

Public Assessment Report
Chlorhexidine Digluconate 0.2% Mouthwash
Chlorhexidine digluconate solution
PL 00079/0608
Beecham Group PLC

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Lay Summary

The MHRA has granted the medicinal product Chlorhexidine digluconate 0.2% solution a Marketing Authorisation (licence) on 28th April 2007. The product was confirmed to be identical to the cross reference product Corsodyl Mint Mouthwash.

Scientific Discussion

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal product Chlorhexidine digluconate 0.2% mouthwash on 26th April 2007. This simple application is submitted in accordance with article 10c of Directive 2001/83/EC as amended. The reference medicinal product is Corsodyl Mint Mouthwash (PL00079/0312). The applicant also holds the marketing authorisation of the reference product and a letter of informed consent is provided.

Therapeutic indications

For inhibition of the formation of dental plaque.

As an aid in the treatment and prevention of gingivitis and in the maintenance of oral hygiene, particularly in situations where toothbrushing cannot be adequately employed (eg following oral surgery, in mentally or physically handicapped patients).

Also for use in a post-peridontal surgery or treatment* regimen to promote gingival healing.

*NB: Use as part of a post-periodontal treatment regimen has only been adequately studied over the short term and following standard root surface instrumentation.

It is useful in the management of aphthous ulceration and oral candidal infections (eg denture stomatitis and thrush).

Pharmaceutical, preclinical and clinical expert statements have been provided. The experts confirmed that the product is identical to the reference product in terms of qualitative and quantitative composition, and therefore the quality/ pharmaceutical, pre-clinical and clinical characteristics of the reference product are applicable to the proposed product. Copies of CV for the experts are included and are satisfactory.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

The manufacturer of chlorhexidine digluconate solution is the same as that for the reference product. A satisfactory drug substance specification was provided which complied with the requirements of the European Monograph.

DRUG PRODUCT

Licensing particulars, including the ATC code, formulation, container and closure, package size, shelf life, storage condition, legal status and manufacturer and specifications of the finished product, are identical to those of the reference product. No material of animal and/ or human origin is used in the manufacturing process of the medicinal product.

Other Ingredients

The other ingredients of the drug product are Ethanol (96 per cent) and Macroglycerol Hydroxystearate, Sorbitol 70 per cent (E420), Peppermint Oil, Purified Water.

Finished product specification

The finished product specification is satisfactory.

ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY AND ADVICE

A Marketing Authorisation was granted.

PRE-CLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for an application of this type.

MEDICAL ASSESSMENT

CLINICAL PHARMACOLOGY

Pharmacodynamics

Chlorhexidine Digluconate 0.2% Mouthwash contains 0.2% w/v chlorhexidine digluconate which is an antimicrobial preparation for external use. 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.

Pharmacokinetics

Because of its cationic nature, chlorhexidine binds strongly to skin, mucosa and tissues and is thus very poorly absorbed. No detectable blood levels have been found following oral use.

Summary of Product Characteristics

A satisfactory SPC which is consistent with the reference product was provided.

Patient Information Leaflet/Label (combined)

Satisfactory colour mock-ups were provided. The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

Assessors Overall Conclusions

A Marketing Authorisation may be granted.

Overall Conclusion and Risk/Benefit Analysis

Quality

The quality aspects of the product were confirmed to be identical to the cross-reference product.

Pre-Clinical

No new preclinical data were submitted and none are required for applications of this type.

Clinical

The clinical aspects of the product were confirmed to be identical to the cross-reference product.

Risk/Benefit Analysis

The product was demonstrated to be identical to the cross-reference product and which has already been found to have a positive risk/benefit ratio.

Steps Taken During Assessment

1	The MHRA received the application on 08/05/2006.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 04/07/2006.
3	Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 04/07/2006.
4	The applicant provided further information in regard to the quality assessment on 19/03/2007 and 28/03/2007.
5	The application was determined on 26/04/2007.

Steps Taken after Assessment

None.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Chlorhexidine Digluconate 0.2% Mouthwash

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Chlorhexidine Digluconate 0.2% w/v
(equivalent to Chlorhexidine Digluconate Solution 1.0% v/v)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oromucosal solution

A clear or slightly opalescent, colourless solution with an odour of peppermint.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For inhibition of the formation of dental plaque.

