be discontinued.

**Rare** $(\geq 0.01\% \text{ but } < 0.1\%)$: (see also section 4.4)
- Angioneurotic oedema (Quincke's oedema)
- Erythema multiforme exsudativum
- Stevens-Johnson syndrome
- Eosinophilia
- Drug fever
- Laryngeal oedema
- Serum sickness
- Haemolytic anaemia
- Allergic vasculitis
- Interstitial nephritis
- Anaphylactic shock

**Blood disorders:**
There have been isolated reports of leucopenia, granulocytopenia, thrombocytopenia, pancytopenia, anaemia, myelosuppression, agranulocytosis, prolongation of bleeding time, and prolongation of prothrombin time. However, these changes were reversible on discontinuation of therapy.

**Gastrointestinal disorders:**
Common $(\geq 1\% \text{ but } < 10\%)$:
Gastric complaints, nausea, loss of appetite, vomiting, flatulence, soft stools, diarrhoea, enanthemas (particularly in the region of the mouth), dry mouth, taste disturbances. These effects on the gastrointestinal system are mostly mild and frequently disappear either during the treatment or very soon after completion of
therapy. The occurrence of these side-effects can generally be reduced by taking Amoxicillin 500mg Capsules during meals or with some food.

If severe and persistent diarrhoea occurs, the very rare possibility of pseudomembranous colitis should be considered. The administration of anti-peristaltic drug is contraindicated.

*Very rare (<0.01%):*
Development of a black tongue.

*Liver disorders:*

*Uncommon (≥0.1% but <1%)*
Moderate and transient increase of liver enzymes. Rare reports of hepatitis and cholestatic jaundice.

*Rare (≥0.01% but <0.1%):*
Acute interstitial nephritis may occur in rare cases.

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

*Other undesirable effects*
Prolonged and repeated use of the preparation can result in superinfections and colonization with resistant organisms or yeasts such as oral and vaginal candidiasis.

### 4.9 OVERDOSE

**Symptoms of overdose:**
Amoxicillin is not generally associated with acute toxic effects, even when accidentally consumed in high doses. Overdosage can lead to symptoms such as gastrointestinal disturbances and fluid and electrolyte imbalance.

**Management of overdose:**
There is no specific antidote for an overdose of amoxicillin. Treatment consists primarily of administration of activated charcoal (gastric lavage is usually not necessary) or symptomatic measures. Particular attention should be paid to the water and electrolyte balance of the patients. In patients with severely impaired renal function, large overdoses can result in signs of renal toxicity; crystalluria is possible. Amoxicillin can be eliminated via haemodialysis.

### 5 PHARMACOLOGICAL PROPERTIES

**Pharmacotherapeutic group:** Beta-lactam antibiotics, penicillins

**ATC-Code:** J01CA04

### 5.1 PHARMACODYNAMIC PROPERTIES

**General Properties**

**ATC CLASSIFICATION**

ATC-Code: J01A04

**MODE OF ACTION**

Amoxicillin is an aminopenicillin that has bacterial action due to its inhibition of the synthesis of the bacterial cell wall

**MECHANISM (S) OF RESISTANCE**

Bacteria may be resistant 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.
Breakpoints
The MIC breakpoints for susceptible organisms vary according to species.

Enterobacteriaceae are considered susceptible when inhibited at ≤ 8 mg/L amoxicillin.

From NCCLS recommendations and using NCCLS-specified methods:
- *M. catarrhalis* (β-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 and 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. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

**SUSCEPTIBLE:**
Frequency of resistance ranges in EU

<table>
<thead>
<tr>
<th>Gram-positive aerobes</th>
<th>Frequency of resistance ranges in EU (extreme values)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus anthracis</em></td>
<td></td>
</tr>
<tr>
<td><em>Corynebacterium spp</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus bovis</em></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> #</td>
<td>4.6 – 51.4%</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus viridans</em> §</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gram-negative aerobes:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Brucella spp</em> #</td>
<td>46.7%</td>
</tr>
<tr>
<td><em>Escherichia oh</em></td>
<td>2 – 31.7%</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>15.3%</td>
</tr>
<tr>
<td><em>Haemophilus parainfluenzae</em></td>
<td></td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em> §</td>
<td>12 – 80%</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em> #</td>
<td></td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>28%</td>
</tr>
<tr>
<td><em>Salmonella spp</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus spp</em> §</td>
<td></td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td></td>
</tr>
</tbody>
</table>

