Safeguarding public health

MHRA

Public Assessment Report

Colgate Whitening Toothpaste
(sodium fluoride and triclosan)

PL 00049/0053

Medicines and Healthcare products Regulatory Agency

COLGATE WHITENING TOOTHPASTE (SODIUM FLUORIDE AND TRICLOSAN) PL 00049/0053

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COLGATE WHITENING TOOTHPASTE (SODIUM FLUORIDE AND TRICLOSAN) PL 00049/0053

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Colgate-Palmolive (UK) Limited a Marketing Authorisation (licence) for the medicinal product Colgate Whitening Toothpaste (PL 00049/0053). This is a general sale list (GSL) medicine for reducing tooth decay and promoting healthier gums.

Colgate Whitening Toothpaste contains sodium fluoride and triclosan. Sodium fluoride blocks the process by which tooth decay occurs while triclosan is an antibacterial with activity against the bacteria that can infect the gums.

This application is a duplicate of a previously granted licence for Colgate Total Plus Whitening Toothpaste (PL 00049/0047).

No new or unexpected safety concerns arose from this simple application and it was therefore judged that the benefits of using Colgate Whitening Toothpaste outweigh the risks, hence a Marketing Authorisation has been granted.

COLGATE WHITENING TOOTHPASTE (SODIUM FLUORIDE AND TRICLOSAN) PL 00049/0053

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Colgate Whitening Toothpaste (PL 00049/0053) to Colgate-Palmolive (UK) Limited on 27 January 2006. The product is a general sale list (GSL) medicine.

This application was submitted as a simple abridged application according to Article 10.1(a)i of Directive 2001/83/EC, cross-referring to Colgate Total Plus Whitening Toothpaste (PL 00049/0047, approved on 5 September 2002).

No new data were submitted for this simple application, nor were any necessary, as the data are identical to that of the previously granted cross-referenced product. As the cross-referenced product was granted prior to the introduction of current legislation, no public assessment report was generated for it.

The product contains the active ingredients sodium fluoride and triclosan. Triclosan is a broad-spectrum non-ionic antibacterial with activity against both aerobic and anaerobic gram-positive and gram-negative microbes. It is widely employed as a disinfectant and as an anti-bacterial in external use OTC products. Sodium fluoride applied topically after tooth eruption reduces caries by inhibiting demineralisation and promoting remineralisation of the tooth surface and by inhibiting the cariogenic microbial process.

The combination of sodium fluoride and triclosan in Colgate Whitening Toothpaste is indicated for improving gingival health, reducing dental caries and reducing the progression of periodontitis.

PHARMACEUTICAL ASSESSMENT

PL number:	**PL 00049/0053**
Name of Product:	**Colgate Whitening Toothpaste**
Active(s):	**Sodium fluoride 0.32%w/w and Triclosan 0.30%w/w**
Company Name:	**Colgate Palmolive (UK) Ltd.**
E.C. Article:	**10.1(a)(i)**
Legal Status:	**GSL**

Legal Basis

This is a simple abridged application for Colgate Whitening Toothpaste, containing sodium fluoride 0.32%w/w (1450 ppm F) and triclosan 0.30%w/w.

The applicant claims essential similarity, under article 10.1(a)(i) of Directive 2001/83/EC, as amended, to Colgate Total Plus Whitening Toothpaste containing the same active ingredients and amounts, sodium fluoride 0.32%w/w (1450 ppm F) and triclosan 0.30%w/w. The reference product, PL 00049/0047, granted 5 September 2002, is held by Colgate Palmolive (UK) Ltd.

Letters of access

A satisfactory letter of access is provided as part of the company's covering letter for the marketing authorisation application (MAA).

The manufacturer for the licensed reference product and the proposed product is the same.

The applicant has also provided satisfactory written confirmation that the reference product MA is identical to the proposed MA, except for the number.

Reference Product

There are no outstanding variations and renewal issues.
There are no outstanding issues with the reference product and the PLUS records are correct.

TSE

The MAA form (Section 2.6.2) indicates no ingredients in the product that are TSE susceptible. The supplier of glycerin has confirmed that it is derived from plant sources.

