Public Assessment Report

Decentralised Procedure

NICOTINE PERRIGO 2MG LOZENGES
NICOTINE PERRIGO 4MG LOZENGES

(Nicotine resinate)

Procedure No: UK/H/4556/001-002/DC

UK Licence No: PL 12063/0113-0114

WRAFTON LABORATORIES LIMITED
LAY SUMMARY

On 15 January 2013, Czech Republic, Germany, Hungary, Italy, Netherlands, Poland and the UK agreed to grant Marketing Authorisations to Wrafton Laboratories Limited (trading as Perrigo) for the medicinal products Nicotine Perrigo 2mg and 4mg Lozenges (PL 12063/0113-0114; UK/H/4556/001-002/DC). The licences were granted via the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS). After a subsequent national phase, Marketing Authorisations were granted in the UK on 15 February 2013. These medicines are available as General Sales List (GSL) medicines and do not require a prescription.

Nicotine Perrigo 2mg and 4mg Lozenges are used to help people stop smoking. This type of treatment is called Nicotine Replacement Therapy (NRT).

Nicotine Perrigo 2mg and 4mg Lozenges can reduce your urge to smoke by providing some of the nicotine previously inhaled from cigarettes and helps you resist cigarettes. Nicotine Perrigo 2mg and 4mg Lozenges do not have the health dangers of tobacco because they do not contain the tar or carbon monoxide of cigarette smoke.

This medicine contains nicotine resin which when sucked, slowly releases nicotine (the active ingredient) from the resin which is then absorbed through the lining of the mouth. This nicotine relieves some of the cravings and unpleasant withdrawal symptoms, such as feeling ill or irritable, that smokers frequently feel when they try to give up.

If possible, when giving up smoking these lozenges should be used with a stop smoking behavioural support programme.

No new or unexpected safety concerns arose from these applications and it was judged that the benefits of taking Nicotine Perrigo 2mg and 4mg Lozenges outweigh the risks and therefore Marketing Authorisations were granted.
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# Module 1

| **Product Name**   | Nicotine Perrigo 2mg Lozenges  
|                   | Nicotine Perrigo 4mg Lozenges |
| **Type of Application** | Generic, Article 10.1 |
| **Active Substances** | Nicotine resinate |
| **Form**           | Lozenge |
| **Strength**       | 2mg and 4mg. |
| **MA Holder**      | Wrafton Laboratories Limited  
|                   | Trading as Perrigo |
|                   | Wrafton |
|                   | Braunton |
|                   | Devon |
|                   | EX33 2DL |
|                   | United Kingdom |
| **Reference Member State (RMS)** | UK |
| **Concerned Member States (CMS)** | Czech Republic, Germany, Hungary, Italy, Netherlands and Poland. |
| **Procedure Number** | UK/H/4556/001-002/DC |
Module 2
Summary of Product Characteristics

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 3
Patient Information Leaflet

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Module 4
Labelling

The following text is the approved labelling text as agreed during the decentralised procedure. No labelling mock-ups have been provided. In accordance with medicines legislation, the product shall not be marketed in the UK until approval of the labelling mock-ups has been obtained.

| PARTICULARS TO APPEAR ON THE CARTON |
| OUTER CARTON |

1. NAME OF THE MEDICINAL PRODUCT

Nicotine Perrigo 2mg Lozenges

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each compressed lozenge contains 2 mg nicotine (as nicotine resinate 13.33 mg).

3. LIST OF EXCIPIENTS

Also contains: aspartame (E951) and mannitol (E421). Each lozenge contains 15 mg of sodium. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

36 lozenges
72 lozenges

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use. The lozenge is designed to be dissolved in the mouth; normally this takes about 30 minutes.
Read the package leaflet carefully before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP ALL MEDICINES OUT OF THE SIGHT AND REACH OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Children under 12 years of age should not use Nicotine Lozenges.
WARNING: Do not exceed the stated dose.
Do not use this medicine if you:
• are allergic to nicotine or any of the other ingredients
• suffer from phenylketonuria (the lozenges contain a source of phenylalanine, which may be harmful to you)
• are a non-smoker
  • are under 12 years of age
• have recently suffered from a heart attack, severe heart rhythm disturbances or a stroke
• have unstable or worsening angina or Prinzmetal’s angina

