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IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Apfen Plus 200 mg/12.8 mg Film-coated Tablets
IBUPROFEN/CODEINE PHOSPHATE HEMIHYDRATE

PA 0678/109/001

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.

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the IMB has granted a marketing authorisation for Apfen Plus 200 mg/12.8 mg Film-coated Tablets, from GlaxoSmithKline Consumer Healthcare (Ireland) Limited, Stonemasons Way, Rathfarnhame, Dublin 16, Ireland on 9th March 2012 for the symptomatic relief of mild to moderate pain in such conditions as soft tissue injuries, including sprains, strains and musculo-tendonitis, backache, non-serious arthritic and rheumatic conditions, rheumatic and muscular pain, migraine, dental pain and dysmenorrhoea.

The applicant has applied under Article 10a of the Directive 2001/83, transposed as S.I. 540/2003 as amended (well-established use), and has provided literature evidence regarding the safety and efficacy of this product used at these doses in the specified indications. The legal basis of this application is considered to be in order.

This product is authorised for retail sale through pharmacies only, and can only be advertised to healthcare professionals. The applicant has not received scientific advice from the Irish Medicines Board.

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

Name of the product	Apfen Plus 200 mg/12.8 mg Film-coated Tablets
Name(s) of the active substance(s) (INN)	Ibuprofen/Codeine Phosphate Hemihydrate
Pharmacotherapeutic classification (ATC code)	N02AA59
Pharmaceutical form and strength(s)	200 mg/12.8 mg Film-coated Tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA 0678/109/001
Marketing Authorisation Holder	GlaxoSmithKline Consumer Healthcare (Ireland) Limited, Stonemasons Way, Rathfarnhame, Dublin 16, Ireland

II QUALITY ASPECTS

II.1. Introduction

This application is for Apfen Plus 200 mg/12.8 mg Film-coated Tablets.

II.2 Drug substance

The active substances are ibuprofen and codeine phosphate hemihydrate. Both are established active substances described in the European Pharmacopoeia and are manufactured in accordance with the principles of Good Manufacturing Practice (GMP).

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

II.3 Medicinal product

P.1 Composition

Apfen Plus are white, capsule-shaped tablets, embossed with a "+" symbol on one side.
Each tablet contains ibuprofen 200mg and codeine phosphate hemihydrate 12.8 mg.
The other ingredients (excipients) are lactose monohydrate, cellulose powder, microcrystalline cellulose, colloidal anhydrous silica, sodium starch glycolate and hydrogenated vegetable oil. The film-coating contains hypromellose and macrogol 400.

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. and are therefore adequately controlled by the agreed specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for tablets 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 have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The product is presented in PVC/ aluminium blisters containing 4, 6, 10, 12, 16, 20, 24, 30, 32, 48, 60, 96, 100 or 108 tablets, however not all pack sizes may be marketed.

Evidence has been provided that the blisters comply with the relevant requirements of the European Pharmacopeia and/or EU legislation for use with foodstuffs.

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 3 years. No special storage precautions are required.

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 Apfen Plus 200 mg/12.8 mg Film-coated Tablets.

III NON-CLINICAL ASPECTS

This combination of active substances has been available on the European/Irish market for several years. Preclinical data have been superseded by clinical experience and therefore no preclinical assessment report is available.

IV CLINICAL ASPECTS

Ibuprofen and Codeine are well known active substances with established efficacy and tolerability.

The content of the SPC approved during the national procedure is in accordance with those accepted for similar products.

For this bibliographic application, the applicant has submitted adequate literature references to demonstrate the pharmacology, efficacy and safety of the combination product. No bioequivalence studies were performed in support of this type of application, and none are required.

The Marketing Authorisation Holder submitted a set of documents describing the Pharmacovigilance System, including information on 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.

V OVERALL CONCLUSIONS

Benefit/Risk Assessment and Recommendation

Apfen Plus 200 mg/12.8 mg Film-coated Tablets, from GlaxoSmithKline Consumer Healthcare (Ireland) Limited, is a well-known active ingredient with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The SPC is consistent with that of other authorised products.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The IMB, on the basis of the data submitted, considered that Apfen Plus 200 mg/12.8 mg Film-coated Tablets demonstrated adequate evidence of efficacy for the approved indication(s) as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.