Expert reports

The writer of the pharmaceutical expert report has relevant experience in the pharmaceutical industry and academia. The report confirms the application to be identical with the reference product in all particulars.

The preclinical expert report confirms the application to be identical with the reference product in all particulars, including preclinical.

The writer of the clinical expert report confirms that the proposed product is identical to the reference product in terms of quality for its intended use with respect to clinical particulars.

The reports are accepted.

Product name

It is based on the company brand name and is acceptable.

Summary of Product Characteristics (SPC)

The SPC has been updated in line with EC5/99 and is in line with the reference product.

Combined label-patient information leaflet

Combined label-leaflet mock-ups have been provided for 19ml, 50ml, 75ml, 100ml, 125ml carton and tubes, together with 100ml,125ml and 150ml stand-up packs.

MAA form

The sites of manufacture, assembly, QC and batch release are in line with the reference product. A satisfactory manufacturing licence is provided.

Section 4 Additional Information

Satisfactory

CONCLUSION

A marketing authorisation may be granted for this product.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

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

OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

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

PRECLINICAL

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

EFFICACY

This application is identical to a previously granted application for Colgate Total Plus Whitening Toothpaste.

No new or unexpected safety concerns arose from this application.

The SPC and combined PIL-labelling are satisfactory and consistent with those of the cross-referenced product.

RISK-BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-referenced product. Extensive clinical experience with the active ingredients sodium fluoride and triclosan is considered to have demonstrated the therapeutic value of the compounds. The risk-benefit assessment is therefore considered to be favourable.

COLGATE WHITENING TOOTHPASTE
(SODIUM FLUORIDE AND TRICLOSAN)
PL 00049/0053

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application for Colgate Whitening Toothpaste on 23 February 2004.
2	Following standard checks the MHRA informed the applicant that its applications were considered valid on 5 March 2004
3	The MHRA's assessment of the submitted data was completed on 13 July 2004
4	Further information was requested from the company on 13 July 2004.
5	The applicant submitted its response to further information request on 9 December 2004.
6	Additional information was requested from the company on 23 March 2005.
7	The applicant submitted its response to additional information request on 31 May 2005.
8	The applicant was asked to resolve some outstanding issues on 3 October 2005.
9	The applicant submitted its response to outstanding issues on 6 October 2005.
10	The MHRA completed its assessment of the application on 13 October 2005.
11	The application was determined on 27 January 2006.

COLGATE WHITENING TOOTHPASTE
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Colgate Whitening Toothpaste

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The active ingredients of Colgate Whitening Toothpaste are:

Triclosan	0.30% w/w
Sodium Fluoride	0.32% w/w (1450 ppm F)

For excipients see 6.1

3. PHARMACEUTICAL FORM

Toothpaste

A dark blue / light blue striped paste.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

To reduce dental caries.

To improve gingival health by:-

1. Significantly reducing the formation of plaque and calculus.
2. Significantly reducing existing levels of gingival bleeding and inflammation.

To reduce the progression of periodontitis.

4.2. Posology and method of administration

The usual dosage is to apply a ribbon of toothpaste across the head of the toothbrush (approximately 1.0g) and to brush the teeth for one minute twice daily.

Children under 7, use a pea-sized amount for supervised brushing to minimise swallowing. If using fluoride supplements, consult your Dentist.

4.3. Contraindications

None known.

Individuals with known sensitivities should consult with their dentist before using.

4.4. Special warnings and precautions for use

Children under 7, use a pea-sized amount for supervised brushing. If using fluoride supplements, consult your Dentist.

4.5. Interactions with other medicinal products and other forms of interaction

None known. It is important to note that as for any fluoride containing toothpaste in children using systemic fluoride therapy, it is important to evaluate the total exposure to fluoride (fluorosis).

4.6. Pregnancy and lactation

Use of this product is not contraindicated during pregnancy or lactation.

4.7. Effects on ability to drive and use machines

None known.

4.8. Undesirable effects

None known.

4.9. Overdose

Not applicable. Use of this type of product would not be expected to result in an overdose.

