IPAR

IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Paracetamol 120mg/5ml Sugar-Free Infant Oral Suspension

Paracetamol

PA0823/010/010

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 Paracetamol 120mg/ 5ml Sugar-Free Infant Oral Suspension, from McNeill Healthcare (Ireland) Ltd on 23rd June 2010.

Therapeutic Indications
PARACETAMOL 120mg/5ml Sugar Free Infant Suspension is indicated for the treatment of pain (including teething pain), and as an antipyretic.

PARACETAMOL 120mg/5ml Sugar Free Infant Suspension is indicated for the relief of headache, migraine, neuralgia, toothache and teething pains, sore throat, rheumatic aches and pains, influenza, feverishness and feverish colds.

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 Calpol 120mg/5ml Sugar-free Infant Oral Suspension, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Paracetamol 120mg/ 5ml Sugar-Free Infant Oral Suspension. Paracetamol 120mg/ 5ml Sugar-Free Infant Oral Suspension has the same qualitative and quantitative composition in terms of active substance and the same pharmaceutical form as Calpol 120mg/5ml Sugar-free Infant Oral Suspension.

Prescription Status
General sale in child resistant packs containing not more than 60ml of the 120mg/5ml unit dosage form.

Retail sale through pharmacies only in child resistant packs containing not more than 140 ml of the120mg/5ml unit dosage form.

Prescription only for any pack size exceeding 140ml content of the 120mg/5ml unit dosage form.

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

Name of the product	Paracetamol 120mg/ 5ml Sugar-Free Infant Oral Suspension
Name(s) of the active substance(s) (INN)	Paracetamol
Pharmacotherapeutic classification (ATC code)	N02B
Pharmaceutical form and strength(s)	120 mg/5ml
Marketing Authorisation Number(s) in Ireland (PA)	PA0823/010/010
Marketing Authorisation Holder	McNeil Healthcare Limited

II QUALITY ASPECTS

II.1. Introduction

This application is for Paracetamol 120mg/ 5ml Sugar-Free Infant Oral Suspension.
This application is for a duplicate licence which is identical to an already licenced product. As all Quality aspects are identical to those of the authorised Calpol 120mg/5ml Sugar-free Infant Oral Suspension product Module 3 data has not been submitted and therefore not assessed.

II.2 Drug substance

The active substance is paracetamol Ph. Eur., an established active substance described in the European Pharmacopoeia, and is

manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Brief description of the dosage form

Composition of the medicinal product

Active Substance
Paracetamol 120mg per 5ml.

Excipients
Maltilol Liquid, Sorbitol Solution (E420) (70% non-crystallising),Glycerol, Dispersible Cellulose, Xanthan Gum, Ethyl Parahydroxybenzoate (E214), Methyl Parahydroxybenzoate (E218), Propyl Parahydroxybenzoate (E216), Polysorbate 80, Flavour Strawberry 500286 E, Carmoisine (E122), Purified Water.

P.2 Pharmaceutical Development

The product is an established/ pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for oral suspensions, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

5 ml sachet composed of a complex made of paper/PE/aluminium/Surlyn.
A spoon with a 5ml and a 2.5ml measure is supplied with this pack.

An amber glass bottle with a two piece child-resistant, tamper-evident closure fitted with a polyethylene or polyvinylidine (PVDC) laminate faced wad.
Or
An amber glass bottle with a three piece plastic, child-resistant, tamper-evident closure fitted with a polyethylene or polyvinylidine (PVDC) laminate faced wad.

A spoon with a 5ml and a 2.5ml measure is supplied with this pack.

Evidence has been provided that the bottle and closures comply with EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines demonstrating the stability of the product for 3years when stored in the original container not above 25°C.

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 Paracetamol Infant 120mg/5ml oral suspension.

III NON-CLINICAL ASPECTS

Not Applicable

IV CLINICAL ASPECTS

IV.1 Introduction

Paracetamol is a well known active substance with established efficacy and tolerability. This medicinal product is the same as the active substance in Calpol Sugar Free Infant Suspension on the Irish market

The content of the SPC approved during the national procedure is in accordance with that accepted for the reference product marketed by MAH.

IV.2 Pharmacokinetics

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 30-90 minutes post dose and the plasma half-life is in the range of 1 to 3 hours after therapeutic doses. Drug is widely distributed throughout most body fluids. Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours almost entirely following hepatic conjugation with glucuronic acid (about 60%), sulphuric acid (about 35%) or cysteine (about 3%). Small amounts of hydroxylated and deacetylated metabolites have also been detected. Children have less capacity for glucuronidation of the drug than do adults. In overdosage there is increased N-hydroxylation followed by glutathione conjugation. When the latter is exhausted, reaction with hepatic proteins is increased leading to necrosis.

IV.3 Pharmacodynamics

Paracetamol has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has weak anti-inflammatory effects.

IV.4 Clinical Efficacy

This Application was made in accordance with Article 10 c of 2001/83/EC. Efficacy data from the reference is used to support the indications for this product.

V OVERALL CONCLUSIONS

BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Paracetamol 120mg/5ml Sugar Free Oral Suspension is the same as Calpol 120mg/5ml Sugar/Color Free Oral Suspension and 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 Paracetamol 120mg/5ml Sugar Free Infant Oral Suspension was the same as the reference product and therefore granted a marketing authorisation.

VI REVISION DATE

June 2010