Seek medical advice before taking this medicine if you:
• are under the care of your doctor or are receiving a prescribed medicine
• are pregnant, breast feeding or planning a pregnancy
• are diabetic.
Note: You are more likely to quit smoking when using this product with help from your pharmacist, doctor, a trained counsellor, or a support programme.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Store in the original packaging in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPLICABLE

Not applicable

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Wraorton Laboratories Limited
Wraorton
Braunton
Devon
EX33 2DL
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

PL 12063/0113

13. BATCH NUMBER,< DONATION AND PRODUCT CODES>

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

GSL

15. INSTRUCTIONS ON USE

These lozenges are for smokers who smoke their first cigarette more than 30 minutes after waking up. Nicotine Lozenges can help you to stop smoking straight away.

Adults (aged 18 years and over):
The recommended treatment schedule is:

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 1 to 6</td>
<td>Weeks 7 to 9</td>
<td>Weeks 10 to 12</td>
</tr>
<tr>
<td>Initial treatment period</td>
<td>Step down treatment period</td>
<td>Step down treatment period</td>
</tr>
<tr>
<td>1 lozenge every 1 to 2 hours</td>
<td>1 lozenge every 2 to 4 hours</td>
<td>1 lozenge every 4 to 8 hours</td>
</tr>
</tbody>
</table>

During weeks 1-6 it is recommended that you take at least 9 lozenges per day.

16. INFORMATION IN BRAILLE
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLISTER</td>
</tr>
<tr>
<td>1.  NAME OF THE MEDICINAL PRODUCT</td>
</tr>
</tbody>
</table>
Nicotine Perrigo 2mg Lozenges
| 2.  NAME OF THE MARKETING AUTHORISATION HOLDER |
Wrafton Laboratories Limited
| 3.  EXPIRY DATE |
EXP
| 4.  BATCH NUMBER<, DONATION AND PRODUCT CODES> |
BN
| 5.  OTHER |
N/a
PARTICULARS TO APPEAR ON THE CARTON

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nicotine Perrigo 4mg Lozenges

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each compressed lozenge contains 4 mg nicotine (as nicotine resinate 26.66 mg).

3. LIST OF EXCIPIENTS

Also contains: aspartame (E951) and mannitol (E421). Each lozenge contains 15 mg of sodium. See enclosed leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

36 lozenges
72 lozenges

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use. The lozenge is designed to be dissolved in the mouth; normally this takes about 30 minutes. Read the package leaflet carefully before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP ALL MEDICINES OUT OF THE SIGHT AND REACH OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Children under 12 years of age should not use Nicotine Lozenges.

WARNING: Do not exceed the stated dose.

Do not use this medicine if you:
• are allergic to nicotine or any of the other ingredients
• suffer from phenylketonuria (the lozenges contain a source of phenylalanine, which may be harmful to you)
• are a non-smoker
  • are under 12 years of age
  • have recently suffered from a heart attack, severe heart rhythm disturbances or a stroke
  • have unstable or worsening angina or Prinzmetal's angina

Seek medical advice before taking this medicine if you:
• are under the care of your doctor or are receiving a prescribed medicine
• are pregnant, breast feeding or planning a pregnancy
• are diabetic.
Note: You are more likely to quit smoking when using this product with help from your pharmacist, doctor, a trained counsellor, or a support programme.

8. **EXPIRY DATE**

EXP:

9. **SPECIAL STORAGE CONDITIONS**

Do not store above 25°C. Store in the original packaging in order to protect from light.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Not applicable

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Wrafton Laboratories Limited  
Wrafton  
Braunton  
Devon  
EX33 2DL  
United Kingdom

12. **MARKETING AUTHORISATION NUMBER(S)**

PL 12063/0114

13. **BATCH NUMBER<, DONATION AND PRODUCT CODES>**

BN

14. **GENERAL CLASSIFICATION FOR SUPPLY**

GSL

15. **INSTRUCTIONS ON USE**

These lozenges are for smokers who smoke their first cigarette less than 30 minutes after waking up. Nicotine Lozenges can help you to stop smoking straight away. 

**Adults (aged 18 years and over):**

The recommended treatment schedule is:

<table>
<thead>
<tr>
<th>Step 1</th>
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During weeks 1-6 it is recommended that you take at least 9 lozenges per day.

16. **INFORMATION IN BRAILLE**
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</tr>
<tr>
<td>Nicotine Perrigo 4mg Lozenges</td>
</tr>
<tr>
<td>2. <strong>NAME OF THE MARKETING AUTHORISATION HOLDER</strong></td>
</tr>
<tr>
<td>Wrafton Laboratories Limited</td>
</tr>
<tr>
<td>3. <strong>EXPIRY DATE</strong></td>
</tr>
<tr>
<td><strong>EXP</strong></td>
</tr>
<tr>
<td>4. <strong>BATCH NUMBER&lt;, DONATION AND PRODUCT CODES&gt;</strong></td>
</tr>
<tr>
<td><strong>BN</strong></td>
</tr>
<tr>
<td>5. <strong>OTHER</strong></td>
</tr>
<tr>
<td>N/a</td>
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</tbody>
</table>
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Member States considered that the applications for Nicotine Perrigo 2mg and 4mg Lozenges (PL 12063/0113-0114; UK/H/4556/001-002/DC) could be approved. These applications were submitted via the decentralised procedure, with the UK as Reference Member State (RMS) and Czech Republic, Germany, Hungary, Italy, Netherlands and Poland as Concerned Member States (CMS). These medicines are available as General Sales List (GSL) medicines and do not require a prescription.

Nicotine Perrigo 2mg and 4mg Lozenges are indicated for the treatment of tobacco dependence by relieving nicotine withdrawal symptoms including cravings, associated with smoking cessation. The eventual objective is the permanent cessation of tobacco use.

Nicotine Perrigo 2mg and 4mg Lozenges should preferably be used in conjunction with a behavioural support programme.

These are abridged applications submitted under Article 10(1) of Directive 2001/83/EC as amended, cross-referring to Nicabate 14mg/24 hours transdermal patches [PL 00079/0346 (formerly PL 04425/0128); Beecham Group PLC, UK], which was first authorised on 23 January 1998. The reference product has been registered in the EEA for more than 10 years, hence the period of data exclusivity has expired. The corresponding UK products are NiQuitin 2mg and 4mg Lozenges which were first authorised in 2001 to Beecham Group PLC as line extensions to the above licence (PL 00079/0346).

Nicotine is an agonist at nicotine receptors in the peripheral and central nervous system and has pronounced central nervous system (CNS) and cardiovascular effects. When consumed in tobacco products, it has been shown to be addictive and abstinence is linked to craving and withdrawal symptoms. These craving and withdrawal symptoms include urge to smoke, depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty in concentrating, restlessness and increased appetite or weight gain. The lozenges replace some of the nicotine provided by tobacco and help reduce the severity of these nicotine craving and withdrawal symptoms.

Two bioequivalence studies (single dose) were submitted to support these applications, comparing the test products Nicotine Perrigo 2mg and 4mg Lozenges (Wrafton Laboratories Limited) with the reference products NiQuitin 2mg and 4mg Lozenges (GlaxoSmithKline Consumer Healthcare, UK).

With the exception of the bioequivalence studies, no new clinical studies were conducted, which is acceptable given that the applications were for products that are intended to be generic versions of the originator products that have been licensed for over 10 years. The bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these product types at all sites responsible for the manufacture, assembly and batch release of these products.
The RMS and CMS considered that the applications could be approved with the end of procedure (Day 210) on 15 January 2013. After the subsequent national phase, the licences were granted in the UK on 15 February 2013.
## II. ABOUT THE PRODUCT

### Module 1

| Name of the product in the Reference Member State | Nicotine Perrigo 2mg Lozenges  
Nicotine Perrigo 4mg Lozenges |
| Name(s) of the active substance(s) (INN) | Nicotine resinate |
| Pharmacotherapeutic classification (ATC code) | Drug in nicotine dependence (NO 7B A01). |
| Pharmaceutical form and strength(s) | 2mg and 4mg lozenge |
| Reference numbers for the Mutual Recognition Procedure | UK/H/4556/001-002/DC |
| Reference Member State | United Kingdom |
| Concerned Member State | Czech Republic, Germany, Hungary, Italy, Netherlands and Poland. |
| Marketing Authorisation Number(s) | PL 12063/0113-0114 |
| Name and address of the authorisation holder | Wrafton Laboratories Limited  
Trading as Perrigo  
Wrafton  
Braunton  
Devon  
EX33 2DL  
United Kingdom |
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

Active substance

INN: Nicotine resinate
Chemical names: 2-Propenoic acid, 2-methyl-, polymer diethenylbenzene, compound with 3-[(2S)-1-methyl-2-pyrrolidinyl] pyridine

Structure:

Appearance: Nicotine resinate a white to off-white free flowing powder.
Solubility: Nicotine resinate is practically insoluble in water.

