Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UK PAR

Azithromycin 250 mg Capsules

(azithromycin dihydrate)

UK Licence No: PL 20416/0548

Crescent Pharma Limited

LAY SUMMARY

Azithromycin 250 mg Capsules

(azithromycin dihydrate)

This is a summary of the Public Assessment Report (PAR) for Azithromycin 250 mg Capsules (PL 20416/0548). For ease of reading, the product may be referred to as 'Azithromycin Capsules' in this lay summary. The Lay summary explains how the application for Azithromycin Capsules was assessed and its authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Azithromycin Capsules.

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

What are Azithromycin Capsules and what are they used for?

This medicine is the same as the medicinal product Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV), which are already authorised in the UK. The licence holder (Jubilant Pharmaceuticals NV) for Azithromycin 250 mg Capsules (PL 19156/0138) has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Azithromycin Capsules (PL 20416/0548) (informed consent).

Azithromycin Capsules are used to treat bacterial infections caused by "microorganisms" such as bacteria. These infections include:

- chest, throat or nasal infections (such as bronchitis, pneumonia, tonsillitis, sore throat (pharyngitis) and sinusitis)
- ear infections
- skin and soft tissue infections (such as an abscess or boil)
- sexually transmitted diseases caused by an organism called Chlamydia.

How do Azithromycin Capsules work?

The active ingredient, Azithromycin is an antibiotic, which belongs to a group of antibiotics called "macrolides".

How are Azithromycin Capsules used?

The pharmaceutical form of this medicine is hard capsules. Azithromycin Capsules are taken by mouth. Azithromycin Capsules can only be obtained on prescription. This medicine should always be taken exactly as instructed by the patient's doctor or pharmacist. The patient should check with his/her doctor or pharmacist if he/she is not sure.

Taking this medicine

The capsules should be swallowed whole with a glass of water.

How much to take

Adults and young people with a body weight of 45kg and above

The usual dose is 500 mg (2 capsules) taken together, once a day, for 3 days.

The dose is different for patients, who have inflammation of the tube that carries urine from the bladder (urethra) or where the womb joins your vagina (cervix). The prescribing doctor will ask the patient to take a single dose of 1000mg (4 capsules) taken all together on one day only.

Children and adolescents under 45kg:
Azithromycin Capsules should not be taken by children weighing less than 45kg. Young people with a body weight of less than 45 kg should use other forms of this medicine such as azithromycin suspension.

Patients with kidney or liver problems
The patient should inform the prescribing doctor if he/she has kidney or liver problems, as the doctor may need to alter the normal dose.

The patient should always continue with the course of treatment, even if he/she feels better. If the patient's infection gets worse or the patient does not begin to feel better within a few days or a new infection develops, the patient should go back and see his/her doctor.

Please read section 3 of the package leaflet for detailed information on dosing recommendations and the duration of treatment.

What benefits of Azithromycin Capsules have been shown in studies?

This application for Azithromycin capsules is considered to be identical to the previously authorised licence for Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV), with the same benefits and risks. So, no new studies have been provided for Azithromycin Capsules (PL 20416/0548). However, reference is made to the studies for Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV).

What are the possible side effects of Azithromycin 250 mg Capsules?

Like all medicines, Azithromycin Capsules can cause side effects, although not everybody gets them.

As Azithromycin Capsules are considered to be identical to Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV), their possible side effects are taken as being the same as those for Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV).

For the full list of all side effects reported with Azithromycin Capsules, see section 4 of the package leaflet.

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

Why are Azithromycin Capsules approved?

No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Azithromycin Capsules outweigh their risks; and the grant of a Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Azithromycin Capsules?

A Risk Management Plan has been developed to ensure that Azithromycin Capsules are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Azithromycin 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 Azithromycin Capsules

A Marketing Authorisation was granted in the UK to Crescent Pharma Limited on 06 August 2018.

The full PAR for Azithromycin Capsules follows this summary.

For more information about treatment with Azithromycin Capsules read the package leaflet, available on the MHRA website, or contact your doctor or pharmacist.

