IPAR

Scientific discussion

Glusamin 750 mg

Glucosamine Sulphate Sodium Chloride
IE/H/244/001/E01

Instructions for use: Choose relevant text and delete alternative. Follow instructions in italic text and then delete.

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) 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 HPRA 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 HPRA 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 RMS considered that the application for Glusamin 750 mg Film Coated Tablets, mild to moderate osteoarthritis of the knee is approvable.

FMC Pharma Ltd initially submitted national application for Glusamin 750 mg Film Coated Tablets and it was first authorised on 26th August 2011. Following the national authorisation MRP was initiated in November 2011 - IE/H/244/01/MR with BG, CZ, HU, LV, PL, RO and SK and IE acting as the RMS. The MRP was concluded positively in June 2012. FMC Pharma Ltd submitted repeat use MRP - IE/H/244/01/MR/E01 in order to include new CMSs namely EE & LT.

The strength 750 mg have already been assessed and authorised via a different MRP as explained below.

Arthriaid 500 mg, 750 mg and 1500 mg Film-Coated Tablets IE/H/243/01-03/MR
Glusamin 750mg Film-Coated Tablets IE/H/244/01/MR
Glucosamine Sulfate 500mg, 750mg, 1500mg Film-Coated Tablets IE/H/245/01-03/MR

The applicant has submitted a well established use application under Article 10a of Directive 2001/83/EC. Under the terms of this procedure, no new clinical or non-clinical data has been provided by the applicant, and as such the evidence for clinical efficacy and safety is bibliographic in nature. This is appropriate for this type of application.

This product is currently subject to medical prescription in the RMS.

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

Name of the product	Glusamin
Name(s) of the active substance(s) (INN)	GLUCOSAMINE SULFATE SODIUM CHLORIDE
Pharmacotherapeutic classification (ATC code)	M01 AX05
Pharmaceutical form and strength(s)	750 mg Film-Coated Tablets
Marketing Authorisation Numbers in Ireland (PA)	PA 1521/2/1
Marketing Authorisation Holder	FMC Pharma Ltd
MRP/DCP No.	IE/H/244/001/E01
Reference Member State	IE
Concerned Member State	IE/H/244/01/MR/E01: EE and LT

II QUALITY ASPECTS

II.1. Introduction

This application is for Glusamin 750mg film-coated tablets

II.2 Drug substance

The active substance is glucosamine sulfate, as glucosamine sulfate sodium chloride an established active substance 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 standards. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Glusamin is an off-white oblong shaped film-coated tablet.

Each tablet contains either 750 mg glucosamine sulfate as glucosamine sulfate sodium chloride. The other ingredients in each tablet core are microcrystalline cellulose, lactose monohydrate, pregelatinised maize starch, crospovidone, stearic acid and the film-coating which consists of polyvinyl-alcohol part hydrolysed, titanium dioxide (E171), talc (E553b) , soya lecithin (E322) and macrogol 3350.

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 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(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 as PVdC coated PVC/Al blister strips or HDPE containers fitted with a tamper-evident HDPE screw cap.

Evidence has been provided that the blisters and the HDPE containers comply with relevant Ph. Eur. and 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 2 years when stored in the original package in order to protect from moisture. The product does not require any special temperature storage conditions.

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 Glusamin 750mg Film-coated Tablets.

III NON-CLINICAL ASPECTS

This active substance has been available on the European and Irish markets 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 SmPC.

Pharmacovigilance System

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.

Risk Management Plan
Summary of safety concerns

Important Identified risks
Interaction with coumarin anticoagulants (e.g.warfarin)
Interaction with tetracyclines
Impaired glucose tolerance
Shellfish allergy
Soya or peanut or other ingredient allergies

Important Potential risks
Off-label use in children and adolescents less than 18 years of age
Off-label use to help with other joint pain caused by osteoarthritis
Worsening of asthma symptoms

Missing information
Hypercholesterolaemia
Safety data in pregnant women

Safety data with breast feeding
Impaired renal and/or liver function

Periodic Safety Update Report (PSUR)

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.
- For medicinal products that do not fall within the categories waived of the obligation to submit routine PSURs by the revised pharmacovigilance legislation, the MAH should follow the DLP according to the EURD list.

IV.6 Discussion on the Clinical Aspects

As this is an abridged application for the authorisation of a generic medicinal product, the need for repetitive tests on humans can be avoided. On the basis of the data submitted, it is considered that adequate evidence of efficacy for the approved indication as well as a satisfactory risk/benefit profile assessment has been provided.

V OVERALL CONCLUSIONS

BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The HPRA, on the basis of the data submitted, considered that Glusamin 750 mg coated tablets demonstrated adequate evidence of efficacy for the approved indication as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI REVISION DATE

August 2016