Public Assessment Report

UK PAR

Erythromycin 250 mg Gastro-resistant Tablets

(Erythromycin)

UK Licence No: PL 44041/0015

Noumed Life Sciences Limited
LAY SUMMARY

Erythromycin 250 mg Gastro-resistant tablets

This is a summary of the Public Assessment Report (PAR) for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015). It explains how the application for Erythromycin 250 mg Gastro-resistant Tablets 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 Erythromycin 250 mg Gastro-resistant Tablets. For practical information about using Erythromycin 250 mg Gastro-resistant Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

The product may be referred to as ‘Erythromycin Gastro-resistant Tablets’ in this report.

**What are Erythromycin Gastro-resistant Tablets and what are they used for?**

Erythromycin Gastro-resistant Tablets are used for the treatment and prevention of infections caused by erythromycin-sensitive organisms, such as:

- upper and lower respiratory tract infections
- eye and ear infections
- oral infections
- skin and soft tissue infections
- gastrointestinal infections
- prophylaxis pre- and post-operative trauma, burns and rheumatic fever
- other infections: osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis and scarlet fever.

**How do Erythromycin Gastro-resistant Tablets work?**

Erythromycin Gastro-resistant Tablets contain the active substance erythromycin. Erythromycin belongs to a group of medicines called antibiotics, which act by preventing the growth and multiplication of bacteria.

**How are Erythromycin Gastro-resistant Tablets used?**

Erythromycin Gastro-resistant Tablets are taken by mouth and should be swallowed whole with a drink of water. The tablet(s) should not be crushed or chewed.

This medicine should always be taken exactly as the patient’s doctor has advised. If unsure, the patient should check with his/her doctor.

**Adults and older children:** The usual dosage is one 250 mg tablet every four to six hours. This can be increased to 4g per day if the infection is very severe. It is important that the patient completes his/her full course of antibiotics; the patient should not stop taking the tablets early even if he/she feels better.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration and the duration of treatment.
Erythromycin Gastro-resistant Tablets can only be obtained with a prescription.

**What benefits of Erythromycin Gastro-resistant Tablets have been shown in studies?**
The application for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) is considered to be identical to the previously authorised licence for Erythromycin 250 mg Gastro-resistant tablets, (PL 21880/0069; Medreich plc), with the same benefits and risks. So, no new studies have been provided for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015). However, reference is made to the studies for Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc).

**What are the possible side effects of Erythromycin Gastro-resistant Tablets?**
Like all medicines, Erythromycin Gastro-resistant tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Erythromycin Gastro-resistant Tablets, see section 4 of the package leaflet.

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

**Why are Erythromycin Gastro-resistant Tablets approved?**
No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Erythromycin Gastro-resistant Tablets 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 Erythromycin Gastro-resistant Tablets?**
A Risk Management Plan has been developed to ensure that Erythromycin Gastro-resistant Tablets 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 Erythromycin Gastro-resistant Tablets, 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 Erythromycin Gastro-resistant Tablets**
A Marketing Authorisation was granted in the UK to Noumed Life Sciences Limited on 26 May 2016.

The full PAR for Erythromycin Gastro-resistant Tablets follows this summary.

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

This summary was last updated in July 2016.
Erythromycin 250 mg Gastro-resistant Tablets

(Erythromycin)

PL 44041/0015

SCIENTIFIC DISCUSSION

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I. INTRODUCTION
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Noumed Life Sciences Limited a Marketing Authorisation for the medicinal product Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) on 26 May 2016. The product is a Prescription Only Medicine (POM) indicated for the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Erythromycin is highly effective in the treatment of a variety of clinical infections such as:
1. upper respiratory tract infections: tonsillitis, peritonsillar abscess, pharyngitis, laryngitis, sinusitis, secondary infections in influenza and common colds.
2. lower respiratory tract infections: tracheitis, acute and chronic bronchitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis and Legionnaire's disease
3. ear infections: mastoiditis, otitis media, otitis externa
4. eye infections: blepharitis
5. oral infections: gingivitis, Vincent's angina
6. skin and soft tissue infections: boils and carbuncles, paronychia, abscesses, pustular acne, impetigo, cellulitis and erysipelas
7. gastro-intestinal infections: cholecystitis and staphylococcal enterocolitis
8. prophylaxis: pre- and post-operative trauma, burns and rheumatic fever
9. other infections: osteomyelitis, urethritis, gonorrhoea, syphilis, lymphogranuloma venereum, diphtheria, prostatitis and scarlet fever.

Note: Erythromycin has also proved to be of value in endocarditis and septicaemia, but in these conditions initial administration of erythromycin lactobionate by the intravenous route is advisable.

The application for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) cross-refers to the reference product Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc), which cross-refers to Erythromycin 250 mg Tablets (PL 16363/0019; Milpharm Limited) and was authorised in the UK on 09 April 2002. Erythromycin 250mg Tablets (PL 16363/0019; Milpharm Limited) was granted a licence on 09 April 2002 and cross-refers to Erythromycin Tablets BP 250mg (PL 06809/0124; Ranbaxy Ireland Limited), which was authorised on 07 December 1994. Erythromycin Tablets BP 250mg (PL 06809/0124; Ranbaxy Ireland Limited) cross-refers to Erythromycin Tablets BP 250 mg (PL 00109/0151; Roussel Laboratories Limited), which was granted a licence on 31 May 1990.

The active substance, erythromycin, belongs to a group of medicines called macrolide antibiotics. Erythromycin exerts its antimicrobial action by binding to the 50S ribosomal sub-unit of susceptible microorganisms and supresses protein synthesis.

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 Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) cross-refers to the reference product Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc), which cross-refers to Erythromycin 250mg Tablets (PL 16363/0019; Milpharm Limited) and was authorised in the UK on 09 April 2002. Erythromycin 250mg Tablets (PL 16363/0019; Milpharm Limited) was granted a licence on 09 April 2002 and cross-refers to Erythromycin Tablets BP 250mg (PL 06809/0124; Ranbaxy Ireland Limited), which was authorised on 07 December 1994. Erythromycin Tablets BP 250mg (PL 06809/0124; Ranbaxy Ireland Limited) cross-refers to Erythromycin Tablets BP 250 mg (PL 00109/0151; Roussel Laboratories Limited), which was granted a licence on 31 May 1990.

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

II.3 Medicinal Product
Name
The proposed name of the product is Erythromycin 250 mg Gastro-resistant Tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each Erythromycin 250 mg Gastro-resistant Tablets contains 250 mg of erythromycin as the active substance. The tablets are administered orally (by mouth).

The product is packaged in 250 um polyvinylchloride/20 um aluminium blisters, in a pack size of 28 tablets.

The proposed shelf life for the product is 3 years, with the special storage conditions ‘Do not store above 25°C. Store in the original container.’

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 Medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Noumed Life Sciences Limited, 1st Floor, Cattle Market, Hexham, Northumberland, NE46 1NJ, U.K.

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
None of the excipients contains materials of animal or human origin. 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 utilises the same processes as the reference product Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc).

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 SmPC is 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 name of the product in Braille on the outer packaging.

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 an 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 is an 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.

| Important Identified Risks | • Cardiac Adverse Events (Cardiac disorders including Cardiac arrhythmias, palpitations, QTc interval prolongation, torsades de pointes, and cardiac rhythm disorders including ventricular tachyarrhythmias).  
| | • Allergic reactions (urticaria, skin eruptions, anaphylaxis, pruritus, exanthema, angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme).  
| | • Use in patients with renal impairment.  
| | • Use in patients with hepatic impairment.  
| | • Use in patients with myasthenia gravis.  
| | • Hearing loss.  
| | • Clostridium difficile associated diarrhoea / Pseudomembranous colitis.  
| | • Infantile Hypertrophic Pyloric Stenosis.  
| | • Interaction with other medicinal products. |
| Important Potential Risks | • None |
| Missing Information | • Exposure during pregnancy |

Routine risk minimisation is provided through the Summary of Product Characteristics and the Patient Information Leaflet and this is sufficient.

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

V. USER CONSULTATION
User-testing of the PIL for Erythromycin 250 mg Gastro-resistant Tablets (PL 44041/0015) has been accepted based on the successful user-testing of the PIL for the reference product Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc) as the ‘parent PIL’.
VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY
The data for this application are consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.

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

EFFICACY
This application is identical to the previously granted licence for Erythromycin 250 mg Gastro-resistant tablets (PL 21880/0069; Medreich plc).

SAFETY
No new safety data were supplied or required for this application. Erythromycin has a well-established safety profile. No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPC and PIL are satisfactory, and consistent with those for the cross-reference product. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT
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 cross-reference product. Extensive clinical experience with erythromycin is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.
The SmPC, PIL and labelling are satisfactory and, where appropriate, in line with current guidance.

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: