Public Assessment Report

UKPAR

Fluoride 5000 ppm Toothpaste

(Sodium fluoride)

UK Licence No: PL 00049/0057

Colgate-Palmolive (UK) Limited.
LAY SUMMARY

Fluoride 5000 ppm Toothpaste
(Sodium fluoride, toothpaste, 5000 parts per million (ppm)).

This is a summary of the Public Assessment Report (PAR) for Fluoride 5000 ppm Toothpaste (PL 00049/0057). It explains how Fluoride 5000 ppm Toothpaste was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Fluoride 5000 ppm Toothpaste.

For practical information about using Fluoride 5000 ppm Toothpaste patients should read the package leaflet or contact their doctor or pharmacist.

What is Fluoride 5000 ppm Toothpaste and what is it used for?
Fluoride 5000 ppm Toothpaste is used to help prevent dental caries (tooth decay) in adolescents aged 16 years and over and adults, particularly amongst patients at risk from multiple caries.

This medicine is the same as Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050) which is already authorised.

The company (Colgate-Palmolive (UK) Limited) that makes Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050) has agreed that its scientific data can be used as a basis for the grant of an identical licence for Fluoride 5000 ppm Toothpaste (informed consent).

How does Fluoride 5000 ppm Toothpaste work?
This toothpaste contains the active ingredient fluoride (as sodium fluoride), which belongs to a group of medicines called caries preventing agents. When Fluoride 5000 ppm Toothpaste is applied to the teeth after tooth eruption, it reduces tooth decay (dental caries) by stopping demineralisation and promoting remineralisation of the tooth surface. It is effective on both enamel and exposed dentine (the 2 outer layers that make up part of the tooth).

How is Fluoride 5000 ppm Toothpaste used?
The pharmaceutical form of this medicine is a toothpaste and the route of administration is for application to the teeth (topical).

Fluoride 5000 ppm Toothpaste is for use by persons aged 16 years and above. The patient should always use Fluoride 5000 ppm Toothpaste exactly as their dentist or pharmacist has told them. The patient should check with their dentist or pharmacist if they are not sure.

The patient should use Fluoride 5000 ppm Toothpaste 3 times a day for brushing their teeth:
- apply a 2cm ribbon onto the toothbrush for each brushing (2cm provides between 3mg and 5mg of fluoride).
- the patient should brush their teeth after each meal.
- vertically, from the gum to the tip of the tooth.
- spit out excess foam and do not swallow.
Careful brushing takes approximately 3 minutes.

Please refer to the package leaflet for further information on how to use this medicine.

This medicine cannot be obtained without a prescription.
For further information on how Fluoride 5000 ppm Toothpaste is used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**What benefits of Fluoride 5000 ppm Toothpaste have been shown in studies?**
Fluoride 5000 ppm Toothpaste is considered identical to previously authorised Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050), with the same benefits and risks. So no new studies have been provided for Fluoride 5000 ppm Toothpaste but reference is made to the studies for Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050).

**What are the possible side effects from Fluoride 5000 ppm Toothpaste?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Fluoride 5000 ppm Toothpaste is considered to be identical to the previously authorised application for Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050) with the same benefits and risks.

For a full list of all the side effects reported with Fluoride 5000 ppm Toothpaste see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

For the full list of restrictions, see the package leaflet.

**Why is Fluoride 5000 ppm Toothpaste approved?**
The MHRA decided that the benefits of Fluoride 5000 ppm Toothpaste are greater than their risks and recommended that it is approved for use.

**What measures are being taken to ensure the safe and effective use of Fluoride 5000 ppm Toothpaste?**
A Risk Management Plan has been developed to ensure that Fluoride 5000 ppm Toothpaste is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the label-leaflet for Fluoride 5000 ppm Toothpaste including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

**Other information about Fluoride 5000 ppm Toothpaste**
A Marketing Authorisation was granted in the UK on 13 March 2017.

The full PAR for Fluoride 5000 ppm Toothpaste follows this summary.

For more information about treatment with Fluoride 5000 ppm Toothpaste read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in April 2017.
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I. INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Colgate-Palmolive (UK) Limited a Marketing Authorisation for the medicinal product Fluoride 5000 ppm Toothpaste (PL 00049/0057) on 13 March 2017. The product is a prescription only medicine (POM) indicated for the prevention of dental caries in adolescents and adults, particularly amongst patients at risk from multiple caries (coronal and/or root caries).

This application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the reference product Duraphat 5000 ppm Fluoride Toothpaste, which was first authorised to Colgate-Palmolive (UK) Limited (PL 00049/0050) on 03 September 2003.

The primary mode of the caries preventative action of fluoride is post-eruptive, i.e. topical. Systemic fluoride supplements are believed to act also mainly topically (e.g. during ingestion, via saliva).

There are three types of effect associated with fluoride:
- the inhibiting effect on demineralisation (lowering the enamel solubility in an acid environment);
- the promotion of remineralisation of enamel during the caries process;
- a bactericidal effect upon dental plaque organisms. This inhibits the proliferation of dental plaque bacteria and prevents formation of the acids that cause caries.

Fluoride alone is not enough to eliminate bacterial plaque, nor as a complete treatment for caries.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to the data for the previously granted cross-referenced product.
II QUALITY ASPECTS

II.1 Introduction
This is an abridged application for Fluoride 5000 ppm Toothpaste (PL 00049/0057) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the reference product Duraphat 5000 ppm Fluoride Toothpaste, which was first authorised to Colgate-Palmolive (UK) Limited (PL 00049/0050) on 03 September 2003. The application is considered valid.

II.2. Drug Substance

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

II.3. Medicinal Product

Name
The proposed product name for this application is Fluoride 5000 ppm Toothpaste. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each 1 gram (g) of toothpaste contains 5 mg fluoride (as sodium fluoride), corresponding to 5000 ppm fluoride. The finished product is packed in tubes (polyethylene (PE)/ polyethylene terephthalate (PET)/aluminium) with a screw cap (polypropylene). The tube is packed inside an outer carton and is available in pack sizes: 1 x 51 g tube or 3 x 51 g tubes. Not all pack sizes may be marketed.

The proposed shelf life of the unopened product is 3 years with the storage condition ‘Do not store above 25°C.’

The proposed packaging, shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

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

Marketing Authorisation Holder/Contact Persons/Company
Colgate-Palmolive (UK) Limited, Guildford Business Park, Middleton Road, Guildford, Surrey, GU2 8JZ, UK.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

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.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.
Manufacturing process
The proposed manufacturing processes are consistent with the details registered for the cross-reference product and the maximum batch size is stated.

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

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

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050).

Expert Report
The applicant cross-refers to the data for Duraphat 5000 ppm Fluoride Toothpaste (PL 00049/0050) to which this application is claimed to be identical. This is acceptable.

Product Name and Appearance
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of the product is identical to that of the cross-reference product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS
Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/environmental risk assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS
Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)
The marketing authorisation holder (MAH) has submitted a risk management plan (RMP), in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Fluoride 5000 ppm Toothpaste.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, are listed below:

Summary table of safety concerns:

<table>
<thead>
<tr>
<th>Summary of safety concerns</th>
<th>Use in children aged less than 10 years</th>
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<tr>
<td>Important identified risks</td>
<td>Fluorosis</td>
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<tr>
<td>Important identified risks</td>
<td>Overdose, particularly in patients who swallow large amounts of toothpaste or are receiving other supplements</td>
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<tr>
<td>Important potential risks</td>
<td>None</td>
</tr>
<tr>
<td>Important missing information</td>
<td>Use during pregnancy and breastfeeding and effects on fertility</td>
</tr>
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</table>

Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.
Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V User consultation
A user consultation with target patient groups on the label-leaflet (PIL) has been performed on the basis of a bridging report making reference to the product for Duraphat 500 mg/100 g Toothpaste (Colgate-Palmolive France). The bridging report submitted by the applicant is acceptable.

VI Overall conclusion, benefit/risk assessment and recommendation
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 cross-reference product. Extensive clinical experience with sodium fluoride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The Summary of Product Characteristics and label-leaflet are consistent with the details registered for the cross-reference product.

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

The approved labelling for this medicine is presented below:
Fluoride 5000 ppm Toothpaste

1.1% w/w Sodium Fluoride

51g

Fluoride: 1g of toothpaste contains 5mg Fluoride (as Sodium Fluoride), corresponding to 5000 ppm Fluoride.

Exciipients: Liquid Sorbitol (Non-crystallising), Dental Type Silica, Dental Type Silica (Precipitated), Macrogol 6000, Tetrapotassium Phosphophosphate, Xanthan Gum, Sodium Benzoate (E211), Sodium Laureth Sulphate, Spearmint Flavouring (containing Peppermint Oil, Carnauba, Spearmint Oil, Menthol, Anethol, and Lemon Oil), Saccharin Sodium, Brilliant Blue FOF (E133) and Purified Water. Contains Sodium Benzoate. See leaflet for further information.

For Dental Use.
Do not swallow.
Keep out of the sight and reach of children.
Do not use in adolescents and children under 16 years of age.
Do not store above 25°C.
Batch and EXP: see end of tube.

Colgate-Palmolive (UK) Limited, Guildford Business Park, Middleton Road, Guildford, Surrey, GU2 8UZ, United Kingdom
Annex 1 - Table of content of the PAR update.

Steps Taken After The Initial Procedure With An Influence On The Public Assessment Report
(Type II variations, PSURs, commitments)

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<th>Product Information affected</th>
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<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
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