Co-amoxiclav 500mg/100mg powder for solution for injection or infusion

Co-amoxiclav 1000mg/200mg powder for solution for injection or infusion

(amoxicillin sodium, clavulanate potassium)

PL 31745/0024-5

UKPAR

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Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion

(amoxicillin sodium, clavulanate potassium)

PL 31745/0024-5

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Ibigen Srl, Italy Marketing Authorisations (licences) for the medicinal products Co-amoxiclav 500mg/100mg powder for solution for injection or infusion (PL 31745/0024) and Co-amoxiclav 1000mg/200mg powder for solution for injection or infusion (PL 31745/0025) on 26 June 2012. These are prescription-only medicines (POM).

Co-amoxiclav is an antibiotic and works by killing bacteria that cause infections. It contains two active ingredients, amoxicillin and clavulanic acid. Amoxicillin belongs to a group of medicines called ‘penicillins’ and can sometimes be stopped from working (made inactive) by resistant bacteria. The other active component (clavulanic acid) stops this from happening.

Co-amoxiclav is used in adults and children to treat the following infections:

- Severe ear, nose and throat infections
- Respiratory tract infections
- Skin and soft tissue infections, including dental infections
- Urinary tract infections
- Bone and joint infections
- Intra-abdominal infections
- Genital organ infections in women

Co-amoxiclav is also used in adults and children to prevent infections associated with major surgical procedures.

These applications are for products considered to be identical to previously granted licences for Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2), authorised to Bowmed Limited on 02 November 2007.
No new or unexpected safety concerns arose from these simple applications. It was judged that the benefits of Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion outweigh the risks; hence Marketing Authorisations have been granted.
Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion

(amoxicillin sodium, clavulanate potassium)

PL 31745/0024-5

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Ibigen Srl, Italy Marketing Authorisations for the medicinal products Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion (PL 31745/0024-5) on 26 June 2012. The products are prescription-only medicines.

These are simple, abridged, ‘informed consent’ applications, submitted according to Article 10(c) of EC Directive 2001/83 (as amended), cross-referencing the Marketing Authorisations for Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2), authorised to Bowmed Limited on 02 November 2007.

Co-amoxiclav is indicated for the treatment of the following infections in adults and children:

- Severe infections of the ear, nose and throat (such as mastoiditis, peritonsillar infections, epiglottitis, and sinusitis when accompanied by severe systemic signs and symptoms)
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis
- Bone and joint infections, in particular osteomyelitis
- Intra-abdominal infections
- Female genital infections.

It is also used for prophylaxis against infections associated with major surgical procedures in adults, such as those involving the gastrointestinal tract, pelvic cavity, head and neck, and biliary tract surgery.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.
Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

The MHRA considers that the pharmacovigilance system described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) 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.

The Marketing Authorisation Holder has provided adequate justification for not submitting a Risk Management Plan (RMP). As the applications are for products that are identical to already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, routine pharmacovigilance activities are proposed and a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profiles of the actives are well-established.

No new data were submitted nor was it necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products. A Public Assessment Report (PAR) is available for the cross-reference products, Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2).
PHARMACEUTICAL ASSESSMENT

1. INTRODUCTION

These are simple abridged applications, submitted under Article 10(c) of Directive 2001/83/EC (as amended) for Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion. The proposed MAH is Ibigen Srl.

The reference products are Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2), authorised to Bowmed Limited on 02 November 2007. The proposed and reference products are identical.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The approved names of the products are Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion. The products have been named in line with current requirements and the product names are acceptable.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion are licensed for marketing in clear, Type III, glass vials fitted with chlorobutyl rubber stoppers and aluminium rings. The vials contain 500 mg amoxicillin (as amoxicillin sodium)/100 mg clavulanic acid (as clavulanate potassium) or 1000 mg amoxicillin (as amoxicillin sodium)/200 mg clavulanic acid (as clavulanate potassium), as a powder for solution for injection or infusion. The vials are packaged with the patient information leaflet (PIL) in cardboard outer cartons in pack sizes of 1, 5, 10, 20 or 50. The MAH has stated that not all pack sizes may be marketed. The container closure systems and pack sizes are consistent with those for the reference products.

The approved shelf-life (2 years) and storage conditions (‘Do not store above 25°C’) before reconstitution/dilution are consistent with the details registered for the reference products. From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used, immediately, in-use storage times and conditions are the responsibility of the user. This is also consistent with the details registered for the reference products.
2.3 Legal status
POM - The products are available subject to a medical prescription.

2.4 Marketing Authorisation Holder / Contact Persons/Company
The proposed Marketing Authorisation Holder is ‘Ibigen Srl, Via Fossignano 2, 04011 – Aprilia (LT), Italy’.

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

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of GMP compliance has been provided.

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

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

2.8 Finished product / shelf-life specification
The proposed finished product specifications are consistent with the details registered for the cross-reference products.

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

2.10 TSE Compliance
There are no materials of human or animal origin contained in or used in the manufacturing process for the proposed products. None of the excipients are sourced from genetically modified organisms.

3. EXPERT REPORT
A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert was provided.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The products are presented in clear glass vials as a white powder for solution for injection or infusion. The appearance of the products is consistent with that of the cross-reference products.
5. SUMMARY OF PRODUCT CHARACTERISTICS
The approved SmPCs are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) / LABELLING
PIL
The approved PIL is satisfactory and in line with the approved SmPCs. The PIL has been prepared in the user-tested format and is consistent with the PIL registered for the cross-reference products.

A mock-up PIL has been provided. PIL user-testing has been accepted based on bridging to the successful user-testing of the PIL for the reference products, Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2). The text, content and layout of the proposed PIL are essentially identical to the approved PIL for the reference product. The bridging is accepted.

Labelling
Mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements.

The MAH has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for currently unmarketed pack sizes to the MHRA for approval before those packs are commercially marketed.

7. CONCLUSIONS
The grounds for these applications are considered adequate. Marketing Authorisations were therefore granted.
NON-CLINICAL ASSESSMENT

These are simple, abridged, ‘informed consent’ applications made under Article 10(c) of EC Directive 2001/83 (as amended).

No new non-clinical data have been supplied with these applications and none are required for applications of this type. A non-clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the non-clinical expert has been supplied.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA). It is not considered that these medicinal products represent any risk to the environment. There is no reason to conclude that marketing of these products will change the overall use pattern of the existing market. The availability of these medicinal products, which are identical to the cited reference products, will not lead to any increase in environmental exposure concentrations of the active ingredient.
CLINICAL ASSESSMENT

These are simple, abridged, ‘informed consent’ applications made under Article 10(c) of EC Directive 2001/83 (as amended), cross-referring to the Marketing Authorisations for Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2; Bowmed Limited).

No new clinical data have been supplied with the applications, and none are required for applications of this type. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-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.

EFFICACY
These applications are considered identical to the previously granted licences for Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2; Bowmed Limited).

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The approved SmPCs, PIL and labelling are satisfactory and consistent with the details registered for the cross-reference products.

A mock-up PIL has been provided. PIL user-testing has been accepted based on bridging to the successful user-testing of the PIL for the reference products, Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for solution for Injection or Infusion (PL 24610/0001-2).

Mock-up labelling has been provided and is satisfactory. The approved labelling artwork complies with statutory requirements. The MAH have committed to submitting mock-ups for unmarketed pack sizes to the MHRA for approval before those packs are marketed.

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 cross-reference products. The benefit: risk ratio is considered to be positive.
Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion

(amoxicillin sodium, clavulanate potassium)

PL 31745/0024-5

**STEPS TAKEN FOR ASSESSMENT**

1. The MHRA received the marketing authorisation applications on 15 February 2012.

2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 10 May 2012.

3. Following assessment of the application the MHRA requested further information relating to the quality dossier on 11 May 2012.

4. The applicant responded to the MHRA’s requests, providing further information for the quality sections on 29 May 2012.

5. The applications were determined on 26 June 2012.
Co-amoxiclav 500mg/100mg and 1000mg/200mg powder for solution for injection or infusion

(amoxicillin sodium, clavulanate potassium)

PL 31745/0024-5

STEPS TAKEN AFTER AUTHORISATION

Not applicable
SUMMARY OF PRODUCT CHARACTERISTICS

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.
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LABELLING

Co-amoxiclav 500mg/100mg powder for solution for injection or infusion (PL 31745/0024)

Carton for vials

Vial label
Co-amoxiclav 1000mg/200mg powder for solution for injection or infusion (PL 31745/0025)

Carton for vials

Vial label

Contains penicillin.
Contents: 1000mg amoxicillin (as sodium salt) and 200mg clavulanic acid (as potassium salt).
For IV use. Read package leaflet before use. POM

PL 31745/0025 Igien Srl