

## **Public Assessment Report**

### **Scientific discussion**

# **Strepfen Sinaasappel Suikervrij 8.75 mg, lozenges (flurbiprofen)**

**NL/H/4615/001/DC**

**Date: 27 February 2023**

This module reflects the scientific discussion for the approval of Strepfen Sinaasappel Suikervrij 8.75 mg, lozenges. The procedure was finalised in the United Kingdom (UK/H/4701/001/DC). After a transfer in 2018, the current RMS is the Netherlands. The report presented below reflects the original procedure at the time of finalisation in the UK and has not been changed or updated since.

# **Public Assessment Report**

## **Decentralised Procedure**

### **Flurbiprofen 8.75 mg Lozenges**

**Flurbiprofen**

**UK/H/4701/001/DC**

**UK licence no: PL 00063/0644**

**Reckitt Benckiser Healthcare (UK) Limited**

## **Flurbiprofen 8.75 mg Lozenges**

**PL 00063/0644**

### **LAY SUMMARY**

On 4<sup>th</sup> December 2012, the Medicines and Healthcare products Regulatory Agency (MHRA) granted a Marketing Authorisation to Reckitt Benckiser Healthcare (UK) Limited for the medicinal product Flurbiprofen 8.75 mg Lozenges (PL 00063/0644; UK/H/4701/001/DC). This medicine is available from the pharmacy (P).

These lozenges contain flurbiprofen. Flurbiprofen belongs to a group of medicines called Non-Steroidal Anti-inflammatory Drugs (NSAIDs). These medicines work by changing how the body responds to pain, swelling and high temperature. Flurbiprofen lozenges are used to relieve the symptoms of sore throats such as throat soreness, pain and swelling.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Flurbiprofen 8.75 mg Lozenges outweigh the risks; hence a Marketing Authorisation was granted.

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## Module 1

<b>Product Name</b>	Flurbiprofen 8.75 mg Lozenges
<b>Type of Application</b>	Article 10.3, Hybrid
<b>Active Substance</b>	Flurbiprofen
<b>Form</b>	Lozenge
<b>Strength</b>	8.75 mg
<b>MA Holder</b>	Reckitt Benckiser Healthcare (UK) Limited 103 – 105 Bath Road Slough SL1 3UH
<b>RMS</b>	UK
<b>CMSs</b>	Austria, Belgium, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Iceland, Lithuania, Luxembourg, Portugal, Slovenia, Spain, Sweden and, The Netherlands
<b>Procedure Number</b>	UK/H/4701/001/DC
<b>Timetable</b>	Day 210: 17 <sup>th</sup> June 2012

## **Module 2**

# **Summary of Product Characteristics**

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

## Module 4 Labelling

**The 24 lozenges pack size is a POM and is not to be marketed under this product licence in the UK**

### 1.3.1 PARTICULARS TO APPEAR ON THE OUTER PACKAGING CARTON (OTC)

- 1 **NAME OF THE MEDICINAL PRODUCT**  
Flurbiprofen 8.75 mg Lozenges
  
- 2 **STATEMENT OF ACTIVE SUBSTANCE**  
Each lozenge contains  
Flurbiprofen 8.75 mg
  
- 3 **LIST OF EXCIPIENTS**  
Contains Glucose, Sucrose.  
See leaflet for further information.
  
- 4 **PHARMACEUTICAL FORM AND CONTENTS**  
8 lozenges  
16 lozenges
  
- 5 **METHOD AND ROUTE OF ADMINISTRATION**  
Read the package leaflet before use:  
For oromucosal administration only.
  
- 6 **SPECIAL WARNING THAT THE MEDICAL PRODUCT MUST BE STORED OUT OF THE REACH OF CHILDREN**  
Keep out of the reach and sight of children.
  
- 7 **OTHER SPECIAL WARNINGS, IF NECESSARY**  
Not applicable.
  
- 8 **EXPIRY DATE**  
Expiry date over printed onto the carton as the following examples:  
EXP: 07 2009
  
- 9 **SPECIAL STORAGE CONDITIONS**  
Not applicable



**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**

Reckitt Benckiser Healthcare (UK) Limited 103 – 105 Bath Road , Slough, SL1 3UH

**12 MARKETING AUTHORISATION NUMBER**

PL 00063/0644

**13 BATCH NUMBER**

Batch number is overprinted onto the carton as following example  
Lot: 12KK

**14 GENERAL CLASSIFICATION FOR SUPPLY**

P

**15 INSTRUCTIONS ON USE**

- Flurbiprofen 8.75 mg Lozenges are used to relieve the symptoms of sore throat
- Works for up to 3 hours
- Contains the anti-inflammatory, flurbiprofen

For adults and children over 12 years:

Suck one lozenge every 3 to 6 hours as required.  
Always move the lozenge around your mouth whilst sucking.

Do not take more than 5 lozenges in any 24 hour period.  
Not suitable for children under 12 years of age.

Do not take for more than 3 days.

If symptoms persist or worsen, consult your doctor.

**16 INFORMATION IN BRAILLE**

Flurbiprofen 8.75 mg Lozenges

NB

Flurbiprofen 8.75 mg Lozenges

**1.3.1 MINIMUM PARTICULARS TO APPEAR ON BLISTERS**

**1. NAME OF THE MEDICINAL PRODUCT**

Flurbiprofen 8.75 mg Lozenges

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Reckitt Benckiser Healthcare (UK) Limited

**3. EXPIRY DATE**

Expiry date is over printed onto the blister foil at the end of the blister strip as follows:  
07 2009

**4. BATCH NUMBER**

The batch number is over printed onto the blister foil at the end of the blister strip as follows: 12KK

**5. OTHER**

Not applicable

## Module 5

### Scientific discussion during initial procedure

#### I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) and Concerned Member States (CMSs) consider that the application for Flurbiprofen 8.75 mg Lozenges for the short term symptomatic relief of sore throat could be approved.

This is a duplicate application to Strepflam 8.75 mg Lozenges (PL 00327/0097; UK/H/0388/001/E01).

This abridged application is submitted under Article 10.3, hybrid, of Directive 2001/83/EC, as amended. The reference product is Strepflam 8.75 mg Lozenges (PL 00327/0097), first authorized to Crookes Healthcare Limited, UK on 31<sup>st</sup> August 1999. This application then underwent a change of ownership procedure to the Marketing Authorisation holder Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0631) on 19<sup>th</sup> March 2010.

With UK as the RMS in this Decentralised Procedure (UK/H/4701/001/DC), Reckitt Benckiser Healthcare (UK) Limited applied for the Marketing Authorisation for Flurbiprofen 8.75 mg Lozenges in the following CMS's:

Austria, Belgium, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Iceland, Lithuania, Luxembourg, Portugal, Slovenia, Spain, Sweden and The Netherlands.

Flurbiprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandins synthesis. In humans flurbiprofen has potent analgesic, antipyretic and anti-inflammatory properties. According to studies using the whole blood assay, flurbiprofen is a mixed COX-1/COX-2 inhibitor with some selectivity towards COX-1.

No new clinical or non-clinical studies were conducted for this application, which is acceptable given that this is a bibliographic application for an active of well-established use.

The RMS has been assured that acceptable standards of GMP are in place for this product type at all sites responsible for the manufacture and assembly of this product. For manufacturing sites within and outside the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

The RMS considers that 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.

All member states agreed to grant a licence for the above product at the end of the procedure (Day 210 – 17<sup>th</sup> June 2012). After a subsequent national phase, the UK granted a licence for this product on 4<sup>th</sup> December 2012 (PL 00063/0644).

**II. ABOUT THE PRODUCT**

Name of the product in the Reference Member State	Flurbiprofen 8.75 mg Lozenges
Name(s) of the active substance(s) (USAN)	Flurbiprofen
Pharmacotherapeutic classification (ATC code)	Other throat preparations, throat preparations. ATC Code: R02AX01
Pharmaceutical form and strength(s)	Lozenge, 8.75 mg
Reference numbers for the Decentralised Procedure	UK/H/4701/001/DC
Reference Member State	United Kingdom
Concerned Member States	Austria, Belgium, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Iceland, Lithuania, Luxembourg, Portugal, Slovenia, Spain, Sweden and The Netherlands
Marketing Authorisation Number(s)	PL 00063/0644
Name and address of the authorisation holder	Reckitt Benckiser Healthcare (UK) Limited 103 – 105 Bath Road Slough SL1 3UH

### III SCIENTIFIC OVERVIEW AND DISCUSSION

#### III.1 QUALITY ASPECTS

##### DRUG SUBSTANCE

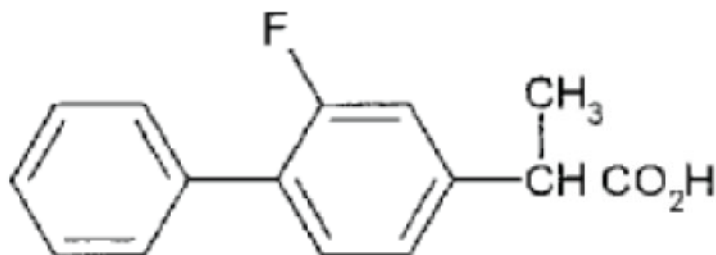
INN: Flurbiprofen

Chemical Names: (2RS)-2-(2-fluorobiphenyl-4-yl) propanoic acid

Chemical formula:  $C_{15}H_{13}FO_2$

Molecular mass: 244.3

Structure:



Physical form: White or almost white, crystalline powder.

