Medicines & Healthcare products Regulatory Agency

MHRA

# Public Assessment Report

# Mutual Recognition Procedure

# Co-amoxiclav 500/125mg and 875/125mg Film-coated Tablets

# (Amoxicillin trihydrate and potassium clavulanate)

# Product Licence Numbers: PL 20075/0733-34

# Procedure Numbers: UK/H/6758/001-2/MR

# Accord Healthcare Limited

# LAY SUMMARY

## Co-amoxiclav 500/125mg and 875/125mg Film-coated Tablets

## (Amoxicillin trihydrate and potassium clavulanate)

This is a summary of the Public Assessment Report (PAR) for Co-amoxiclav 500/125mg and 875/125mg Film-coated Tablets. It explains how these products 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 these products.

These products will be referred to as Co-amoxiclav Tablets in this lay summary for ease of reading.

For practical information about using Co-amoxiclav Tablets, patients should read the package leaflets or contact their doctor or pharmacist.

**What are Co-amoxiclav Tablets and what are they used for?**
These applications are for generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised in the European Union (EU) called Augmentin 500/125 and 875/125 mg film-coated tablets.

Co-amoxiclav Tablets are used in adults and children to treat the following infections:
• middle ear and sinus infections
• respiratory tract infections
• urinary tract infections
• skin and soft tissue infections including dental infections
• bone and joint infections.

**How do Co-amoxiclav Tablets work?**
These medicines contain the active ingredients amoxicillin and clavulanic acid. Amoxicillin is an antibiotic that belongs to a group of medicines called penicillins. Amoxicillin works by killing the bacteria that cause the infection. Amoxicillin can sometimes be stopped from working (made inactive). The other active component, clavulanic acid, stops this from happening.

**How are Co-amoxiclav Tablets used?**
The pharmaceutical form of these medicines is a tablet and the route of administration is oral (by mouth). The whole tablet must be swallowed with a glass of water at the start of a meal or slightly before. The doses must be spaced evenly during the day, at least 4 hours apart. Do not take 2 doses in 1 hour. Co-amoxiclav should not be taken for more than 2 weeks. If patients still feel unwell, they should go back to see a doctor.

***Adults and children weighing 40 kg and over***
• The usual dose is 1 tablet three times a day

***Children weighing less than 40 kg***
Children aged 6 years or less should preferably be treated with Amoxicillin/Clavulanic acid oral suspension (in bottles or sachets).

Advice must be sought from a doctor when giving Co-amoxiclav tablets to children weighing less than 40 kg.

**Patients with kidney and liver problems**

• If patients have kidney problems, the dose might be changed. A different strength or a different medicine may be chosen by a doctor.

• If patients have liver problems, they may have more frequent blood tests to check how their liver is working.

For further information on how Co-amoxiclav Tablets are used, refer to the package leaflets and Summaries of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take these medicines exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

**What benefits of Co-amoxiclav Tablets have been shown in studies?**

Because Co-amoxiclav Tablets are generic medicines, studies in healthy volunteers have been limited to tests to determine that they are bioequivalent to the reference medicines. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

**What are the possible side effects of Co-amoxiclav Tablets?**

Because Co-amoxiclav Tablets are generic medicines and are bioequivalent to the reference medicines, its benefits and possible side effects are considered to be the same as the reference medicines.

For the full list of all side effects reported with these medicines, see Section 4 of the package leaflets or the Summaries of Product Characteristics (SmPC) available on the MHRA website.

**Why were Co-amoxiclav Tablets approved?**

It was concluded that, in accordance with EU requirements, Co-amoxiclav Tablets has been shown to be comparable to and to be bioequivalent to the reference medicines. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

**What measures are being taken to ensure the safe and effective use of Co-amoxiclav Tablets?**

A Risk Management Plan (RMP) has been developed to ensure that Co-amoxiclav Tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPCs and the package leaflets, 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 and reviewed continuously.

**Other information about Co-amoxiclav Tablets**

First-wave mutual recognition procedures were concluded on 03 September 2013 with the Netherlands as Reference Member State (RMS) and Austria, Belgium, Denmark (500/125

mg strength only), Finland, Hungary, Iceland, Ireland, Luxembourg, Portugal, Sweden, and the United Kingdom as Concerned Member States (CMSs; NL/H/2782/001-2/MR).
. Marketing Authorisations were granted to Actavis Group PTC ehf (PL 30306/0456-7) in the UK on 25 September 2013.

Repeat-use mutual recognition procedures (NL/H/2782/001-2/E/001) with the Netherlands as RMS and Czech Republic, Estonia, Greece, Lativia, Lithuania, Poland, Slovakia and Slovenia as CMSs were concluded on 04 December 2014.

