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IRISH MEDICINES BOARD

PUBLIC ASSESSMENT REPORT FOR A MEDICINAL PRODUCT FOR HUMAN USE

Scientific discussion

Arthriaid 500mg, 750mg & 1500mg Film-Coated Tablets

GLUCOSAMINE SULFATE as Glucosamine sulfate sodium chloride

PA1521/001/001-003

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 Arthriaid 500mg, 750mg & 1500mg Film-Coated Tablets, from FMC Pharma Ltd on 22nd July 2011 for the treatment of osteoarthritis of low to moderate degree.

This application was made under Article 10a of Directive 2001/83/EC, a well established use procedure, and therefore the evidence provided to demonstrate the safety and efficacy of this product in bibliographic in nature, this is appropriate for this type of procedure.

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	Arthriaid 500mg, 750mg & 1500mg Film-Coated Tablets
Name(s) of the active substance(s) (INN)	GLUCOSAMINE SULFATE
Pharmacotherapeutic classification (ATC code)	M01AX05
Pharmaceutical form and strength(s)	500mg, 750mg & 1500mg Film Coated Tablets
Marketing Authorisation Number(s) in Ireland (PA)	PA 1521/001/001-003
Marketing Authorisation Holder	FMC Pharma Ltd

II QUALITY ASPECTS

II.1. Introduction

This application is for Arthriaid 500mg, 750mg and 1500mg Film Coated Tablets.

II.2 Drug substance

The active substance is glucosamine sulfate, as glucosamine sulfate sodium chloride, an established active substance not described in the European or British Pharmacopoeia. It 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 standards. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Arthriaid are off-white, oblong shaped, film-coated tablets.

Each tablet contains 500mg, 750mg or 1500mg glucosamine sulfate as glucosamine sulfate sodium chloride.

The other ingredients in each tablet core are microcrystalline cellulose, lactose monohydrate, pregelatinised maize starch, crospovidone and stearic acid. The film-coating of the 500mg strength contains titanium dioxide, yellow iron oxide, Hypromellose and Macrogol 400. The film-coating of the 750mg and 1500mg strength contains polyvinyl-alcohol part hydrolysed, titanium dioxide, Talc, Macrogol 3350 and soya lecithin.

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 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 manufacturers' specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for a coated tablet, 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

The product is presented either in blister packs of PVdC coated PVC/Aluminium blister strips or in HDPE containers fitted with a tamper-evident screw cap.

Evidence has been provided that the blister materials and plastic bottles comply with Ph. Eur 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 2 years when stored in the original package in order to protect from moisture, with no specific temperature storage precautions.

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 Arthriaid 500mg, 750mg and 1500mg Film-coated tablets.

III NON-CLINICAL ASPECTS

This active substance has been available on the European/Irish market for more than 10 years. Preclinical data have been superseded by clinical experience and therefore no additional preclinical data has been provided to support this application.

IV CLINICAL ASPECTS

IV.1 Introduction

Glucosamine is a well known active substance with established efficacy and tolerability. As this is a well-established use application, the evidence supporting its safety and efficacy is bibliographic in nature.

IV.2 Pharmacokinetics

The human pharmacokinetic documentation for glucosamine consists of published papers and is very limited. Glucosamine is a rather small molecule, which is very soluble in water. No definite figures on absolute oral bioavailability and degree of absorption of glucosamine are available, but the absorption is probably at least 10% based on urinary excretion data. The half-life of free glucosamine is short (2 hours), while the half-life of protein-incorporated glucosamine is about 70 hours.

There is no data on interactions or pharmacokinetics in special patient groups for glucosamine. These deficiencies are adequately covered in the product information.

IV.3 Pharmacodynamics

A mechanism of action for symptom-modifying effects of glucosamine is not well understood, but it is thought to be related in part to increased synthesis of glucosaminoglycans in the chondrocytes. Additionally, in experiments using chondrocytes isolated from human osteoarthritic femoral heads, glucosamine was shown to induce a significant and dose dependent increase in proteoglycan synthesis, while DNA synthesis or prostaglandin E2 production was unaffected.

IV.4 Clinical Efficacy

From published clinical studies, it is concluded that the effect on pain, stiffness and mobility of glucosamine in osteoarthritis is similar to that of ibuprofen. In the referred published studies there is an efficacy shown for symptomatic relief in patients with mild to moderate osteoarthritis.

IV.5 Clinical Safety

The safety profile for glucosamine is favourable with mainly mild reactions, particularly from the gastrointestinal region. Some concerns are raised regarding patients with diabetes mellitus and the regulation of blood glucose homeostasis. Caution is warranted for patients with predisposing factors for diabetes mellitus and patients with diabetes mellitus should not be treated unless they are carefully monitored. Appropriate information and warnings are included in the SPC.

The schedule for Periodic Safety Update Reports (PSUR) submission should be addressed

Risk Management Plan
No additional risk management measures are required, apart from those necessary for routine pharmacovigilance.

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

From a quality perspective the overall assessment outcome of Arthriaid 500mg, 750mg and 1500mg film-coated tablets is positive.

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 Arthriaid 500mg, 750mg & 1500mg 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.

VI REVISION DATE

July 2011