As an aid in the treatment and prevention of gingivitis and in the maintenance of oral hygiene, particularly in situations where toothbrushing cannot be adequately employed (eg following oral surgery, in mentally or physically handicapped patients).

Also for use in a post-peridontal surgery or treatment* regimen to promote gingival healing.

*NB: Use as part of a post-periodontal treatment regimen has only been adequately studied over the short term and following standard root surface instrumentation.

It is useful in the management of aphthous ulceration and oral candidal infections (eg denture stomatitis and thrush).

4.2 Posology and method of administration

Thoroughly rinse the mouth for about one minute with 10 ml twice daily. In the dental surgery the patient should be instructed to rinse the mouth for one minute prior to treatment.

Chlorhexidine Digluconate 0.2% Mouthwash is incompatible with anionic agents which are usually present in conventional dentifrices. These should therefore be used before Chlorhexidine Digluconate 0.2% Mouthwash (rinsing the mouth between applications) or at a different time of day.

For the treatment of gingivitis a course of about one month is advisable although some variation in response is to be expected. In the case of aphthous ulceration and oral candidal infections treatment should be continued for 48 hours after clinical resolution. For the treatment of dental stomatitis the dentures should be cleansed and soaked in Chlorhexidine Digluconate 0.2% Mouthwash for fifteen minutes twice daily.

Children and the elderly: There are no special dosage recommendations for either elderly patients or children. The normal adult dose is appropriate unless otherwise recommended by the dentist or the physician.

Route of administration

Oromucosal use. [This product is not intended to be swallowed].

4.3 Contraindications

Chlorhexidine Digluconate 0.2% Mouthwash is contraindicated for patients who have previously shown a hypersensitivity reaction to chlorhexidine. However, such reactions are extremely rare.

4.4 Special warnings and precautions for use

For oromucosal use only - keep out of the eyes and ears.

If the mouthwash comes into contact with the eyes, wash out promptly and thoroughly with water.

4.5 Interaction with other medicinal products and other forms of interaction

Chlorhexidine is incompatible with anionic agents.

4.6 Pregnancy and lactation

There is no evidence of any adverse effects on the foetus arising from the use of chlorhexidine digluconate during pregnancy or lactation. Therefore no special precautions are recommended.

4.7 Effects on ability to drive and use machines

None have been reported or are known.

4.8 Undesirable effects

Discoloration: A superficial discoloration of the dorsum of the tongue may occur. This disappears after treatment is discontinued. Discoloration of the teeth and silicate or composite restorations may also occur. This stain is not permanent and can largely be prevented by brushing with a conventional toothpaste daily before using the mouthwash, or, in the case of dentures, cleaning with a conventional denture cleaner. However, in certain cases a professional prophylaxis (scaling and polishing) may be required to remove this stain completely. Stained anterior tooth-coloured restorations with poor margins or rough surfaces which are not adequately cleaned by professional prophylaxis may require replacement. Similarly where normal toothbrushing is not possible, for example with intermaxillary fixation, or with extensive orthodontic appliances, scaling and polishing may also be required once the underlying condition has been resolved.

Taste: Transient disturbance of taste sensation and a burning sensation of the tongue may occur on initial use of the mouthwash. These effects usually diminish with continued use.

Oral desquamation: In cases where oral desquamation occurs dilution of the mouthwash with an equal volume of tap water, freshly mixed, will often allow continued use of the mouthwash.

Parotid gland swelling: Very occasionally, swelling of the parotid glands during the use of chlorhexidine mouthrinses has been reported. In all cases spontaneous resolution has occurred on discontinuing treatment.

Irritative skin reactions: Irritative skin reactions to chlorhexidine preparations can occasionally occur. Generalised allergic reactions to chlorhexidine have also been reported but are extremely rare.

4.9 Overdose

This has not been reported.

Accidental ingestion: Chlorhexidine taken orally is poorly absorbed. Systemic effects are unlikely even if large volumes are ingested. However, gastric lavage may be advisable using milk, raw egg, gelatin or mild soap. Employ supportive measures as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectives and antiseptics for local oral treatment

ATC code: A01AB03

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5.2 Pharmacokinetic properties

Because of its cationic nature, chlorhexidine binds strongly to skin, mucosa and tissues and is thus very poorly absorbed. No detectable blood levels have been found following oral use.

