PHENOXYMETHYLPPENICILLIN 125MG/5ML AND 250MG/5ML GRANULES FOR ORAL SOLUTION
PL 20416/0203-4

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited Marketing Authorisations (licences) for the medicinal products Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0203-4) on 31 January 2013. These medicines are only available on prescription from your doctor. Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution may be referred to as Phenoxymethylpenicillin Granules for Oral Solution throughout the rest of this report.

The active ingredient, phenoxymethylpenicillin (as phenoxymethylpenicillin potassium), belongs to the penicillin group of antibiotics.

Phenoxymethylpenicillin Granules for Oral Solution is an antibacterial drug used in the:

- treatment of mild to moderately severe infections such as chest and throat infections, skin and soft tissue infections, infections of the mouth, gums and teeth, scarlet fever (characterised by high fever, sore throat and skin rashes, and mild erysipelas (disease marked by red skin eruptions, chills and fever)
- prevention of rheumatic fever and chorea (a group of disorders characterised by brief rapid involuntary movements of limbs, face trunk and head).

No new or unexpected safety concerns arose from these simple applications and it was therefore judged that the benefits of using Phenoxymethylpenicillin Granules for Oral Solution outweigh the risks; hence Marketing Authorisations have been granted.
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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Marketing Authorisations for the medicinal products Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0203-4) to Crescent Pharma Limited on 31 January 2013. The products are prescription-only medicines (POM) indicated in the treatment of mild to moderately severe infections associated with micro-organisms whose susceptibility to penicillin is within the range of serum levels attained with these dosage forms. The following infections will usually respond to adequate doses:

- streptococcal infections (without bacteraemia): mild to moderate infections of the upper respiratory tract, scarlet fever and mild erysipelas.
- pneumococcal infections: mild to moderately severe infections of the respiratory tract.
- staphylococcal infections sensitive to penicillin: mild infections of the skin and soft tissues.
- Fusospirochaetosis (Vincent’s gingivitis and pharyngitis): mild to moderately severe infections of the oropharynx usually respond to therapy with oral penicillin.

Phenoxymethylpenicillin Granules for Oral Solution is also indicated for prophylactic use. Prophylaxis with oral penicillin has proved effective in preventing recurrence of rheumatic fever and chorea.

Patients with a past history of rheumatic fever receiving continuous prophylaxis may harbour penicillin-resistant organisms. In these patients, the use of another prophylactic agent should be considered.

It is to be noted that severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with phenoxymethylpenicillin during the acute phase.

These applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0131-2) which were originally granted Marketing Authorisations (PL 00549/5239R-40R) to Regent Laboratories Limited on 29 August 1986. On 17 October 1994, the Marketing Authorisation Holder was updated by a change of ownership to Regent-GM Laboratories Limited. Thereafter, on 24 March 2004 the Marketing Authorisation holder was again updated by a change of ownership to Crescent Pharma Limited.

The active ingredient, phenoxymethylpenicillin (as phenoxymethylpenicillin potassium), belongs to the pharmacotherapeutic group class called ‘beta-lactamase sensitive penicillins’.

No new data were submitted nor were they necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products.
1. INTRODUCTION
These are abridged applications for Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution, submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0131-2) which are currently authorised to Crescent Pharma Limited after changes in authorisation holder on 29 August 1986 (PL 00549/5239R-40R), 17 October 1994 (PL 12724/0013-14) and 24 March 2004 (PL 20416/0131-2). The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed names of the products are Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each 5 ml of reconstituted product contains 125 mg or 250 mg of the active ingredient phenoxymethylpenicillin (as phenoxymethylpenicillin potassium). The granules for oral solution are packaged in amber glass or plastic bottles with screw caps. After reconstitution of the product, each bottle contains 100 ml of oral solution.

The packaging, proposed shelf-life (36 months before reconstitution and 1 week after reconstitution) and storage conditions (‘Do not store above 25 °C. Keep the bottle tightly closed.’ for the dry granules, and ‘Store in a refrigerator (2 – 8 °C). Keep the bottle tightly closed. Use within one week of reconstitution.’, for the reconstituted product) are consistent with the details for the cross-reference products.

2.3 Legal status
On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hants, RG25 3ED.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.
2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of Good Manufacturing Practice (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 size is stated.

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

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

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

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged applications, as the proposed products are manufactured to the same formula and utilise the same processes as the reference products.

3. EXPERT REPORT
The applicant cross-refers to the data for Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0131-2), to which these applications are claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The appearances of the products are identical to the respective cross-reference products.

5. SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed Summaries of Product Characteristics are consistent with the details registered for the respective cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
The patient information leaflets (label-leaflets) have been prepared in line with the details registered for the cross-reference products and are attached to the product information provided for the bottle labels.
The applicant has previously submitted results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive 2001/83/EC for the reference products Phenoxy methylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0131-2). The results indicate that the label-leaflets are 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.

As the proposed and reference label-leaflets are considered the same, no further user testing of the label-leaflets for these products is necessary.

**Bottle label**
The proposed artwork is consistent with the artwork registered for the respective cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the names of the products in Braille on the outer packaging.

7. **CONCLUSION**
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Suitable justification has been provided for non-submission of an Environment Risk Assessment (ERA). This is consistent with the cross-reference products.

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

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.

As the applications are for identical versions of already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profile of the active ingredient is well-established.

The grant of Marketing Authorisations is recommended.
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 identical to previously granted applications for Phenoxymethylpenicillin 125mg/5ml and 250mg/5ml Granules for Oral Solution (PL 20416/0131-2).

SAFETY
No new safety data were supplied or required for these applications. Phenoxymethylpenicillin has a well-established safety profile. No new or unexpected safety concerns arise from these applications.

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

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. Extensive clinical experience with phenoxymethylpenicillin is considered to have demonstrated the therapeutic value of the products. The benefit/risk balance is, therefore, considered to be positive.
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STEPS TAKEN FOR ASSESSMENT

1  The MHRA received the Marketing Authorisation applications on 10 May 2012.
2  Following standard checks and communication with the applicant the MHRA
considered the applications valid on 14 June 2012.
3  Following assessment of the applications the MHRA requested further
information relating to the dossier on 18 June 2012.
4  The applicant responded to the MHRA’s request, providing further information
on the 15 November 2012.
5  The applications were granted on 31 January 2013.
SUMMARY OF PRODUCT CHARACTERISTICS

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