Public Assessment Report

UKPAR

AMOXICILLIN 250 MG CAPSULES
AMOXICILLIN 500 MG CAPSULES

(amoxicillin trihydrate)

PL 30464/0105-6

Athlone Pharmaceuticals Limited.
LAY SUMMARY

Amoxicillin 250 mg Capsules
Amoxicillin 500 mg Capsules
(amoxicillin trihydrate, capsules, 250 mg and 500 mg)

This is a summary of the Public Assessment Report (PAR) for Amoxicillin 250 mg Capsules (PL 30464/0105) and Amoxicillin 500 mg Capsules (Pl 30464/0106). It explains how Amoxicillin 250 mg and 500 mg Capsules were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Amoxicillin 250 mg and 500 mg Capsules.

The medicines will be collectively referred to as Amoxicillin Capsules throughout the remainder of this public assessment report (PAR).

For practical information about using Amoxicillin Capsules patients should read the package leaflet or contact their doctor or pharmacist.

What are Amoxicillin Capsules and what are they used for?
Amoxicillin Capsules are used to treat infections caused by bacteria in different parts of the body. Amoxicillin Capsules may also be used in combination with other medicines to treat stomach ulcers.

These medicines are the same as Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8) which are already authorised. The company (Athlone Laboratories Limited) that makes Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8) has agreed that its scientific data can be used as a basis for the grant of identical licences for Amoxicillin Capsules (informed consent).

How do Amoxicillin Capsules work?
Amoxicillin Capsules contain the active ingredient amoxicillin. Amoxicillin is one of a group of antibiotic medicines called penicillins. Amoxicillin works by interfering with the bacteria that cause infections.

How are Amoxicillin Capsules used?
The pharmaceutical form of this medicine is a capsule and the route of administration is oral.

The patient must always take this medicine exactly as their doctor or pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

- Swallow with water without opening capsule.
- Space the doses evenly during the day, at least 4 hours apart.

The usual dose is:

**Children weighing less than 40 kg**
All doses are worked out depending on the child’s body weight in kilograms.

- The patient’s doctor will advise how much Amoxicillin Capsules should be given to a baby or child.
- The usual dose is 40 mg to 90 mg for each kilogram of body weight a day, given in two or three divided doses.
- The maximum recommended dose is 100 mg for each kilogram of body weight a day.
Adults, elderly patients and children weighing 40 kg or more
The usual dose of Amoxicillin Capsules is 250 mg to 500 mg three times a day or 750 mg to 1 g every 12 hours, depending on the severity and type of infection.

- **Severe infections**: 750 mg to 1 g three times a day
- **Urinary tract infections**: 3 g twice daily for one day.
- **Lyme disease (an infection spread by parasites called ticks)**: Isolated erythema migrans (early stage – red or pink circular rash): 4 g a day, Systemic manifestations (late stage – for more serious symptoms or when the disease spreads around your body): up to 6 g a day.
- **Stomach ulcers**: one 750 mg or one 1 g dose twice a day for 7 days with other antibiotics and medicines to treat stomach ulcers.
- **To prevent heart infection during surgery**: the dose will vary according to the type of surgery. Other medicines may be given at the same time. The patient’s doctor, pharmacist or nurse can give the patient more details.
- The maximum recommended dose is 6 g per day.

**Kidney problems**
If the patient has kidney problems the dose might be lower than the usual dose.

Amoxicillin Capsules can only be obtained with a prescription.

For further information on how Amoxicillin Capsules are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**What benefits of Amoxicillin Capsules have been shown in studies?**
Amoxicillin Capsules are considered identical to previously authorised Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8), with the same benefits and risks. So no new studies have been provided for Amoxicillin Capsules but reference is made to the studies for Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8).

**What are the possible side effects from Amoxicillin Capsules?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

The applications for Amoxicillin Capsules are considered to be identical to the previously authorised applications for Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8) with the same benefits and risks.

For a full list of all the side effects reported with Amoxicillin Capsules see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

For the full list of restrictions, see the package leaflet.

