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IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Paracetamol Infant Oral Suspension
Paracetamol

PA0823/010/009

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 Infant Oral Suspension" (PA823/10/9), from McNeill Healthcare (Ireland) Ltd on June 23 rd 2010 for

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

PARACETAMOL 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 Infant Suspension", an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for "Paracetamol 120mg/5ml Infant Oral Suspension". "Paracetamol 120mg/5ml Infant Oral Suspension" has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as "Calpol 120mg/5ml Infant 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 (SPC) for this medicinal product is available on the IMB's website at www.imb.ie.

Name of the product	Paracetamol 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)	PA0823/010/009
Marketing Authorisation Holder	McNeil Healthcare Limited

II QUALITY ASPECTS

II.1. Introduction

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

II.2 Drug substance

The active substance is Paracetamol, an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

II.3 Medicinal product

P.1 Composition

A pink suspension with a strawberry flavour.

The suspension contains the active substance Paracetamol - 120 mg in 5ml. Also the following excipients:
Sucrose,
Sorbitol Solution (E420) (70% non-crystallising),
Glycerol,
Dispersible Cellulose, Xanthan Gum,
Ethyl Parahydroxybenzoate (E214)
Methyl Parahydroxybenzoate (E218)
Propyl Parahydroxybenzoate (E216)
Polysorbate 80
Acesulfame Potassium
Flavour, Strawberry 500018E
Carmoisine (E122)
Purified water

P.2 Pharmaceutical Development

The product is an established pharmaceutical form.

.3 Manufacture of the Product

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

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 identical to "Calpol Infant 120mg/5ml Oral Suspension". This specification is based on is based on the pharmacopoeial monograph for oral suspensions, and the tests and control limits are considered appropriate for this type of product.

Using the information previously supplied for the above product, the analytical methods used are described in sufficient detail and are supported by validation data and batch analytical data for a number of batches from the proposed production site. This demonstrates the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

As for the reference product, the product is presented as either:
An amber glass bottle with a two piece child-resistant, tamper-evident closure fitted with a polyethylene or polyvinylidine (PVDC) laminate faced wad.
or
A 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.

P.7 Stability of the Finished Product

Using data provided in supporting the reference product, the products are considered stable for 3 years when kept in the original container and not above 25°C.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are as those accepted for the reference product marketed by Mallinckrodt Healthcare. Based on this the consistent quality of Paracetamol Infant 120mg/5ml Oral Suspension is assured.

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

VI REVISION DATE

June 2010