# IPAR

# HEALTH PRODUCTS REGULATORY AUTHORITY

## PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension
IBUPROFEN
PA0979/066/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

## I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension from Reckitt Benckiser Healthcare (UK) Limited on 24th October 2014 indicated for reduction of fever and relief of mild to moderate pain, such as cold and flu symptoms, teething pain, headache, sprains and strains and to ease the pain of sore throats and earache.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension. In this case the same MAH owns both medicinal products.

Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension. has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA website.

| | |
|---|---|
| Name of the product | Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension |
| Name(s) of the active substance(s) (INN) | IBUPROFEN |
| Pharmacotherapeutic classification (ATC code) | M01AE01 |
| Pharmaceutical form and strength(s) | 100mg/5ml |

| | |
|---|---|
| Marketing Authorisation Number(s) in Ireland (PA) | PA0979/066/001 |
| Marketing Authorisation Holder | Reckitt Benckiser Ireland Ltd |

# II QUALITY ASPECTS

## II. QUALITY ASPECTS

### II.1. Introduction

This application is for Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension.

Since this application is an informed consent of Nurofen for Children Orange100mg/5ml Oral Suspension PA 0979/032/001, the quality data in support of this product is identical to the up-to-date quality data of the Nurofen for Children Orange dossier which has been assessed and approved. A more detailed quality comment is not required.

### II.2 Drug substance

Since this application is an informed consent of Nurofen for Children Orange 100mg/5ml Oral Suspension PA 0979/032/001, the quality data in support of the drug substance, i.e. Ibuprofen, is identical to the quality data of the Nurofen for Children Orange dossier which has been assessed and approved.

### II.3 Medicinal product

Since this application is an informed consent of Nurofen for Children Orange 100mg/5ml Oral Suspension PA 0979/032/001, the quality data in support of this medicinal product is identical to the quality data of the Nurofen for Children Orange dossier which has been assessed and approved.

### II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension.

# III NON-CLINICAL ASPECTS

### III.1 Introduction

This active substance is the same as that present in Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

### III.2 Pharmacology

See clinical section

### III.3 Pharmacokinetics

See clinical section

### III.4 Toxicology

The toxicity of ibuprofen in animal experiments was observed as lesions and ulcerations in the gastrointestinal tract. Ibuprofen did not show a mutagenic potential in vitro and was not carcinogenic in rats and mice. Experimental studies have demonstrated that ibuprofen crosses the placenta, but there is no evidence of any teratogenic action.

### III.5 Ecotoxicity/environmental risk assessment

Not Applicable

### III.6 Discussion on the non-clinical aspects

As this is an informed consent application, additional non clinical data is not necessary for this application. The active substance ibuprofen is well known and its preclinical effects are well documented. Relevant preclinical aspects are mentioned in section 5.3 of the SPC.

## IV CLINICAL ASPECTS

### IV.1 Introduction

Ibuprofen is a well known active substance with established efficacy and tolerability. This medicinal product is the same as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 on the European market.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Nurofen for Children Orange 100mg/5ml Oral Suspension marketed by Reckitt Benckiser Ireland Ltd.

### IV.2 Pharmacokinetics

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring about 45 to 70 minutes after administration of Nurofen for Children. The elimination half life is approximately 2 hours. Ibuprofen is metabolised in the liver to two major inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins

### IV.3 Pharmacodynamics

Ibuprofen is an NSAID that has demonstrated its efficacy in the common animal experimental inflammation models by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swelling and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

The clinical efficacy of ibuprofen has been demonstrated in fever and in pain associated with headache, toothache and dysmenorrhoea. Furthermore it has been demonstrated in patients with pain and fever associated with cold and flu and in pain models such as sore throat, muscular pain, soft tissue injury, backache.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelets aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use

### IV.4 Clinical Efficacy

Ibuprofen is a well known active substance with established efficacy and tolerability. This medicinal product is the same as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 on the European market and therefore both medicinal products will have the same efficacy.

### IV.5 Clinical Safety

Ibuprofen is a well known active substance with established efficacy and tolerability. This medicinal product is the same as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 on the European market with the same indications and posology and therefore both medicinal products will have the same safety profile.

The marketing authorisation holder (MAH) submitted a summary describing the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

The MAH has submitted a risk management plan, 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 Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension.

Based on consideration of the identified risks, the potential risks and the need for additional information on the medicinal product, it is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

The schedule for Periodic Safety Update Reports (PSUR) will be on a three year cycle.

### IV.6 Discussion on the clinical aspects

Ibuprofen is a well known active substance with established efficacy and tolerability. This medicinal product is the same as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1 on the European market. As both medicinal products also have the same indications and posology both medicinal products will have the same efficacy and safety profile.

## V OVERALL CONCLUSIONS

Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension PA 979/66/1 is the same as Nurofen for Children Orange 100mg/5ml Oral Suspension PA 979/32/1. Ibuprofen is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The HPRA, on the basis of the data submitted considered that Nurofen for Children Orange 100mg/5ml Cold, Flu & Pain Oral Suspension PA 979/66/1 was the same as the reference product and therefore granted a marketing authorisation.

This section reflects the significant changes following finalisation of the initial procedure.

| Scope | Procedure number | Product Information affected | Date of start of procedure | Date of end of procedure | Approval/ non approval |
|---|---|---|---|---|---|
| | | | | | |