**Anaerobes**
- *Bacteroides melaninogenicus* §
- *Clostridium spp* §
- *Fusobacterium spp.* §
- *Peptostreptococci* §

**RESISTANT**

**Gram-positive aerobes**
Staphylococci (β-lactamase producing strains)

**Gram-negative aerobes**
- *Acinetobacter spp* §
- *Citrobacter spp* §
- *Enterobacter spp* §
- *Klebsiella spp* §
- *Moraxella catarrhalis* §

MHRA PAR-Amoxicillin 250mg and 500mg Capsules 24
Proteus spp (indole positive)
Proteus vulgaris
Providencia spp
Pseudomonas spp
Serratia 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.

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 250 mg and 750 mg 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 500 mg amoxicillin results in plasma concentrations of 6-11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/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.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/min, very similar to the inulin clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different 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
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
Capsule contents
Magnesium Stearate
Gelatin

MHRA PAR-Amoxicillin 250mg and 500mg Capsules
Capsule (Body)
Erythrosine E 127
Patent Blue E 131
Sunset Yellow E 110
Titanium Dioxide E 171

Capsule (Cap)
Yellow Iron Oxide E 172
Titanium Dioxide E 171

6.2 INCOMPATIBILITIES
None stated.

6.3 SHELF LIFE
36 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25°C.
Store in the original container

6.5 NATURE AND CONTENTS OF CONTAINER
Polypropylene container with pilfer proof polyethylene closure containing 100, 500 and 1000 capsules.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
None.

7 MARKETING AUTHORISATION HOLDER
LPC Medical (UK) Limited
30 Chaul End Lane
Luton
Bedfordshire LU4 8EZ
U. K.

8 MARKETING AUTHORISATION NUMBER(S)
PL 19348/0054.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
09/03/2011

10 DATE OF REVISION OF THE TEXT
09/03/2011
PATIENT INFORMATION LEAFLET

AMOXICILLIN 250mg/500mg CAPSULES

What is Amoxicillin 250/500mg Capsules and what is it used for?

The name of your medicine is Amoxicillin 250mg capsules or Amoxicillin 500mg capsules.

250mg Capsules: Each capsule contains 250mg of Amoxicillin as the active ingredient. Each capsule is size "0", ivory/scarlet hard gelatin capsule. In addition, the capsules contain magnesium stearate.

500mg Capsules: Each capsule contains 500mg of Amoxicillin as the active ingredient. Each capsule is size "0", ivory/scarlet hard gelatin capsule. In addition, the capsules contain magnesium stearate.

The capsule shell is made of gelatin and contains the following colouring agents: E110 Sunset yellow, E127 Erythrosine, E131 Patent Blue, E171 Titanium dioxide. Amoxicillin capsules come in containers of 100, 500 and 1000 capsules.

Amoxicillin is an antibiotic. It works by killing bacteria that cause some types of infections. Amoxicillin belongs to a group of antibiotics called penicillins.

Amoxicillin 250/500mg Capsules are used to treat a range of bacterial infections including those of the - chest (bronchitis or pneumonia) - ears - sinuses - throat - kidneys and bladder - gut and areas around the gut

They may also be used to help prevent infections of the heart valves that may follow some surgical and dental operations in patients who have a particular risk of developing such infections.

Who makes your Amoxicillin 250/500mg Capsules?

The Product Licence Holder of Amoxicillin capsules is LPC Medical (UK) Limited, 30 Chaull End Lane, Luton, Bedfordshire LU4 8EZ, U.K.

Before you take Amoxicillin 250/500mg Capsules

Do not take Amoxicillin 250/500mg Capsules if any of the following apply to you:

- If you think you are, or you have been told you are, sensitive or allergic to penicillin, amoxicillin or to certain other antibiotics such as cephalosporins.
- You have a viral infection, including a viral infection called infectious mononucleosis or glandular fever.
- You have blood disease called acute lymphatic leukaemia.

Amoxicillin 250/500mg Capsules may or may not be suitable for you if any of the following apply. If you are not sure, discuss these with your doctor or pharmacist before you take Amoxicillin 250/500mg Capsules. Make sure that you tell your doctor about all medicines that you are taking, whether or not these have been prescribed or have been bought over the counter.

- If you are suffering from diarrhoea and vomiting. This may reduce the effect of your medicine.
- If you have asthma
- If you suffer from any allergies
- If you have any problems with your kidneys or have a catheter to enable you to pass urine.
- If you are having blood or urine tests for sugar or a substance found in bile called urobilinogen because false positive results may occur. If you are diabetic, it is important that you know that Amoxicillin 250/500mg Capsules can affect the results of certain glucose tests.
- If you are pregnant, the levels of a hormone called oestriol in your urine may fall. It is important that your doctor and midwife know that you are taking amoxicillin so that they can interpret the test results correctly.
- In premature children and during the neonatal period: renal, hepatic and haematological functions should be monitored.

Amoxicillin capsules contain Sunset Yellow. This may cause allergic reactions.

Breast feeding and pregnancy

If you are pregnant, think you are pregnant or are planning become pregnant, discuss this with your doctor for advice before taking any medicine.

Small amounts of amoxicillin may enter the breast milk and can occasionally cause diarrhoea or mouth infections in infants. Infants may also become allergic to amoxicillin. If you are breastfeeding, discuss this with your doctor before you take Amoxicillin 250/500mg Capsules.

Taking other medicines

Amoxicillin 250/500mg Capsules are not recommended for use with some other medicines and special care is needed when it is given with others. Make sure that you will tell your doctor about all medicines that you are taking, whether
or not these are prescribed or have been bought over the counter. Amoxicillin 250/500mg Capsules may or may not be suitable for you if:

- You are taking allopurinol (a medicine for gout) because the risk of allergic skin rashes is increased
- You are taking probenecid because this can cause the blood concentrations of amoxicillin to increase
- You are taking digoxin (a heart medicine) because blood concentrations of this drug may increase
- You are taking warfarin or any other medicine that prevents blood clotting because the time it takes for your blood to clot may be even longer while you are taking amoxicillin and you may need extra blood tests because of this
- You are taking certain other antibiotics called macrolides, tetracyclines, chloramphenicol, or sulphonamides because the effect of amoxicillin may be reduced
- You are taking the contraceptive pill. Amoxicillin 250/500mg Capsules may reduce the effect of the pill. You should therefore take additional contraceptive precautions such as using a condom or diaphragm with a spermicide

How to take Amoxicillin 250/500mg Capsules

You should always take this medicine as prescribed by your doctor. Do not take more than the doctor told you to. Follow the instructions on the pharmacist’s label. If you are not sure about anything please ask your doctor or pharmacist.

The dose you are prescribed will depend on the type and severity of your infection.

The usual dose for adults and adolescents (13 years or more) weighing over 40kg is one 250mg capsule three times a day. For more severe infections your doctor may prescribe a higher total daily dose.

In simple bladder infections (cystitis), you may be instructed to take only two doses 12 hours apart to treat the infection. Each dose is usually of 3g.

If you are given amoxicillin because you have a risk of developing an infection of the heart valves during a surgical or dental procedure and you are not having a general anaesthetic, you would usually be given 3g within one hour of the start of the procedure and, possibly, another dose of 3g about 6 hours later.

Amoxicillin 250/500mg Capsules are not recommended for children (under 13 years) or those weighing less than 40kg. In order to give the right dose, other size capsules, tablets and suspensions containing amoxicillin are available for these persons as below.

Children:

Children weighing less than 40 kg
The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen

Dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

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

Other dosages which may be given are:

- 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 regimen should be guided by national/local recommendations.
- Early Lyme disease (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.
- Prophylaxis for endocarditis: 50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure.
- Impaired renal function: The dose should be reduced. 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.

If you have kidney problems your doctor may decide to give you lower dose.

Swallow the capsules with drink e.g. water. Do not chew the capsules. The capsules can be taken before, with or after food. Space the doses as evenly as possible throughout the day.

Your doctor will tell you how long your treatment with Amoxicillin 250/500mg Capsules will last. Treatment is usually continued for two or three days after the symptoms of the infection have disappeared.

It is important that you keep taking Amoxicillin 250/500mg Capsules until the prescribed course is finished. Do not stop taking the capsules just because you feel better. If you stop too soon, the infection may start up again.

If you still feel unwell at the end of your prescribed course of treatment, or feel worse during treatment, tell your doctor.

If you forget to take Amoxicillin 250/500mg Capsules at the right time, take it as soon as you remember. Do not take a double dose to make up for forgotten individual doses.

If you have taken more Amoxicillin 250/500mg Capsules than you should, drink plenty of water and consult your doctor or the nearest hospital casualty department immediately. Take this leaflet or some capsules with you so that people will know what you have taken.
Possible side effects

Like all medicines, Amoxicillin 250/500mg Capsules can have side effects. In this section, common side effects occur in less than one in ten patients but more than one in a hundred. Uncommon side effects occur in less than one in a hundred patients but more than one in a thousand patients. Rare side effects occur in less than one in a thousand patients but more than one in ten thousand patients. Very rare side effects occur in less than one in ten thousand patients.

Allergic reactions may occur commonly during treatment with amoxicillin but severe allergic reactions are rare. If any of the following happen, stop taking Amoxicillin 250/500mg Capsules and tell your doctor (or an emergency doctor) immediately. You may need urgent medical attention or hospitalisation.

- skin rash, redness or itching; some sort of skin rash may occur commonly.
- swelling of the face or neck: Mild forms occur commonly, but severe forms are rare.
- blistering or peeling of the skin, with or without ulceration in the mouth and sore eyes or sore genitals. These are rare side effects.
- In rare cases there may be joint pain and fever, breathing problems, sweating, rapid heart beat or loss of consciousness.

Other rare side effects that may be due to allergy are increases in number of one type of white blood cells called eosinophils, drops in number of red blood cells causing anaemia, inflammation and damage to the blood vessels causing purple spots or blotches in and under the skin, and inflammation of the kidney.

Also, tell your doctor immediately if you experience any of the following rare or very rare possible side effects of treatment because they are, or may be, serious:

- If your skin or the whites of your eyes turn yellow, your urine turns dark or faeces become very pale.
- If you have severe diarrhoea, with or without bleeding.
- If you have a fit.
- If you have abnormal bruising or notice that you bleed for longer after minor wounds.
- If you have pain in the area of the kidneys (this will feel like low back pain).

Other possible side effects:

The following have been reported commonly:
Stomach complaints, loss of appetite, feeling sick, being sick, wind, soft stools, diarrhoea, ulceration of the mouth, dry mouth, and disturbances in taste. These symptoms are usually mild and disappear either during treatment or very soon after completion of treatment. These symptoms may be reduced by taking the capsules with food. If diarrhoea is severe or you see blood, you should contact your doctor immediately (see above).

Some people develop thrush (a yeast infection of the vagina, mouth or skin folds) whilst they are taking antibiotics.

Uncommonly, the blood levels of enzymes made by the liver may be increased.

Rarely, inflammation of the liver, acute inflammation of kidneys, uncontrolled or restless movements of the arms and legs, and dizziness have been reported. Fits have been reported particularly in patients with kidney disorders or if high doses are being taken.

In very rare cases the tongue turn black.

There have been isolated reports of change in the composition of the blood. These include decreases in the number of various different types of white blood cells, decreases in the numbers of red blood cells or platelets or of all types of blood cells. There have also been isolated reports of prolonged bleeding time and an increase in the time taken for blood to clot.

These blood changes have returned to normal after stopping treatment.

If you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

Storing Amoxicillin 250/500mg Capsules

Amoxicillin capsules should be kept out of the reach and sight of children.

Do not store the capsules above 25°C.

Store in the original pack.

If your doctor decides to stop the treatment, return any capsules left over to the pharmacist. Only keep them if your doctor tells you to.

Do not use after the expiry date printed on the package.

Important reminder: Do not give your capsules to anyone else, even if they suffer from the same condition as you. This medicine could be harmful to them or interfere with other treatments. Your medicine has been prescribed by your doctor specifically for you.

Legal status: POM

This package leaflet is revised in December 2010.

PL 19348/0053 and 19348/0054
Each capsule contains 294mg Amoxicillin Trihydrate equivalent to 250mg Amoxicillin.
Also contains E110.
- Read the package leaflet before use.
- Use as directed by the physician.

500 Capsules
- Do not store above 25°C.
- Store in the original container.
- Keep the container tightly closed.

For oral administration.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

MA Holder: LPC Medical (UK) Ltd., 30 Chaul End Lane, Luton, Bedfordshire, LU4 8EZ, UK.
PL No. 19348/0054 POM

Each capsule contains 588mg Amoxicillin Trihydrate equivalent to 500mg Amoxicillin.
Also contains E110.
- Read the package leaflet before use.
- Use as directed by the physician.

500 Capsules
- Do not store above 25°C.
- Store in the original container.
- Keep the container tightly closed.

For oral administration.

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MA Holder: LPC Medical (UK) Ltd., 30 Chaul End Lane, Luton, Bedfordshire, LU4 8EZ, UK.
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