**Why is Amoxicillin Capsules approved?**
The MHRA decided that the benefits of Amoxicillin Capsules are greater than their risks and recommended that they be approved for use.
What measures are being taken to ensure the safe and effective use of Amoxicillin Capsules?
Safety information has been included in the Summaries of Product Characteristics and the package leaflet for Amoxicillin Capsules including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Amoxicillin Capsules
Marketing Authorisations were granted in the UK on 03 February 2012.

The full PAR for Amoxicillin Capsules follows this summary.

For more information about treatment with Amoxicillin Capsules read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in September 2016.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I  Introduction</td>
<td>6</td>
</tr>
<tr>
<td>II Quality aspects</td>
<td>7</td>
</tr>
<tr>
<td>III Non-clinical aspects</td>
<td>10</td>
</tr>
<tr>
<td>IV  Clinical aspects</td>
<td>11</td>
</tr>
<tr>
<td>V   User consultation</td>
<td>11</td>
</tr>
<tr>
<td>VI  Overall conclusion, benefit/risk assessment and Recommendation</td>
<td>12</td>
</tr>
<tr>
<td>Summary of steps taken after authorisation</td>
<td>25</td>
</tr>
</tbody>
</table>
I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the MHRA granted Marketing Authorisations for the medicinal products Amoxicillin 250 mg and 500 mg Capsules (PL 30464/0105-6) to Athlone Pharmaceuticals Ltd on 03 February 2012. These are prescription-only medicines (POM).

Amoxicillin Capsules are indicated for the treatment of the following infections in adults and children (see sections 4.2, 4.4 and 5.1 of the SmPC):

- Acute bacterial sinusitis
- Acute otitis media
- Acute streptococcal tonsillitis and pharyngitis
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Acute cystitis
- Asymptomatic bacteriuria in pregnancy
- Acute pyelonephritis
- Typhoid and paratyphoid fever
- Dental abscess with spreading cellulitis
- Prosthetic joint infections
-Helicobacter pylori eradication
- Lyme disease

Amoxicillin Capsules are also indicated for the prophylaxis of endocarditis.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Amoxicillin is a semisynthetic penicillin, which is acid resistant and has a similar antibacterial spectrum to ampicillin. It is, however, better absorbed after oral administration, yielding blood levels approximately twice as high as those obtained with similar doses of ampicillin.

Amoxicillin is used for the same purposes as ampicillin and is especially suitable for the treatment of infections of the urinary and respiratory tracts by ampicillin sensitive organisms.

These applications were submitted as simple abridged applications according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, as amended, cross-referring to Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8) approved on 04 November 1988 to the Marketing Authorisation Holder Athlone Laboratories 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.
II QUALITY ASPECTS

II.1 Introduction
These are simple, informed consent applications for Amoxicillin 250 mg and 500 mg Capsules, submitted under Article 10(c) of Directive 2001/83/EC, as amended. The applications cross-refer to Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8) approved on 04 November 1988, to Athlone Laboratories Limited.

The current applications are considered valid.

II.2 Drug Substance
Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3 Medicinal Product
Name(s)
The proposed names of the products are Amoxicillin 250 mg and 500 mg Capsules. The products have been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
The products contain 250 mg and 500 mg amoxicillin, as amoxicillin trihydrate and are packaged in:

- an opaque white polypropylene securitainer with a polyethylene air proof security cap and a polyethylene jayfilla in pack sizes of 15, 18, 20, 21, 28, 30, 50, 100 or 500 (250 mg strength only) capsules.
- an opaque white polypropylene securitainer with a polyethylene air proof security cap and a polyethylene bag in pack sizes of 500 (500 mg strength only) or 1000 capsules (250 mg strength only).
- an opaque polyvinylidene chloride/polyvinylchloride blister 250/40 with an aluminium lidding foil 20 micron containing 15, 18, 20, 21, 28, 30, 50, 100, 500 or 1000 (250 mg strength only) capsules.

The proposed shelf life (48 months) and storage conditions (Store below 25°C. Protect from light and moisture) are consistent with the details registered for the cross-referenced products.

Legal status
On approval, the products will be available by supply through pharmacies, subject to a medical prescription (POM).

Marketing Authorisation Holder/Contact Persons/Company
The proposed Marketing Authorisation Holder is Athlone Pharmaceuticals Limited, Ballymurray, Co. Roscommon, Ireland.
The Qualified Person (QP) responsible for pharmacovigilance is stated and their CV is included.

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

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

Manufacturing process
The manufacturing process is consistent with the details registered for the reference products and the maximum batch sizes are stated.

Finished product/shelf-life specification
The finished product specifications are in line with the details registered for the reference products.

TSE Compliance
With the exception of magnesium stearate and gelatin, none of the excipients contain materials of animal or human origin. The suppliers of magnesium stearate and gelatin have provided Certificates of Suitability from the European Directorate for the Quality of Medicines (EDQM) which cover all aspects of the manufacture and control of these excipients. No genetically modified organisms (GMO) have been used in the preparation of the excipients. This is consistent with the reference products.

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 Capsules BP 250 mg and 500mg (PL 06453/0017-8).

Expert Report
The applicant has included a detailed pharmaceutical expert report, written by an appropriately qualified person.

Product Name and Appearance
See 2.1 for details of the proposed product names. The appearance of the products is identical to that of the reference products.

Summaries of product characteristics (SmPC)
The proposed SmPCs are consistent with the details registered for the reference products.

Patient Information Leaflet/labelling
PIL
The patient information leaflet has been prepared in line with the details registered for the reference products.

Carton and blister
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.
II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with these applications is acceptable. The grant of Marketing Authorisations is recommended.
III NON-CLINICAL ASPECTS
As these applications are identical to the reference products Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8), no new non-clinical data have been supplied with these applications and none are required. A non-clinical expert report has been written by a suitably qualified person and is satisfactory.
IV CLINICAL ASPECTS
As these applications are identical to the reference products Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8), 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.

The Marketing Authorisation Holder has provided a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Risk Management Plan (RMP)
Suitable justification has been provided for not submitting a Risk Management Plan for these products.

Discussion on the clinical aspects
The grant of Marketing Authorisations is recommended.

V User consultation
The package leaflet has been evaluated via a user consultation study, in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the package leaflet was English.

The results show that the package leaflet meets the criteria for readability, as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.
VI Overall conclusion, benefit/risk assessment and recommendation

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

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

CLINICAL
These applications are identical to the previously granted applications for Amoxicillin Capsules BP 250 mg and 500mg (PL 06453/0017-8), granted to Athlone Laboratories Limited on 04 November 1988.

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

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with that for 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 non-clinical 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.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for the original grant of this medicine is presented below:

Carton:
Each capsule contains amoxicillin 250mg as amoxicillin trihydrate Ph eur. Each capsule also contains magnesium stearate Ph eur., starch Ph eur., gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172).

For oral use. Swallow with water.

KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN.

Use as directed by the physician.

Store below 25°C. Protect from light and moisture.

Please read the enclosed leaflet before you start to take this medicine.
Amoxicillin Capsules BP 250mg

Contains amoxicillin 250mg as amoxicillin trihydrate. Each capsule also contains magnesium stearate, starch, gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172).

For oral use. Swallow with water.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Use as directed by the physician. Please read the enclosed leaflet before you start to take this medicine. Store below 25°C. Store in the original package. Return any unused medication to your pharmacist.

Amoxicillin 250mg
5 day treatment pack
15 Capsules BP
CONTAINS PENICILLIN

Take ONE capsule THREE times a day for five days. Take at regular intervals. Complete the prescribed course unless otherwise directed.

Name..............................................................
Date.......................... Disp By.............................

Amoxicillin 250mg
15 Capsules BP
5 day pack

WHITE TTA AREA TO REMAIN VARNISH FREE
PAR Amoxicillin 250 mg and 500 mg Capsules PL 30464/0105-6
Amoxicillin Capsules BP 500mg
Contains amoxicillin 500mg as amoxicillin trihydrate. Each capsule also contains magnesium stearate, starch, gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172). For oral use. Swallow with water. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Use as directed by the physician. Please read the enclosed leaflet before you start to take this medicine. Store below 25°C. Store in the original package. Return any unused medication to your pharmacist.
Each capsule contains amoxicillin 500mg as amoxicillin trihydrate Ph. eur. Each capsule also contains magnesium stearate Ph. eur., starch Ph. eur., gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172). For oral use. Swallow with water.

KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN. Use as directed by the physician. Store below 30°C.

Protect from light and moisture. Please read the enclosed leaflet before you start to take this medicine.

Distributor: KENT Pharmaceuticals
Worton Road Aylesford
Kent, TN26 3LL, UK.

P. Holder: Akhane Pharmaceuticals Ltd.
Derry, Co. Derry, N. Ireland.

Batch No.: 
Expiry: 

Container:
Amoxicillin Capsules BP 500mg
Contains amoxicillin 500mg as amoxicillin trihydrate. Each capsule also contains magnesium stearate, starch, gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172). For oral use. Swallow with water.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Use as directed by the physician. Please read the enclosed leaflet before you start to take this medicine. Store below 25°C. Store in the original package. Return any unused medication to your pharmacist.
Amoxicillin Capsules BP 500mg

Contains amoxicillin 500mg as amoxicillin trihydrate. Each capsule also contains magnesium stearate, starch, gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172).

For oral use. Swallow with water.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Use as directed by the physician. Please read the enclosed leaflet before you start to take this medicine. Store below 25°C. Store in the original package. Return any unused medication to your pharmacist.
Amoxicillin Capsules BP 500mg

Contains amoxicillin 500mg as amoxicillin trihydrate. Each capsule also contains magnesium stearate, starch, gelatin, erythrosin (E127), quinoline yellow (E104), titanium dioxide (E171), red iron oxide (E172).

For oral use. Swallow with water.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Use as directed by the physician. Please read the enclosed leaflet before you start to take this medicine. Store below 25°C. Store in the original package. Return any unused medication to your pharmacist.

Bar code
Place address label here

PL Holder: Athlone Pharmaceuticals Ltd., Ballymurray, Co Roscommon, Ireland.
Distributed by: Kent Pharmaceuticals Limited, Wotton Road, Ashford, Kent, TN23 9LL, U.K.
The following table lists non-urgent safety updates to the Marketing Authorisations for these products that have been approved by the MHRA since the products were first licensed. The table includes updates that have been added as an annex to this PAR. This is not a complete list of the post-authorisation changes that have been made to these Marketing Authorisations.

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/06/2016</td>
<td>Type IB</td>
<td>PL 30464/0105-0037 and PL 30464/0106-0038: To update the SmPC sections 2, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2, 5.3, 6.2, 6.3, 6.4, 6.5, 6.6 and PILs due to the Commission Decision of 20/08/2015 for any product that contains amoxicillin to bring our SPCs and PILs in line with Article 30.</td>
<td>Approved on 10/08/2016.</td>
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</tbody>
</table>
ANNEX 1

Our Reference: PL 30464/0105-0037
               PL 30464/0106-0038

Product: Amoxicillin 250mg Capsules
          Amoxicillin 500mg Capsules

Marketing Authorisation Holder: Athlone Pharmaceuticals Limited
ActiveIngredient(s): Amoxicillin trihydrate

Type of Procedure: National
Submission Type: Variation
Submission Category: Type IB
Submission Complexity: Standard
EU Procedure Number (if applicable): Not applicable

Reason:
To update the SmPC sections 2, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2, 5.3, 6.2, 6.3, 6.4, 6.5, 6.6 and PILs due to the Commission Decision of 20/08/2015 for any product that contains amoxicillin to bring our SmPCs and patient information leaflets (PILs) in line with Article 30.

Supporting Evidence
Revised SmPC fragments and PILs.

Evaluation
The proposed changes to the SmPCs and PILs are in line with Article 30. The updated SmPC fragments and PILs have been incorporated into the Marketing Authorisations.

Conclusion
The proposed changes to the SmPCs and PILs are acceptable.

Decision - Approved on 10 August 2016.