The RMS was changed to the UK on 19 July 2017 (UK/H/6758/001-2).

Following a change of ownership procedure, these licenses were transferred to Accord Healthcare Limited (PL 20075/0733-4) on 03 October 2018.

The full PAR for Co-amoxiclav Tablets follows this summary.

This summary was last updated in July 2019.

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## Contents

# I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Co-amoxiclav 500/125mg and 875/125mg Film-coated Tablets (PL 30306/0456-7) could be approved.

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

- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- 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

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

These mutual recognition procedures were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic medicines. the innovator products Augmentin 500/125 mg film-coated tablets (NL license RVG 09840), which has been registered in the Netherlands by GlaxoSmithKline BV since 2 December 1983, and Augmentin 875/125 mg film-coated tablets (NL license RVG 18553), which was registered in the Netherlands on 22 August 1996. The higher strength is no longer registered in the Netherlands. In addition, reference is made to Augmentin authorisations in the individual member states (reference products).

The Reference Member State (RMS) for these procedures was the Netherlands and the Concerned Member States (CMSs) were Austria, Belgium, Denmark (500/125 mg strength only), Finland, Hungary, Iceland, Ireland, Luxembourg, Portugal, Sweden, and the United Kingdom (NL/H/2782/001-2/MR).

These products contain the active substances amoxicillin and clavulanic acid. 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.

No new non-clinical studies were conducted, which is acceptable given that the applications are based on being a generic medicinal products of a reference products that has been licensed for over 10 years.

With the exception of the bioequivalence studies, no new clinical studies were conducted, which is acceptable given that the applications are based on being generic medicinal products of reference products that have been in clinical use for over 10 years. The bioequivalence study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

The RMS and CMSs considered that the applications could be approved at the end of procedure (Day 90) on 03 September 2013. Marketing Authorisations were granted to Actavis Group PTC ehf (PL 30306/0456-7) in the UK on 25 September 2013.

Repeat-use mutual recognition procedures (NL/H/2782/001-2/E/001) with the Netherlands as RMS and Czech Republic, Estonia, Greece, Lativia, Lithuania, Poland, Slovakia and Slovenia as CMSs were concluded on 04 December 2014.

The RMS was changed to the UK on 19 July 2017 (UK/H/6758/001-2).

Following a change of authorisation holder (CoA), these licenses were transferred to Accord Healthcare Limited (PL 20075/0733-4) on 03 October 2018.

# II QUALITY ASPECTS

## II.1 Introduction

These products consist of film-coated tablets. Each film-coated tablet contains amoxicillin trihydrate equivalent to 500 or 875 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.

Co-amoxiclav 500/125mg, Film-coated Tablets are white, oval, film-coated tablets inscribed with 'A' on one side and '64' on the other side.

Co-amoxiclav 875/125mg, Film-coated Tablets are white, capsule shaped, film-coated tablets inscribed with 'A' on one side and with '6' and '5' on the other side with a score line in between.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

In addition to amoxicillin and potassium clavulanate, these products also contain the excipients microcrystalline cellulose (E460), colloidal silicon dioxide, magnesium stearate (E470b), sodium starch glycolate (type A) making up the tablet core. The tablet coat is composed of hypromellose (E464), macrogol 400 and titanium dioxide (E171).

The finished products are packaged in Alu/Alu blister packs and Al/ Al strip in a cardboard box. The tablets are available in blister packs with 4, 5, 6, 7, 8, 10, 12, 14, 15, 16, 20, 21, 25, 30, 35, 40,50, 100 and 500 film-coated tablets.

Not all listed pack sizes will be marketed.

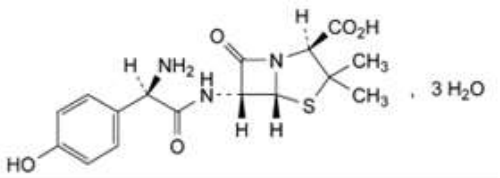
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

## II.2 ACTIVE SUBSTANCES

INN: Amoxicillin trihydrate

Chemical names: (2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate

Structural formula:




Molecular formula: $C_{16}H_{19}N_3O_5S.3H_2O$

Molecular mass: 419.4 g/mol

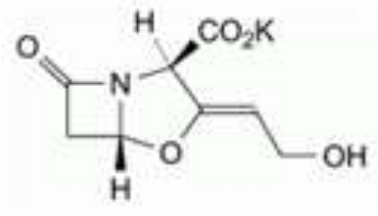
Appearance: White or almost white, crystalline powder.

Solubility: Amoxicillin trihydrate is slightly soluble in water, very slightly soluble in ethanol (96 per cent) and practically insoluble in fatty oils. It dissolves in dilute acids and dilute solutions of alkali hydroxides.

Amoxicillin trihydrate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

INN: Potassium clavulanate
Chemical names: potassium (2R,3Z,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate
Structural formula:




Molecular formula: $C_8H_8KNO_5$
Molecular mass: 237.3 g/mol
Appearance: White or almost white powder, hygroscopic (diluted).
Solubility: Potassium clavulanate is freely soluble in water, slightly soluble in ethanol (96 per cent) and very slightly soluble in acetone (diluted).

Potassium clavulanate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

## II.3 DRUG PRODUCTS

### Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution and impurity profiles have been provided for the proposed and reference products.

The two strengths for both the reference and the test products are not dose-weight proportional, therefore bioequivalence studies were performed for both strengths separately.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the final products.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

### Manufacture of the products

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

Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

**Finished Product Specifications**
The finished product specifications are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years, with no special temperature storage conditions. The products must be stored in the original package in order to protect from light and moisture.

### II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of marketing authorisations is recommended.

## III NON-CLINICAL ASPECTS

### III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of amoxicillin and potassium clavulanate are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

### III.2 Pharmacology
No new pharmacology data were provided and none were required for these applications.

### III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for these applications.

### III.4 Toxicology
No new toxicology data were provided and none were required for these applications.

### III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of an already authorised product, an increase in environmental exposure is not anticipated following approval of the Marketing Authorisations for the proposed products.

### III.6 Discussion on the non-clinical aspects
The grant of marketing authorisations is recommended.

## IV CLINICAL ASPECTS

### IV.1 Introduction
The clinical pharmacology, efficacy and safety of amoxicillin and potassium clavulanate are well-known. With the exception of data from two bioequivalence studies, no new clinical data are provided or are required for this type of applications. An overview based on a literature review and a review of these studies is, thus, satisfactory.

## IV. 2 Pharmacokinetics

In support of the applications, the applicant submitted the following bioequivalence studies.

**Study 1**

This study was a single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study comparing the test product Amoxicilline/Clavulaanzuur Actavis 500/125 mg film-coated tablets versus the reference product, Augmentin 500/125 mg film-coated tablets (GlaxoSmithKline, United Kingdom) in subjects under fasted conditions.

Each subject received a single dose (500 mg amoxicillin/125 mg clavulanic acid) of one of the 2 formulations. The tablet was orally administered with 240 ml water after an overnight fast. There were 2 dosing periods, separated by a washout period of 3 days.
Blood samples were collected pre-dose and up to 24 hours post dose.

The design of the study is acceptable. These products must be taken with food only in order to prevent gastro-intestinal adverse events; there is no pharmacokinetic reason for intake with food. Therefore, the study design using fasting conditions is acceptable.

A summary of the pharmacokinetic results are presented below:

**Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, $t_{max}$ (median, range)) of amoxicillin under fasting conditions.**

| Treatment N=48 | $AUC_{0-t}$ µg.h/ml | $AUC_{0-\infty}$ µg.h/ml | $C_{max}$ µg/ml | $t_{max}$ h | $t_{1/2}$ h |
|---|---|---|---|---|---|
| Test | 24.80 ±5.36 | 25.37 ± 5.43 | 8.21 ± 2.29 | 2.0 (0.75 – 4.0) | 1.16 ± 0.19 |
| Reference | 26.44 ± 6.04 | 26.92 ± 6.06 | 8.21 ± 2.29 | 2.0 (1.0 – 5.0) | 1.15 ± 0.18 |
| *Ratio (90% CI) | 0.95 (0.92 – 0.97) | 0.94 (0.92-0.97) | 0.94 (0.89-0.99) | - | - |
| CV (%) | 8.1 | 7.9 | 14.9 | | |

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
$AUC_{0-t}$ area under the plasma concentration-time curve from time zero to t hours
$C_{max}$ maximum plasma concentration
$t_{max}$ time for maximum concentration
$t_{1/2}$ half-life
*ln-transformed values

**Table 2. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, $t_{max}$ (median, range)) of clavulanic acid under fasting conditions**

| Treatment N=48 | $AUC_{0-t}$ µg.h/ml | $AUC_{0-\infty}$ µg.h/ml | $C_{max}$ µg/ml | $t_{max}$ h | $t_{1/2}$ h |
|---|---|---|---|---|---|
| Test | 6.40 ±2.52 | 6.62 ± 2.52 | 2.63 ± 0.98 | 1.25 (0.75 – 3.0) | 1.10 ± 0.15 |
| Reference | 6.72 ± 2.41 | 6.96 ± 2.41 | 2.71 ± 0.96 | 1.5 (1.0 – 3.0) | 1.13 ± 0.19 |
| *Ratio (90% CI) | 0.93 (0.87 – 1.01) | 0.93 (0.87-1.00) | 0.96 (0.89-1.03) | - | - |
| CV (%) | 22.1 | 20.8 | 22.8 | | |

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
$AUC_{0-t}$ area under the plasma concentration-time curve from time zero to t hours

$C_{max}$ maximum plasma concentration
$t_{max}$ time for maximum concentration
$t_{1/2}$ half-life
*ln-transformed values

In line with the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**), the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

**Study 2**
This study was a single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study comparing the test product Amoxicilline/Clavulaanzuur Actavis 875/125 mg film-coated tablets versus the reference product, Augmentin 875/125 mg film-coated tablets (GlaxoSmithKline, United Kingdom) in subjects under fed conditions.

Each subject received a single dose (875 mg amoxicillin/125 mg clavulanic acid) of one of the 2 formulations. The tablets were administered in solid form with 240 ml water 30 minutes after intake of a high fat, high caloric meal containing 955 Kcal, approximately 60% of total calories consisted of fat. For each subject there were 2 dosing periods, separated by a washout period of 8 days.

Blood samples were collected pre-dose and up to 12 hours post dose

The single-dose, crossover study under fed conditions meets the requirement of the applicable guidelines and is in accordance with the recommendation for intake with food as stated in the SmPC.

**Results**

**Table 3. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, $t_{max}$ (median, range)) of amoxicillin under fed conditions.**

| **Treatment N=48** | **$AUC_{0-t}$ µg.h/ml** | **$AUC_{0-\infty}$ µg.h/ml** | **$C_{max}$ µg/ml** | **$t_{max}$ h** | **$t_{1/2}$ h** |
|---|---|---|---|---|---|
| Test | 50.7 ±8.9 | 51.4 ± 9.0 | 15.7 ± 3.5 | 2.33 (1.0 – 5.0) | 1.5 ± 0.3 |
| Reference | 48.8 ± 8.6 | 49.4 ± 8.5 | 15.3 ± 3.4 | 2.33 (1.33 – 5.0) | 1.5 ± 0.3 |
| *Ratio (90% CI) | 1.03 (1.00 – 1.07) | 1.03 (1.00-1.07) | 1.02 (0.97-1.08) | - | - |
| CV (%) | 8.3 | 8.2 | 15.1 | | |

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
$AUC_{0-t}$ area under the plasma concentration-time curve from time zero to t hours
$C_{max}$ maximum plasma concentration
$t_{max}$ time for maximum concentration
$t_{1/2}$ half-life
*ln-transformed values

**Table 4. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, $t_{max}$ (median, range)) of clavulanic acid under fed conditions.**

| Treatment N=48 | $AUC_{0-t}$ µg.h/ml | $AUC_{0-\infty}$ µg.h/ml | $C_{max}$ µg/ml | $t_{max}$ h | $t_{1/2}$ h |
|---|---|---|---|---|---|
| Test | 4.0 ±2.3 | 4.6 ± 2.5 | 1.9 ± 1.1 | 2.33 (1.33 – 5.0) | 1.0 ± 0.2 |
| Reference | 3.7 ± 1.6 | 4.3 ± 1.7 | 1.7 ± 0.8 | 2 (1.33 – 3.0) | 1.0 ± 0.2 |
| *Ratio (90% CI) | 1.01 (0.91 – 1.13) | 1.01 (0.88-1.15) | 1.04 (0.92-1.16) | - | - |
| CV (%) | 30.9 | 30.4 | 32.4 | | |

$AUC_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
$AUC_{0-t}$ area under the plasma concentration-time curve from time zero to t hours
$C_{max}$ maximum plasma concentration
$t_{max}$ time for maximum concentration
$t_{1/2}$ half-life
*ln-transformed values

**Conclusion**
The 90% confidence intervals calculated for the $AUC_{0-t}$ and $C_{max}$ are within the bioequivalence acceptance range of 0.80–1.25 for both active substances. Based on the submitted bioequivalence study Amoxicilline/ Clavulaanzuur Actavis 875/125 mg is considered to be bioequivalent with Augmentin 875/125 mg film-coated tablets under fed conditions.

