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IRISH MEDICINES BOARD

PUBLIC ASSESSEMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Nurofen Sinus and Pain Film-Coated Tablets
Ibuprofen 200 mg, Pseudoephedrine Hydrochloride 30 mg
PA 0979/065/001

The Public Assessment Report reflects the scientific conclusion reached by the Irish Medicines Board (IMB) 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 IMB 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 IMB 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 IMB has granted a marketing authorisation for Nurofen Sinus and Pain film-coated tablets, from Reckitt Benckiser Ireland Ltd on the 20th June 2014 for the symptomatic relief of head colds and influenza, including nasal congestion, and to ease the pain of sore throats.

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 Cold & Flu film-coated tablets, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Nurofen Sinus and Pain film-coated tablets. Nurofen Sinus and Pain film-coated tablets have the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Nurofen Cold & Flu film-coated tablets.

Nurofen Sinus and Pain film-coated tablets are not subject to medical prescription but are supplied through pharmacies only.

The Summary of Product Characteristics (SmPC) for this medicinal product is available on the IMB's website at www.imb.ie

Name of the product	Nurofen Sinus and Pain film-coated tablets
Names of the active substances (INN)	Ibuprofen, pseudoephedrine hydrochloride
Pharmacotherapeutic classification (ATC code)	M01AE01
Pharmaceutical form and strength(s)	200 mg/30 mg
Marketing Authorisation Number in Ireland (PA)	PA 979/65/1
Marketing Authorisation Holder	Reckitt Benckiser Ireland Ltd

II QUALITY ASPECTS

Nurofen Sinus and Pain film-coated tablets are identical to Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1). No additional pharmaceutical data were submitted in support of the current application. This is acceptable for an informed-consent application.

III NON-CLINICAL ASPECTS

III.1 Introduction

The active substances are the same as that present in Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1) 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

The use of ibuprofen and pseudoephedrine HCl in this present fixed dose combination is thus a combination of two drugs with entirely separate modes of action, relying on COX inhibition and direct and indirect agonist activity at both α- and β-adrenoceptors, respectively. Neither agent has any secondary pharmacological activities of relevance in the present context, or any toxicological properties of significance for the intended use.

Ibuprofen
The anti-inflammatory, analgesic and antipyretic actions of ibuprofen are all mediated by inhibition of COX, the enzyme responsible for the conversion of arachidonic acid to the endoperoxide, prostaglandin H_2 (PGH_2), which is the critical intermediate in the biosynthesis of prostaglandins, thromboxanes and other mediators.

Ibuprofen is remarkably devoid of typical NSAID toxicities in therapeutic use (Henry et al 1996; Rainsford et al 1997), a variety of studies show that racemic ibuprofen does not show COX-2 selectivity in a range of in vitro systems (Mitchell et al 1993; Laneuville et al 1994; Young et al 1996).

Pseudoephedrine
Pseudoephedrine is a natural product found in various plants of the Ephedra family and is present in many herbal Ephedra products. It is a stereoisomer of the well-known adrenergic agent ephedrine: the side chain of these agents contains two chiral centres and pseudoephedrine is a diastereoisomer of ephedrine with similar but less potent pharmacological activity. The actions of pseudoephedrine arise from both direct and indirect activation of α- and β-adrenoceptors, notably in the respiratory tract. Its principal effects are vasoconstriction and bronchodilation, thereby producing a series of characteristic effects including a reduction in swelling of the nasal mucosa, in tissue hyperaemia, oedema and nasal congestion.

A large number of such combination products on the market in many countries.

III.3 Pharmacokinetics

See clinical section

III.4 Toxicology

Not applicable

III.5 Ecotoxicity/environmental risk assessment

Not applicable

III.6 Discussion on the non-clinical aspects

In summary, it is concluded that the available preclinical information provides adequate support for the safe therapeutic use of this fixed combination of ibuprofen and pseudoephedrine HCl in a 100:15 ratio by weight in soft gelatin capsules, in terms of its potency and activity, general pharmacodynamics, pharmacokinetics and toxicity and the absence of any relevant pharmacological or toxicological interaction between the two agents.

IV CLINICAL ASPECTS

IV.1 Introduction

Both Ibuprofen and pseudoephedrine are well known active substances with established efficacy and tolerability. A large number of such combination products on the market in many countries.
Nurofen Sinus and Pain film-coated tablets are identical to Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1). No additional clinical data were submitted in support of the current application. This is acceptable for an informed-consent application.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Nurofen Cold & Flu film-coated tablets (PA 979/33/1) marketed by Reckitt Benckiser.

IV.2 Pharmacokinetics

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1 to 2 hours after administration.

Ibuprofen is extensively bound to plasma proteins

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. The elimination half-life is approximately 2 hours. Excretion by the kidney is both rapid and complete.

Pseudoephredine is absorbed from the gastrointestinal tract and is largely excreted in the urine unchanged, together with small amounts of a hepatic metabolite. It has an elimination half-life of several hours, which may be reduced by acidifying the urine.

IV.3 Pharmacodynamics

Ibuprofen is a propionic acid derivative, having analgesic, anti-inflammatory and antipyretic activity. The therapeutic effects of ibuprofen as a NSAID are thought to result from its inhibitory activity on the enzyme prostaglandin synthetase.

Pseudoephedrine is a sympathommetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta stimulant adrenergic activity and some stimulant effect on the central nervous system. The sympathomimetic effect of pseudoephredine produces vasoconstriction which in turn relieves nasal congestion.

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

The efficacy of the combination is well known and as Nurofen Sinus and Pain film-coated tablets are identical to Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1) similar efficacy can be assumed.

IV.5 Clinical Safety

The safety of the combination is well known and as Nurofen Sinus and Pain film-coated tablets are identical to Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1) similar safety profile can be assumed.

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 Sinus and Pain Film-Coated Tablets (Ibuprofen 200 mg, Pseudoephedrine Hydrochloride 30 mg).

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.

A summary of the pharmacovigilance system has been provided.

Periodic Safety Update Reports (PSUR) should be submitted every 3 years.

IV.6 Discussion on the clinical aspects

This is an informed consent application, no clinical data was submitted for this application, this is acceptable for this type of application. The medicinal product is identical to the reference Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1) therefore similar efficacy and safety can be assumed.

V OVERALL CONCLUSIONS

Nurofen Sinus and Pain film-coated tablets are identical to Nurofen Cold & Flu film-coated tablets, a product which is already authorised (PA 979/33/1) Nurofen Cold & Flu film-coated tablets is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The IMB, on the basis of the data submitted considered that Nurofen Sinus and Pain film-coated tablets was the same as the reference product and therefore granted a marketing authorisation.