This summary was last updated in September 2018.

Azithromycin 250 mg Capsules

(azithromycin dihydrate)

PL 20416/0548

SCIENTIFIC DISCUSSION

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I. INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited a Marketing Authorisation for the medicinal product Azithromycin Capsules 250 mg (PL 20416/0548) on 06 August 2018. For ease of reading, the product may be referred to as 'Azithromycin Capsules' in this scientific discussion.

Azithromycin capsules are indicated in the treatment of the following bacterial infections induced by micro-organisms susceptible to azithromycin:

- infections of the lower respiratory tract: acute exacerbation of chronic bronchitis (adequately diagnosed) and mild to moderate community-acquired pneumonia
- infections of the upper respiratory tract: sinusitis and pharyngitis/tonsillitis
- acute otitis media
- infections of the skin and soft tissues of mild to moderate severity e.g. folliculitis, cellulites, erysipelas
- uncomplicated genital infections due to *Chlamydia trachomatis.*

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

The application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended. The application for Azithromycin Capsules (PL 20416/0548) cross-refers to the medicinal product Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV), which was granted in the UK on 24 April 2015.

Azithromycin Capsules contain the active ingredient azithromycin (as azithromycin dihydrate). Azithromycin is a macrolide antibiotic belonging to the azalide group.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to those of the previously granted cross-reference product.

II. QUALITY ASPECTS

II.1 INTRODUCTION

This is an informed consent application for Azithromycin capsules (PL 20416/0548) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application for Azithromycin Capsules (PL 20416/0548) cross-refers the medicinal product Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV), which was granted in the UK on 24 April 2015. The application is considered valid.

II.2 Drug substance

The proposed drug substance specification is consistent with the details registered for the reference product.

II.3 Medicinal Product

Name

The proposed name of the product is Azithromycin 250 mg Capsules (PL 20416/0548). The product has been named in line with current requirements.

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

Each hard capsule for oral use contains 250 mg of azithromycin (as azithromycin dihydrate). The product is packaged in white opaque , polyvinylchloride/polyvinylidene chloride-aluminium blister, in a pack size of 6 hard capsules:

The proposed shelf life for the products is 2 years, with the special storage conditions 'Store below 25°C. Store in the original package.'

The packaging, proposed shelf life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
The product is available as a Prescription Only Medicines (POM).

Marketing Authorisation Holder/Contact Persons/Company
Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hampshire RG25 3ED, United Kingdom

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

Finished product/shelf-life specification
The proposed finished product specification is consistent with the details registered for the cross-reference product.

TSE Compliance
With the exception of gelatin, none of the excipients contain materials of animal or human origin. The suppliers of gelatin have provided Certificates of Suitability from the European Directorate for the Quality of Medicines (EDQM) to show that they are manufactured in-line with current European guidelines concerning the minimising of risk of transmission of Bovine Spongiform Encephalopathy/transmissible Spongiform Encephalopathies (BSE/TSE).

This is consistent with the cross-reference product.

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula and use the same processes as the reference product Azithromycin 250 mg Capsules (PL 19156/0138; Jubilant Pharmaceuticals NV).

Product Name and Appearance
See Section II.3 'Medicinal Product, Name' for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

Summary of Product Characteristics (SmPC)

The proposed Summary of Product Characteristics are consistent with the details registered for the cross-reference product.

Patient Information Leaflet (PIL) and Labelling

PIL

The PIL has been prepared in line with the details registered for the cross-reference product.

Carton and label

The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the names 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 the application are acceptable. The grant of a Marketing Authorisation is recommended.

III. NON-CLINICAL ASPECTS

Introduction

As this is an informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/Environmental Risk Assessment (ERA)

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects

The grant of a Marketing Authorisation is recommended.

IV. CLINICAL ASPECTS

Introduction

As this informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Pharmacovigilance and Risk Management Plan (RMP)

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

An acceptable Risk Management Plan (RMP) has been submitted. A summary of safety concerns is listed in the following table.

