TRIMETHOPRIM 200 MG TABLETS

(Trimethoprim)

PL 17907/0180

UK PAR

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Lay Summary

The MHRA granted Bristol Laboratories Limited, a Marketing Authorisation (licence) for the medicinal product Trimethoprim 200 mg Tablets (PL 17907/0180) on 05 March 2013. This product is a prescription-only medicine (POM).

Trimethoprim 200 mg Tablets contain the active ingredient trimethoprim. Trimethoprim is an antibacterial medicine used to treat bacterial infections of the urinary or respiratory tract caused by organisms that are sensitive to trimethoprim. It is also used to prevent the patient from getting further urinary tract infections.

No new or unexpected safety concerns arose from this application and it was therefore, judged that the benefits of taking Trimethoprim 200 mg Tablets outweigh the risks; hence a Marketing Authorisation has been granted.
TRIMETHOPRIM 200 MG TABLETS

PL 17907/0180

SCIENTIFIC DISCUSSION

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Pharmaceutical assessment
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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Bristol Laboratories Limited, a Marketing Authorisation for the medicinal product Trimethoprim 200 mg Tablets (PL 17907/0180) on 05 March 2013. This product is indicated for the treatment of susceptible infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections and for the prophylaxis of recurrent urinary tract infections.

This product belongs to a pharmacotherapeutic group of medicines called ‘anti-infectives for systemic use’ (ATC code: J01EA01) and contains the active ingredient trimethoprim.

Trimethoprim is an antimicrobial agent. The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase.

Trimethoprim is effective in vitro against Gram-positive and Gram-negative aerobic organisms, including enterobacteria – E. coli, Proteus, Klebsiella pneumoniae, Streptococcus faecalis, Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus.

It is not active against Mycobacterium tuberculosis, Neisseria gonorrhoeae, Pseudomonas aeruginosa, Treponema pallidum, or anaerobic bacteria.

This application was submitted as a simple abridged application according to Article 10(c) of Directive 2001/83/EC, cross-referring to Trimethoprim 200 mg Tablets (PL 17907/0093), which was granted to the Marketing Authorisation Holder Bristol Laboratories Limited on 26 November 2006.

No new data were submitted nor were they necessary for this simple application, as the data is identical to that of the previously granted cross-reference product.
1 INTRODUCTION
This is a simple, informed consent application for Trimethoprim 200 mg Tablets, submitted under Article 10(c) of Directive 2001/83/EC. The application cross-refers to Trimethoprim 200 mg Tablets (PL 17907/0093), which was granted to the Marketing Authorisation Holder Bristol Laboratories Limited on 26 November 2006.

The current application is considered valid.

2 MARKETING AUTHORISATION APPLICATIONS (MAA)
2.1 Name(s)
The proposed name of the product is Trimethoprim 200 mg Tablets. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 200 mg trimethoprim. The tablets are available in the following presentations:
- high density polyethylene (HDPE) containers in pack sizes of 100, 250 and 500 tablets.
- aluminium/polyvinyl chloride (PVC) blisters in pack sizes of 14, 28, 56 and 84 tablets.

It has been stated that not all pack sizes may be marketed. However, the Marketing Authorisation Holder has committed to submitting the mock-ups for any pack size to the relevant regulatory authorities for approval before marketing.

The proposed shelf life (36 months for both presentations) and storage conditions (‘Do not store above 25°C. Store in the original package’ for the blister packs and ‘Do not store above 25°C. Store in the original package. Keep the container tightly closed’ for the HDPE containers) is consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a prescription-only medicine (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
The proposed Marketing Authorisation Holder is Bristol Laboratories Limited, Unit 3, Canalside, Northbridge Road, Berkhamsted, Herts, HP14 1EG, United Kingdom

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

2.5 Manufacturers
The proposed manufacturing site is consistent with that registered for the reference product and evidence of compliance with current Good Manufacturing Practice has been provided.
2.6 Qualitative and quantitative composition
The composition is consistent with the details registered for the reference product.

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

2.8 Finished product/shelf-life specification
The finished product specification is in line with the details registered for the reference product.

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

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin.

None of the excipients are sourced from genetically modified organisms.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the reference product Trimethoprim 200 mg Tablets (PL 17907/0093).

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

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to that of the reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING
PILs
The patient information leaflet has been prepared in line with the details registered for the reference product.

A package leaflet has been submitted to the MHRA together with results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.
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.

7. CONCLUSIONS
The data submitted with this application is acceptable. The grant of a Marketing Authorisation is recommended.
**NON-CLINICAL ASSESSMENT**

As this application is identical to the reference product Trimethoprim 200 mg Tablets (PL 17907/0093), no new non-clinical data have been supplied with this application and none are required. A non-clinical expert report has been written by a suitably qualified person and is satisfactory.
CLINICAL ASSESSMENT

As this application is identical to the reference product Trimethoprim 200 mg Tablets (PL 17907/0093), no new clinical data have been supplied with this application 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.

Suitable justification has been provided for not submitting a Risk Management Plan for this product.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application is consistent with that previously assessed for the reference product and as such has been judged to be satisfactory.

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

EFFICACY
This application is identical to the previously granted application for Trimethoprim 200 mg Tablets (PL 17907/0093), granted to Bristol Laboratories Limited on 26 November 2006.

SAFETY
No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and consistent with that for the reference product.

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 product is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the reference product. Extensive clinical experience with trimethoprim is considered to have demonstrated the therapeutic values of the compounds. The benefit/risk is therefore considered to be positive.
TRIMETHOPRIM 200 MG TABLETS

PL 17907/0180

STEPS TAKEN FOR ASSESSMENT

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<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation Application on 03 February 2010.</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 09 February 2010.</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 25 June 2010 and 03 November 2010.</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 09 July 2010 and 09 February 2011.</td>
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<td>5</td>
<td>The application was determined on 05 March 2013.</td>
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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.
PATIENT INFORMATION LEAFLET

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.
Trimethoprim 200mg Tablets

Do not store above 25°C.

Keep out of the reach and sight of children.

For further information please read the patient information leaflet.

Take as directed by your physician.

Each tablet contains Trimethoprim 200mg as the active ingredient.

Each strip contains Trimethoprim 200mg as the active ingredient.

Each tablet contains Trimethoprim 200mg as the active ingredient.

28 Tablets

Artwork Same Size
Size: 116 x 16 x 50 mm

Kaypee Design
05 01 10
Container Label:

Trimethoprim

Each tablet contains Trimethoprim 200 mg as the active ingredient. Also contains lactose. For oral administration only. Take as directed by the physician. Refer to the enclosed leaflet for further information. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN. Do not store above 25°C. Store in the original container. Keep the container tightly closed.

100 Tablets

Bristol Laboratories Ltd.
Seckhamsted, Hersham, HP4 1EG, UK.

Blister:

TRIMETHOPRIM 200 mg TABLETS
PL Holder: Bristol Laboratories Ltd.
Batch No. Exp. Date

TRIMETHOPRIM 200 mg TABLETS
PL Holder: Bristol Laboratories Ltd.
Batch No. Exp. Date

TRIMETHOPRIM 200 mg TABLETS
PL Holder: Bristol Laboratories Ltd.
Batch No. Exp. Date