Nicotine resinate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance nicotine resinate are covered by a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability.

Medicinal Product

Other Ingredients

Other ingredients consist of the pharmaceutical excipients mannitol, magnesium stearate, sodium alginate, xanthan gum, potassium bicarbonate, sodium carbonate anhydrous, aspartame and peppermint flavour.

All excipients comply with their respective European Pharmacopoeia monographs with the exception of peppermint flavour which is controlled to a suitable in-house specification. Satisfactory certificates of analysis have been provided for all excipients. Suitable batch analysis data have been provided for each excipient.

No genetically modified organisms (GMO) have been used in the preparation of these products.

Pharmaceutical Development

The objective of the development programme was to formulate stable, robust, lozenges containing 2mg or 4mg nicotine (as resinate), which could be considered generic medicinal products of NiQuitin 2mg and 4mg Lozenges (GlaxoSmithKline Consumer Healthcare, UK).

A satisfactory account of the pharmaceutical development has been provided.
Comparative in vitro dissolution profiles have been provided for the proposed and originator products.

Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated at commercial scale and has shown satisfactory results.

Finished Product Specification
The proposed finished product specifications are acceptable. Test methods have been described and have been adequately validated. Batch data have been provided, which comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Container-Closure System
Both strengths of the finished product are packaged in:

- Clear, colourless laminate comprising: 76 micron UltRx3000 ACLAR / adhesive / 254 micron polyvinyl chloride (PVC) blister packs comprising of 20 micron aluminium (Al) foil with heat seal lacquer.
- Clear, colourless laminate comprising: 60 micron PVC/240 micron cyclic olefin copolymer (COC) / 90gsm polyvinylidene chloride (PVdC) blister packs comprising of 20 micron aluminium foil with heat seal lacquer.

All presentations are available in pack sizes of 36 or 72 lozenges enclosed in a cardboard carton.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

Stability of the product
Stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 24 months for the ACLAR/PVC/Al blisters and 21 months for the COC/PVdC/Al blisters with the storage conditions ‘Do not store above 25°C. Store in the original packaging in order to protect from light.’

Bioequivalence/bioavailability
Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence studies.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPCs, PIL and labels are acceptable.

The MAH has committed to perform (and submit via a variation before marketing the products) consultations with target patient groups for the patient information leaflet (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended.

Marketing Authorisation Application (MAA) form
The MAA forms are satisfactory.
Quality Overall Summary
The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
There are no objections to the approval of these products from a pharmaceutical view-point.

III.2 NON-CLINICAL ASPECTS
As the pharmacodynamic, pharmacokinetic and toxicological properties of nicotine are well-known, no new non-clinical studies are required and none have been provided.

The applicant’s non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant pharmacology and toxicology.

Since Nicotine Perrigo 2mg and 4mg Lozenges are intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment (ERA) is therefore not deemed necessary.

There are no objections to the approval of these products from a non-clinical view-point.

III.3 CLINICAL ASPECTS
Pharmacokinetics
In support of these applications, the marketing authorisation holder has submitted results from the following two bioequivalence studies:

Study 1
An open, randomised, single-dose, two-way crossover study to compare the pharmacokinetics of the test product Nicotine Perrigo 2mg Lozenges (Wrafton Laboratories Limited) versus the reference product NiQuitin 2mg Lozenges (GlaxoSmithKline Consumer Healthcare, UK) in healthy adult smoker volunteers under fasted conditions.

All volunteers received a single oral dose of either the test or reference product as a 1 x 2 mg lozenge administered after 36 hours from abstinence of smoking. Every 4 seconds (as prompted by a metronome) subjects moved the lozenge from side to side in the mouth until the lozenge had completely dissolved (approximately 20-30 minutes). After every 30 seconds the subjects were instructed to swallow their saliva at a verbal command. Blood samples were taken for the measurement of pharmacokinetic parameters at pre- and up to 16 hours post dose. The washout period was at least 7 days.