Solubility: Practically insoluble in water, freely soluble in alcohol and in methylene chloride. It dissolves in aqueous solutions of alkali hydroxides and carbonates.

Flurbiprofen is the subject of a European Pharmacopoeia monograph.

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

#### DRUG PRODUCT

##### Other Ingredients

Other ingredients consist of the pharmaceutical excipients macrogol 300, potassium hydroxide, lemon flavour, levomenthol, liquid sucrose, liquid glucose and honey. A rationale for the inclusion of each excipient is provided.

All excipients comply with the relevant European Pharmacopoeia monographs with the exception of levomenthol, liquid sucrose and lemon flavour, which comply with an in-house specification. Satisfactory Certificates of Analysis have been provided for these excipients.

The above excipients do not contain materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of this product.

##### Pharmaceutical Development

The objective of the pharmaceutical development programme was to obtain a lozenge containing flurbiprofen that could provide with honey and lemon flavour.

##### Manufacture

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Satisfactory process validation data on

pilot-scale batches have been provided. The applicant has committed to perform process validation on future commercial-scale batches.

### **Finished Product Specifications**

The finished product specification is satisfactory. Test methods have been described and adequately validated. Batch data have been provided and comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

### **Container Closure System**

The finished product is supplied in a push through strip consisting of opaque PVC/PVdC (polyvinyl chloride/polyvinyl di-chloride) blister, heat sealed to hard tempered aluminium foil. Each blister contains either 8 or 12 lozenges and there may be one or two blister strips in each pack. Pack size of 8, 16 or 24 lozenges.

The 24 lozenges pack size is a prescription-only medicine (POM) and is not to be marketed under this product licence in the UK

Specifications and Certificates of Analysis for the primary packaging material have been provided. These are satisfactory. All primary packaging is controlled to European Pharmacopoeia standards and complies with relevant guidelines.

### **Stability**

Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 3 year with no special storage condition has been set. This is satisfactory.

### **Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling**

The SmPC, PIL and labels are pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA together with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

The Marketing Authorisation Holder has committed to submit mock-ups for unmarketed pack size to the relevant regulatory authorities for approval before those packs are marketed.

### **Marketing Authorisation Application (MAA) Form**

The MAA form is pharmaceutically satisfactory.

### **Expert Report/Quality Overall Summary**

A pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

### **Conclusion**

There are no objections to the approval of this product from a pharmaceutical point of view.

### **III.2 NON-CLINICAL ASPECTS**

#### **PHARMACODYNAMICS, PHARMACOKINETICS, TOXICOLOGY**

The pharmacological, pharmacokinetic and toxicological properties of flurbiprofen are well-known.

No new non-clinical data have been supplied with this application and none are required for applications of this type. The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

An environmental risk assessment has been conducted by a suitably qualified person. The applicant has committed to conduct a Phase II assessment as a post approval commitment (PAC). This is acceptable.

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

### **III.3 CLINICAL ASPECTS**

#### **CLINICAL PHARMACOLOGY**

The clinical pharmacology of flurbiprofen is well known. No new pharmacodynamic or pharmacokinetic data are provided or required for this duplicate application.

#### **Efficacy**

No new efficacy data were submitted or required for this application.

#### **Safety**

No new safety data were submitted and none are required for this application. The applicant has provided an acceptable safety review from the literature. No new safety issues have been raised from this application.

#### **EXPERT REPORT/Clinical Overall Summary**

The clinical overview is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

#### **SUMMARY OF PRODUCT CHARACTERISTICS**

The SmPC is medically satisfactory and consistent with that for the reference product.

#### **PATIENT INFORMATION LEAFLET**

The PIL is medically satisfactory and consistent with the SmPC.

#### **LABELLING**

The packaging is medically satisfactory.

#### **MAA FORM**

The MAA form is medically satisfactory.

#### **CONCLUSIONS**

There are no objections to the approval of this product from a clinical point of view.

### **IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT QUALITY**

The important quality characteristics of Flurbiprofen 8.75 mg 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.

#### **CLINICAL**

No new data were submitted and none were required for this type of application.

The efficacy of the active substance is well described and no new studies have been conducted. The applicant has summarised the current state of knowledge in their literature review.

#### **SAFETY**

The safety profiles of flurbiprofen are well-known. The literature review identified no new or unexpected safety issues or concerns.

The SmPC, PIL and labelling are satisfactory and in line with current guideline.

#### **RISK-BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with flurbiprofen is considered to have demonstrated the therapeutic value of the compound. The risk-benefit is, therefore, considered to be positive.



## Module 6

### STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

Date submitted	Application type	Scope	Outcome