5.3 Preclinical safety data

No information further to that contained in other sections of the SPC is included.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96 per cent)

Macrogolglycerol Hydroxystearate
Sorbitol 70 per cent (non-crystallising) (E420)
Peppermint oil
Purified water.

6.2 Incompatibilities

Hypochlorite bleaches may cause brown stains to develop in fabrics that have previously been in contact with preparations containing chlorhexidine.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Oriented amber polyethylene terephthalate bottle with plastic screw cap made from white food grade polypropylene.

Each bottle contains 300 ml or 600 ml.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Beecham Group plc
980 Great West Road
Brentford
Middlesex
TW8 9GS
United Kingdom

Trading as:

GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9GS, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00079/0608

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

26/04/2007

10 DATE OF REVISION OF THE TEXT

26/04/2007

Labels and Leaflet (Combined)

WHAT IS CHLORHEXIDINE DIGLUCONATE 0.2% MOUTHWASH FOR?
It is an antibacterial solution which inhibits the formation of dental plaque, & is used to:

- Treat & prevent gingivitis (gum disease - usual sign is gums that bleed when brushed)
- Promote gum healing after dental surgery or treatment
- Control mouth ulcers
- Maintain mouth hygiene • Manage oral thrush & denture sore mouth

HOW TO USE Use only if plastic wrap is present and intact before opening
Use twice daily. Fill cap to 10 ml line. Rinse mouth thoroughly for 1 minute then spit out.
Gum disease: One month course (600 ml) is recommended.
Mouth ulcers & oral thrush: Continue to use for 2 days after healing has occurred.
Denture sore mouth: Dentures should be cleaned & soaked in the mouthwash for 15 mins twice daily.
Dental surgery: Rinse as directed by your dentist.

CONSULT YOUR DENTIST If symptoms persist.

CONTAINS 0.2% w/v chlorhexidine digluconate. Also contains ethanol 7% v/v, macroglycol hydroxystearate, sorbitol (E420), peppermint oil, water.
Store below 25°C.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Do not use after the expiry date shown on the pack.

GlaxoSmithKline
Consumer Healthcare, Brentford, TW8 9GS, U.K.
PL 00079/0608 XX0000 XX000000
Text prepared: December 2006.
Made by SmithKline Beecham Consumer Healthcare, Maidenhead, SL6 4BL, U.K.

PLEASE READ BEFORE USING

- Use only if you are not sensitive to chlorhexidine or any of the other listed ingredients.
- Toothpastes may stop the mouthwash working properly if used immediately afterwards. To prevent this, use toothpaste at a different time of day, or use toothpaste first, rinse thoroughly with water & wait 5 minutes before using the mouthwash.
- When using the mouthwash, discolouration of the tongue & teeth may occur which is not permanent. Tongue staining disappears after treatment stops & tooth discolouration is normally removed by brushing. Staining can generally be avoided by:
 - 1) not drinking tea, coffee or red wine - especially for the first hour after use
 - 2) brushing daily with toothpaste before using the mouthwash
 Should tooth discolouration remain, this can be removed by a simple scale & polish from your dentist or hygienist.
- If discolouration of dentures occurs, clean with a conventional denture cleaner.
- No special precautions are needed if you are pregnant or breast feeding but consult your dentist or doctor before use.

WHEN USING FOR OROMUCOSAL USE ONLY
Not intended to be swallowed but accidental swallowing is unlikely to cause harm. Avoid contact with eyes & ears, & wash thoroughly if this occurs. 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 skin inside the mouth occurs, dilute the mouthwash with an equal amount of water. Occasionally the mouthwash may cause skin irritation. Very rarely allergic reactions may occur. Very occasionally the mouthwash may cause swelling of the salivary glands in the mouth but this should go away if you stop using the product. If you are concerned about these or any other unwanted effects, stop using the mouthwash & consult your dentist or doctor.
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300 ml

10mm | 19mm | 35mm

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600 ml