**IPAR**

**Public Assessment Report for a**
**Medicinal Product for Human Use**

Scientific Discussion

Glucosamine sulfate 1500mg Film-coated Tablets
Glucosamine sulfate
PA1521/003/003

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.

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## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Glucosamine sulfate 500 mg, 750 mg and 1500 mg Film-coated Tablets from FMC Pharma Ltd on 26th August 2011 for the treatment of osteoarthritis of low to moderate degree.

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 (MAH) for Arthrimel, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for GLUCOSAMINE SULFATE. GLUCOSAMINE SULPHATE has the same qualitative and quantitative composition in terms of the active substance and the same pharmaceutical form as Arthrimel.

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

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

## II. QUALITY ASPECTS

### II.1. Introduction
This application is for Glucosamine sulfate 500 mg, 750 mg and 1500 mg 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, 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
Glucosamine sulfate are off-white, oblong shaped, film-coated tablets

Each tablet contains 500 mg, 750 mg or 1500 mg 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 500 mg strength contains titanium dioxide, yellow iron oxide, hypromellose and macrogol 400.

The film-coating of the 750 mg and 1500 mg strength contains polyvinyl-alcohol part hydrolysed, titanium dioxide (E171), talc (E553b), macrogol 3350 and soya lecithin (E322).

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.4Control of Other Substances
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 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 as PVdC coated PVC/Al blister strips or HDPE containers fitted with a tamper-evident HDPE screw cap containing 7, 8, 9 10, 12, 14, 15, 20, 21, 28, 30, 56, 60, 84, 90,112, 120, 168, 180, 252, 270, 336, 360, 504 and 540 tablets per package. Not all pack sizes may be marketed.
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, 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 glucosamine sulfate 500 mg, 750 mg and 1500 mg film-coated tablets.

## III. NON-CLINICAL ASPECTS

**III.1 Introduction**
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 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**

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

## V. OVERALL CONCLUSIONS

**BENEFIT/RISK ASSESSMENT AND RECOMMENDATION**

From a quality, efficacy and safety perspective the overall assessment outcome of Glucosamine sulfate 500mg, 750 mg & 1500 mg film-coated tablets is positive.

The HPRA, on the basis of the data submitted considered that Glucosamine sulfate 500 mg, 750 mg and 1500 mg tablets were the same as the reference product and therefore granted a marketing authorisation.

## VI. REVISION DATE

August 2011