IPAR

IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Brupro for Children 100 mg/5 ml Oral Suspension
IBUPROFEN
PA 711/225/001

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 Brupro for Children 100 mg/5 ml Oral Suspension, from Rowex Ltd. on 07th March 2014 for the short-term symptomatic treatment of mild to moderate pain and fever.

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 Rowex Ltd., which currently holds a Marketing Authorisation for 'Brupro for Children 100 mg/5 ml Oral Suspension' (PA 711/205/1), has cross-referred to that dossier in support of the present application. This product has the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form as the existing Brupro product.

The product is not subject to medical prescription and is supplied through pharmacies only.

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

Name of the product	Brupro for Children
Name(s) of the active substance(s) (INN)	Ibuprofen
Pharmacotherapeutic classification (ATC code)	M01AE01
Pharmaceutical form and strength(s)	100 mg/5 ml
Marketing Authorisation Number(s) in Ireland (PA)	PA 711/225/1
Marketing Authorisation Holder	Rowex Ltd.

II QUALITY ASPECTS

This is an 'informed consent' application which cross-refers to the dossier for a currently authorised product (PA 711/205/1). No new pharmaceutical data were submitted in support of this application. The pharmaceutical dossier received as part of the application for PA 711/205/1 has not been reassessed.

III NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is the same as that present in Brupro for children 100mgs/5ml oral suspension PA0711/205/001 on the European market (MRP DE/H/3341/001 CRN 2099760). 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.

The IMB has been assured that GLP standards were followed in an appropriate manner in the studies conducted.

III.2 Pharmacology

The Pharmacology of Ibuprofen is well established. The MAH has not conducted additional pharmacology tests, this is accepted for this application.

III.3 Pharmacokinetics

The pharmacokinetics of Ibuprofen is well established. The MAH has not conducted additional pharmacology tests, this is accepted for this application.

III.4 Toxicology

The subchronic and chronic toxicity of ibuprofen in animal experiments showed up mainly in form of lesions and ulcerations in the gastro-intestinal tract.

In vitro and *in vivo* studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of ibuprofen was found.

Ibuprofen inhibited ovulation in rabbits and impaired implantation in various animal species (rabbit, rat, mouse). Experimental studies in rat and rabbit have shown that ibuprofen crosses the placenta. Following administration of maternotoxic doses, an increased incidence of malformations (ventricular septal defects) occurred in the progeny of rats.

III.5 Ecotoxicity/environmental risk assessment

Not applicable as this is a generic application.

III.6 Discussion on the non-clinical aspects

As this is an informed consent on a generic application the company has not conducted preclinically studies which is acceptable for this type of application.
The non clinical aspects are deemed to be the same as for the innovator reference product.

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 Brupro for children 100mgs/5ml PA0711/205/001 oral suspension on the European market (MRP DE/H/3341/001).

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product, Brupro for children 100mgs/5ml PA0711/205/001 on the European market.

IV.2 Pharmacokinetics

On oral application, ibuprofen is already partly absorbed in the stomach and then completely in the small intestine. Peak plasma levels following oral administration of a normal-release pharmaceutical form are reached after 1−2 hours. Following hepatic metabolisation (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 − 3.5 hours, plasma-protein binding about 99 %.

IV.3 Pharmacodynamics

Ibuprofen is a non-steroidal anti-inflammatory drug that, in the conventional animal-experiment inflammation models, has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen has an antipyretic effect, reduces inflammatory-related pain and swelling. Furthermore, ibuprofen reversibly inhibits ADP- and collagen-induced platelet aggregation.

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid (ASA) on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release acetylsalicylic acid dosing (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 and Safety

This is an informed consent application and is identical to Brupro for children 100mg/5ml oral suspension PA0711/205/001 licensed to Rowex on the 11/1/2013, therefore the efficacy and safety are the same.

No new data were submitted nor were necessary for this simple application, as the data is identical to that previously granted product Brupro for children 100mg/5ml oral suspension PA0711/205/001.

However any issues with the reference license will also be relevant for this National informed consent license and it is recommended that the product information is updated as necessary and in line with the reference product.

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 Brupro for Children 100 mg/5 ml 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) submission should be the same as PA0711/205/001. The international birth date (IBD) is known and the renewal date is 31.01.2015.

V OVERALL CONCLUSIONS

The quality of this product is acceptable and no new non clinical or clinical safety concerns have been identified. The applicant product is identical to the cross reference product, Brupro for children 100mg/5ml oral suspension PA0711/205/001. The benefit risk is therefore considered to be positive.

The IMB, on the basis of the data submitted considered that was the same as the cross reference product and therefore granted a marketing authorisation.