No acute effects would be expected from the low level of Triclosan (489 mg in a 125 ml tube). Even in the extreme case of prolonged exposure, serious adverse effects would not be expected from Triclosan.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Triclosan: Triclosan is a broad-spectrum non-ionic antibacterial with activity against both aerobic and anaerobic gram-positive and gram-negative microbes. It is widely employed as a disinfectant and as an anti-bacterial in external use OTC products. In Colgate Whitening Toothpaste it is combined with a copolymer which enhances the delivery of Triclosan to the site of action.

Sodium Fluoride: Sodium fluoride applied topically after tooth eruption reduces caries by inhibiting demineralisation and promoting remineralisation of the tooth surface and by inhibiting the cariogenic microbial process.

5.2. Pharmacokinetic properties

Triclosan: When administered in a dentifrice by toothbrushing, salivary and plaque triclosan levels range between 1-6 ppm and 25 ppm respectively at 1-2 hours after using a 0.3% dentifrice. Following usage of a dentifrice containing up to 0.6% triclosan, mean blood levels range between 15 to 25 ppb.

Blood levels of triclosan in subjects brushing with a dentifrice are about 14 per cent of those in subjects who directly ingested an aqueous solution in an equivalent dose level.

Sodium Fluoride: After oral administration, fluoride absorption is rapid and extensive with (90 - 100%) peak fluoride plasma levels reached within 30 to 60 minutes after ingestion. Fluoride is widely distributed through the body and concentrates in the bone and teeth. About 50% of fluoride absorbed is stored. Excretion is primarily through the kidneys with less than 10% being excreted in the faeces and less than 1% in sweat and saliva.

5.3. Preclinical safety data

Triclosan: In subchronic oral ingestion studies with rats dentifrices containing triclosan were administered for 13 weeks at levels that are conservatively up to 100 times expected human use levels. Animals received daily doses of up to 12 mg/kg of triclosan and showed no indications of treatment related effects. This dose would be equivalent to 600 mg of triclosan in 50 kg human. Ingestion of 125 ml of a toothpaste (approximately one tube) containing 0.3% triclosan would give an intake of approximately 489 mg and would not be expected to produce untoward effects.

Sodium Fluoride: The total amount of sodium fluoride in a 125 ml tube of Colgate Whitening Toothpaste is 516 mg. This is within the acceptable limits for

the amount to be dispensed at one time for safety purposes. Prolonged daily ingestion of excessive fluoride may result in varying degrees of fluorosis.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Glycerine
Dental Grade Silicas
Sorbitol (70% Solution)
Water
Poly (Methyl Vinyl Ether) Maleic Acid
Sodium Hydroxide
Sodium Lauryl Sulphate
89332 mint Flavour
Sodium Carboxymethylcellulose
Titanium Dioxide
Titanium dioxide coated mica
Iota Carrageenan
Sodium Saccharin
Blue colour (E133)

6.2. Incompatibilities

None.

6.3. Shelf life

Three years.

6.4. Special precautions for storage

Do not store above 25ºC.

6.5. Nature and contents of container

Colgate Whitening Toothpaste is packaged in 19, 50, 75, 100 and 125 ml squeeze tubes consisting of three elements, a conical shoulder with threaded neck manufactured from high density polyethylene, a barrier material of polyester (PBT) or polyester (PET) below and inside the conical shoulder, and a cylindrical laminated tube barrel. The laminated tube barrel is manufactured from 5-ply laminated webstock consisting of:

Outer layer : Low density polyethylene
Ethylene acrylic acid copolymer
Aluminium foil
EAA copolymer

Inner layer : Linear medium density polyethylene

100, 125 and 150 ml stand up tube of polyethylene laminate consisting of:

Medium density polyethylene
EMA/EvOH barrier
Medium density polyethylene.

The cap is a conventional screw-type flip top manufactured from polypropylene.

6.6. Instruction for use and handling

None.

7. MARKETING AUTHORISATION HOLDER

Colgate-Palmolive (UK) Ltd
Guildford Business Park
Middleton Road
Guildford
Surrey GU2 8JZ
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 00049/0053

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/01/2006

10 DATE OF REVISION OF THE TEXT

27/01/2006

Combined Labelling and Patient Information Leaflet

COLGATE WHITENING TOOTHPASTE
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