### IV.3 Pharmacodynamics
No new pharmacodynamic data have been submitted for these applications and none were required.

### IV.4 Clinical efficacy
No new efficacy data were submitted with these applications and none were required.

### IV.5 Clinical safety
With the exception of the safety data submitted with the bioequivalence studies, no new safety data were submitted with these applications.

The safety data from the bioequivalence studies showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence studies.

### IV.6 Risk Management Plan (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

### IV.7 Discussion on the clinical aspects
The grant of marketing authorisations is recommended for these applications.

## V USER CONSULTATION
The Patient Information Leaflet (PIL) 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 results show that the PIL 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

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with amoxicillin and potassium clavulanate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPCs and PILs for these products are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided for Co-amoxiclav 500/125mg Film-coated Tablets (PL 20075/0733).


accord
500
125
mg
Co-amoxiclav
Film-coated Tablets
Amoxicillin/Clavulanic acid
Contains Penicillin
21 Tablets
For oral use
READ ENCLOSED LEAFLET
Co-amoxiclav
Film-coated Tablets
Amoxicillin/Clavulanic acid
21 Tablets
5 055565 748015
Each film-coated tablet contains amoxicillin trihydrate corresponding to 500mg amoxicillin and potassium clavulanate corresponding to 125mg clavulanic acid.
Read the package leaflet before use.
Use as directed by your doctor.
Keep out of the sight and reach of children.
Store in the original package in order to protect from light and moisture.
MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK
PL 20075/0733
POM
Place dispensing label here
BBBA2008
85 x 33 x 122

The following text is the currently approved label text. No label mock-ups have been provided for PL 20075/0734. In accordance with medicines legislation, the 875/125 mg film-coated tablets shall not be marketed in the UK until approval of the label mock-ups has been obtained.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**Carton**

**1. NAME OF THE MEDICINAL PRODUCT**

Co-amoxiclav 875/125mg, Film-coated Tablets
Amoxicillin/Clavulanic acid

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each film-coated tablet contains amoxicillin trihydrate corresponding to 875mg amoxicillin and potassium clavulanate corresponding to 125mg clavulanic acid.

**3. LIST OF EXCIPIENTS**

**4. PHARMACEUTICAL FORM AND CONTENTS**

**Film-coated tablets**

4 film-coated tablets
5 film-coated tablets
6 film-coated tablets
7 film-coated tablets
8 film-coated tablets
10 film-coated tablets
12 film-coated tablets
14 film-coated tablets
15 film-coated tablets
16 film-coated tablets
20 film-coated tablets
21 film-coated tablets
25 film-coated tablets
30 film-coated tablets
35 film-coated tablets
40 film-coated tablets
50 film-coated tablets
100 film-coated tablets
500 film-coated tablets

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

For oral use.

Read the package leaflet before use.

Use as directed by your doctor.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING (S), IF NECESSARY**

**8. EXPIRY DATE**

EXP:

**9. SPECIAL STORAGE CONDITIONS**

Store in the original package in order to protect from light and moisture.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

MA holder
Accord Healthcare Ltd, North Harrow, HA1 4HF, UK

**12. MARKETING AUTHORISATION NUMBER(S)**

PL 20075/0734

**13. BATCH NUMBER**

Batch:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

POM

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

co-amoxiclav 875/125mg film-coated tablets

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS**

**Blister**

**1. NAME OF THE MEDICINAL PRODUCT**

Co-amoxiclav 875/125mg, Film-coated Tablets
Amoxicillin/Clavulanic acid

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Accord logo

**3. EXPIRY DATE**

EXP:

**4. BATCH NUMBER**

Batch:

**5. OTHER**

# TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
|---|---|---|---|---|---|
| IB | To update sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in line with reference product Augmentin 625 mg Tablets, PL 00038/0362, UK/H/4735/002 (Beecham Group plc) dated 28.02.2018. Consequently, the patient information leaflet has also been updated | SmPC and PIL | 06/06/2019 | Approved | Y |

# Annex 1

**Reference:** PL 20075/0733–0006; PL 20075/0734-0006

**Product:** Co-amoxiclav 500/125mg and 875/125mg Film-coated Tablets

**Type of Procedure**: Mutual recognition

**Submission category**: Type IB Variation

**Reason:** To update sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in line with reference product Augmentin 625 mg Tablets, PL 00038/0362, UK/H/4735/002 (Beecham Group plc) dated 28.02.2018. Consequently, the patient information leaflet has also been updated

**Supporting evidence**
The Company has submitted updated sections of the SmPC and PIL.

**Evaluation**
The updated documents are satisfactory.

**Conclusion**
The proposed changes are acceptable.

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

**Decision:** Grant

**Date:** 06 June 2019