The pharmacokinetic results for nicotine are presented below (mean, standard deviation (SD) and % confidence intervals):
Table of Pharmacokinetic Parameters:

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameters</th>
<th>Test (T)</th>
<th>Reference (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/ml)</td>
<td>9.18 ± 2.87</td>
<td>8.52 ± 2.43</td>
</tr>
<tr>
<td>AUC0-t (hr ng/ml)</td>
<td>39.59 ± 19.78</td>
<td>37.54 ± 12.27</td>
</tr>
<tr>
<td>AUC0-∞ (hr ng/ml)</td>
<td>45.14 ± 26.60</td>
<td>42.46 ± 14.93</td>
</tr>
<tr>
<td>T_max (hr)</td>
<td>0.50 (0.33-1.50)</td>
<td>0.50 (0.33-2.02)</td>
</tr>
<tr>
<td>K_el (1/hr)</td>
<td>0.179 ± 0.069</td>
<td>0.191 ± 0.060</td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>4.54 ± 2.05</td>
<td>3.97 ± 1.22</td>
</tr>
</tbody>
</table>

*Median (range)

Study 2

An open, randomised, single-dose, two-way crossover study to compare the pharmacokinetics of the test product Nicotine Perrigo 4mg Lozenges (Wrafton Laboratories Limited) versus the reference product NiQuitin 4mg Lozenges (GlaxoSmithKline Consumer Healthcare, UK) in healthy adult smoker volunteers under fasted conditions.

All volunteers received a single oral dose of either the test or reference product as a 1 x 4 mg lozenge administered after 36 hours from abstinence of smoking. Every 4 seconds (as prompted by a metronome) subjects moved the lozenge from side to side in the mouth until the lozenge had completely dissolved (approximately 20-30 minutes). After every 30 seconds the subjects were instructed to swallow their saliva at a verbal command. Blood samples were taken for the measurement of pharmacokinetic parameters at pre- and up to 16 hours post dose. The washout period was at least 3 days.

The pharmacokinetic results for nicotine are presented below (mean, standard deviation (SD) and % confidence intervals):
The 90% confidence intervals for AUC and $C_{\text{max}}$ for test versus reference product for nicotine for both studies (2mg and 4mg strengths) are within predefined acceptance criteria specified in the "Guideline on the Investigation of Bioequivalence" (CPMP/EWP/QWP/1401/98 Rev 1/, Corr). Thus, the data support the claim that the test products are bioequivalent to the reference products.

**Pharmacodynamics**
No new pharmacodynamic data were submitted and none were required for these applications.

**Efficacy**
No new efficacy data were submitted and none were required for these applications.

**Safety**
With the exception of the data generated during the bioequivalence studies, no new safety data were submitted and none were required for these applications. No new or unexpected safety issues were highlighted by the bioequivalence data.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels**
The SmPCs, PIL and labels are acceptable. The SmPCs are consistent with those for the originator products. The PIL is consistent with the SmPCs and in line with current guidelines. The labelling is in-line with current guidelines.

**MAA Forms**
The MAA forms are satisfactory.
Clinical Overview
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Pharmacovigilance System and Risk Management Plan
The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for these products.

Conclusion
There are no objections to the approval of these products from a clinical view-point.

IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The quality characteristics of Nicotine Perrigo 2mg and 4mg Lozenges 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. The pharmacodynamic, pharmacokinetic and toxicological properties of nicotine are well-known.

Efficacy
With the exception of the bioequivalence studies, no new data were submitted and none are required for applications of this type.

Bioequivalence has been demonstrated between the applicant’s Nicotine Perrigo 2mg and 4mg Lozenges and their respective reference products NiQuitin 2mg and 4mg Lozenges (GlaxoSmithKline Consumer Healthcare, UK).

SAFETY
With the exception of the bioequivalence studies, no new data were submitted and none are required for applications of this type. As the safety profile of nicotine is well-known, no additional data were required. No new or unexpected safety concerns arose from the safety data from the bioequivalence studies.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with the product literature for the reference products, and in line with current guidelines.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence studies support the claim that the applicant’s products and the originator products are interchangeable. Extensive clinical experience with
nicotine is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Module 6

**STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY**

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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