Table 1 Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Hypersensitivity reactions (including anaphylaxis) • Acute generalised enxanthematous pustulosis (AGEP) • Hepatotoxicity • *Clostridium difficile* associated diarrhoea • Use in patients with severe renal impairment • Myasthenia gravis • Drug interactions with ciclosporin • Cytopenias (Leukopenia, neutropenia, thrombocytopenia, haemolytic anaemia) • Deafness • Pancreatitis • Severe cutaneous adverse reactions (Stevens-Johnson syndrome, Toxic epidermal necrolysis and Erythema Multiforme)
Important potential risks	• Concomitant administration with ergot derivatives • Drug interactions with digoxin, colchicine (P-gp substrates) or coumarin-type oral anticoagulants • Prolongation of the QT interval
Missing information	• Use during breastfeeding • Use during pregnancy • Use in patients with severe hepatic impairment

Routine pharmacovigilance and routine risk minimisation activities are proposed for all safety concerns.

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

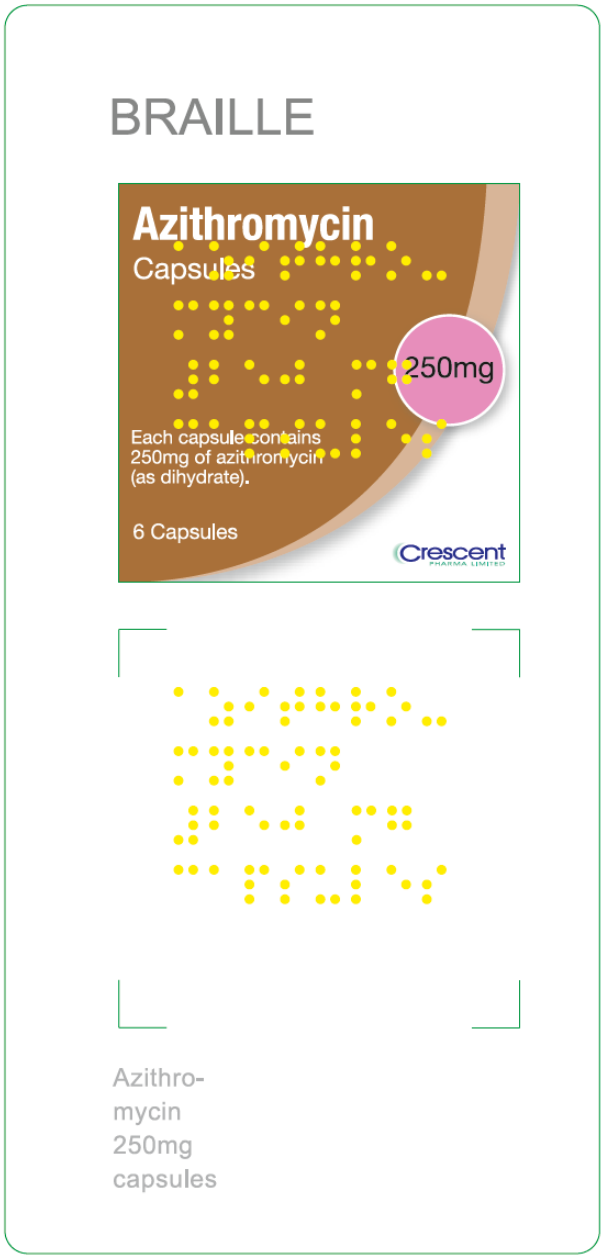
V. USER CONSULTATION

A user consultation with target patient groups on the Patient Information Leaflet (PIL) has been performed on the basis of a bridging report making reference to the PIL for Azithromycin Jubilant 250 mg and 500 mg Film-coated tablets. The bridging report is acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the respective cross-reference product. Extensive clinical experience with azithromycin is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.

In accordance with Directive 2010/84/EU, the current version of the SmPC and PIL is available on the MHRA website. The current labelling is presented below:



BN and EXP will be added at the production.

Azithromycin 250 mg Capsules

(azithromycin dihydrate)

PL 20416/0548

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome