CHLORHEXIDINE DIGLUCONATE
0.2% W/V MOUTHWASH
PL 00079/0677

UKPAR

TABLE OF CONTENTS

Lay Summary .............................................. Page 2
Scientific discussion ................................ Page 3
Steps taken for assessment ......................... Page 9
Steps taken after authorisation – summary .... Page 10
Summary of Product Characteristics .......... Page 11
Product Information Leaflet ..................... Page 11
Labelling .................................................... Page 12
CHLORHEXIDINE DIGLUCONATE
0.2% W/V MOUTHWASH
PL 00079/0677

LAY SUMMARY

On 06 June 2013, the MHRA granted Beecham Group plc a Marketing Authorisation (licence) for the medicinal product Chlorhexidine Digluconate 0.2% w/v Mouthwash (PL 00079/0677). This is a General Sales List medicine (legal status GSL), which can be purchased at pharmacies, supermarkets and other retail outlets without the supervision of a pharmacist.

This product contains the active ingredient chlorhexidine digluconate, which is an antibacterial agent that reduces the formation of dental plaque. It is used to treat and prevent gum disease, promote gum healing after dental surgery or treatment, control mouth ulcers, maintain mouth hygiene and manage oral thrush and denture sore mouth.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of using Chlorhexidine Digluconate 0.2% w/v mouthwash (PL 00079/0677) outweigh the risks; hence a Marketing Authorisation has been granted.
# SCIENTIFIC DISCUSSION

**TABLE OF CONTENTS**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Pharmaceutical assessment</td>
<td>5</td>
</tr>
<tr>
<td>Nonclinical assessment</td>
<td>7</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>7</td>
</tr>
<tr>
<td>Overall conclusions and benefit-risk assessment</td>
<td>8</td>
</tr>
</tbody>
</table>
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation to Beecham Group plc for the medicinal product Chlorhexidine Digluconate 0.2% w/v Mouthwash (PL 00079/0677) on 06 June 2013. This product is available as a General Sales List (GSL) medicine and does not require a prescription.

Chlorhexidine Digluconate 0.2% w/v Mouthwash is used for inhibition of the formation of dental plaque. It is also used as an aid in the treatment and prevention of gingivitis and in the maintenance of oral hygiene, particularly in situations where tooth brushing cannot be adequately employed (e.g. following oral surgery or in mentally or physically handicapped patients). Moreover, it is suitable for use in a post-peridontal surgery or treatment regimen to promote gingival healing. The mouthwash is useful in the management of aphthous ulceration and oral candidal infections (e.g. denture stomatitis and thrush).

This application was submitted as an abridged simple application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Corsodyl 0.2% Mouthwash (PL 00079/0608), which was granted to the Marketing Authorisation Holder Beecham Group plc on 26 April 2007.

The product contains the active substance chlorhexidine digluconate, which is an antimicrobial agent. It is effective against a wide range of Gram negative and Gram positive vegetative bacteria, yeasts, dermatophyte fungi and lipophilic viruses. It is active against a wide range of important oral pathogens and is therefore effective in the treatment of many common dental conditions.
1. INTRODUCTION
This is a simple, piggyback application for Chlorhexidine Digluconate 0.2% w/v Mouthwash, submitted under Article 10c of Directive 2001/83/EC as amended. The proposed MA holder is Beecham Group plc, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK.

The application cross-refers to Corsodyl 0.2% Mouthwash (PL 00079/0608), which was granted to the Marketing Authorisation Holder Beecham Group plc on 26 April 2007.

The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Chlorhexidine Digluconate 0.2% w/v Mouthwash. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The finished product contains 0.2% w/v chlorhexidine digluconate.

The finished product is packaged in an oriented amber polyethylene terephthalate bottle with a plastic screw cap made from white food grade polypropylene. Each bottle contains either 300 ml or 600 ml.

The proposed shelf-life (30 months unopened, 3 months after opening) and storage conditions (“Store below 25°C”) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a General Sales List medicine (GSL).

2.4 Marketing authorisation holder/Contact Persons/Company
Beecham Group plc, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK.

The QP responsible for pharmacovigilance is stated and their CV is included.
2.5 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.

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

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product.

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

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

2.10 TSE Compliance
No materials of animal or human origin are included in this product. This is consistent with the cross-reference product.

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 Corsodyl 0.2% Mouthwash (PL 00079/0608).

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

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

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

6. PATIENT INFORMATION LEAFLET (PIL)/LABEL
Label-Leaflet
Mock-ups and results of consultations with target patient groups (to ensure readability in accordance with Article 59 of Council Directive 2001/83/EC, as amended) have not been provided with this application. The applicant states that there are no plans to
market the product at present but has committed to providing full colour mock-ups, together with results of consultations with target patient groups, for assessment and approval prior to placing the product onto the market in the future.

7. CONCLUSIONS
The data submitted with the application is acceptable. From a quality perspective, a Marketing Authorisation may be granted.

NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with this application and none are required for applications of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for applications of this type.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Chlorhexidine Digluconate 0.2% w/v Mouthwash are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

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

CLINICAL PHARMACOLOGY/EFFICACY
No new clinical pharmacology/efficacy data have been submitted with this application and none are required for applications of this type.

SAFETY
No new safety data have been submitted with this application and none are required for applications of this type.

No new or unexpected safety concerns arise from this application.

The SmPC is satisfactory and consistent with the reference product. The applicant has committed to providing full colour mock-ups of the PIL/label, together with results of consultations with target patient groups, for assessment and approval prior to placing the product onto the market in the future.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with chlorhexidine digluconate is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
CHLORHEXIDINE DIGLUCONATE  
0.2% w/v MOUTHWASH  
PL 00079/0677

**STEPS TAKEN FOR ASSESSMENT**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation application on 26 October 2011.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant, the MHRA considered the application valid on 22 November 2011.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application, the MHRA requested further information relating to the dossier on 17 February 2012, 28 September 2012 and 16 January 2013.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 16 August 2012, 18 December 2012 and 15 April 2013.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 06 June 2013.</td>
</tr>
</tbody>
</table>
**CHLORHEXIDINE DIGLUCONATE**

*0.2% W/V MOUTHWASH*

PL 00079/0677

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Summary of Product Characteristics and Patient Information Leaflet
In accordance with Directive 2010/84/EU, the current approved UK versions of the Summaries of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for this product are available on the MHRA website.
Labelling

The following text is the approved label text for Chlorhexidine Digluconate 0.2% w/v Mouthwash (PL 00079/0677). No label mock-ups have been provided for this product. In accordance with medicines legislation, the product shall not be marketed in the UK until approval of the label mock-ups has been obtained.

1.3.1 Label-Leaflet

Chlorhexidine Digluconate 0.2% w/v Mouthwash
(PL 00079/0677)

December 2012

GlaxoSmithKline Consumer Healthcare

The label-leaflet for the product will be split into 3 sections as indicated by the diagram below:

<table>
<thead>
<tr>
<th>Left Section</th>
<th>Middle Section</th>
<th>Right Section</th>
</tr>
</thead>
</table>

The middle section is the front facing section and will be the branded part of the product. Braille will also be printed on this section.

The left and right sections will contain all the relevant patient information for the product such as directions for use, possible side effects, storage and handling etc. Exact details are provided below.

Text to appear in the Middle Section

Chlorhexidine Digluconate 0.2% w/v Mouthwash
chlorhexidine digluconate
ALCOHOL FREE

- Bleeding Gums
- Irritated Gums
- Mouth Ulcers

TREATS GUM PROBLEMS

Mint flavour

300 ml

<Text in Braille – Chlorhexidine Digluconate 0.2% w/v Mouthwash>

Text to appear in the Right Section

What is Chlorhexidine Digluconate 0.2% w/v Mouthwash for?

The active ingredient is chlorhexidine digluconate which is an antibacterial agent that reduces the formation of dental plaque and is used to:

- Treat & prevent gum disease (where gums may bleed when brushed)
- Promote gum healing after dental surgery or treatment
- Control mouth ulcers
- Maintain mouth hygiene
- Manage oral thrush and denture sore mouth

Check before you use

Do not use:
- If you have ever had an allergic reaction to chlorhexidine digluconate or any of the other ingredients. (see Storage and further information).
- In children under 12 years unless recommended by a dentist.
- Anywhere other than your mouth. Wash thoroughly if you get any in your eyes or ears.
- Immediately after brushing your teeth. See How to use for more information.

Take special care with Chlorhexidine Digluconate 0.2% w/v Mouthwash
- Do not bleach fabrics that have been in contact with the mouthwash.

Pregnancy and breast feeding
- You can use the mouthwash if you are pregnant or breast feeding.

How to use
Use only if seal on cap is present and intact before opening.
- Do not swallow
- Do not exceed stated dose.
- Toothpastes can stop the mouthwash working. Rinse your mouth thoroughly with water and wait 5 minutes after brushing your teeth before using the mouthwash. You can also use the mouthwash at a different time of day.
- Use twice a day. Fill the cap to 10 ml line. Rinse mouth thoroughly for 1 minute then spit out.
- Gum disease: A one mouth course (600 ml) is recommended.
- Mouth ulcers & oral thrush: Continue to use for 2 days after healing has occurred.
- Denture sore mouth: Clean & soak your dentures in the mouthwash for 15 minutes twice a day.
- Dental surgery: Rinse as directed by your dentist.

If your symptoms persist, see your dentist.

Text to appear in the Left Section

Possible side effects
This mouthwash can have side effects, but not everybody gets them.
- Stop using the mouthwash and seek immediate medical help if you get a rash, swelling of the mouth or face or have difficulty breathing. These effects may be symptoms of a severe allergic reaction which is very rare.
- Stop using the mouthwash and tell your dentist if you get irritation of the mouth, soreness, or swelling of the inside of the cheeks. These effects should go away when treatment is stopped.

Other side effects that may occur:
- Temporary staining of the tongue. This disappears when treatment is stopped.
- Temporary staining of teeth. This can normally be removed by brushing. You can avoid staining by not drinking tea, coffee or red wine – especially one hour after use, and by brushing daily with toothpaste (see How to use). If staining continues it can be removed
with a scale & polish from your dentist or hygienist. You can clean your dentures with
denture cleaner.
- You may notice a change of taste or burning sensation when you first use the
mouthwash. This usually goes away with continued use.
- If peeling of the skin inside the mouth occurs, dilute the mouthwash with an equal
amount of water.

If you do get any side effects, even those not mentioned above, tell your doctor, dentist or
pharmacist.

Storage and further information

Keep out of the reach and sight of children.
Do not use after the ‘EXP’ date shown on the pack.
Store below 25°C.
Use within 3 months of opening.

Active ingredient: Chlorhexidine Digluconate 0.2% w/v.
Other ingredients: Glycerol, macrogolglycerol hydroxystearate, sorbitol liquid (non-
crystallising), peppermint flavour and purifying water.

Macrogolglycerol hydroxystearate may cause skin reactions.

MA Holder: GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9GS, U.K. and all
enquiries should be sent to this address.

The manufacturer is Omega Pharma Manufacturing GmbH & Co. KG, Herrenberg,
Germany.

PL 00079/0677

Text prepared: 12/2012

BN:

EXP: