LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Glamin
(glucosamine hydrochloride)

Asp no: 2017-0800

This module reflects the scientific discussion for the approval of Glamin. The procedure was finalised on 2018-06-25. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Matrix Pharmaceuticals has applied for marketing authorisations for Glamin contain 625 mg glucosamine per capsule.
The active substance is glucosamine hydrochloride (Relief of symptoms of mild to moderate OA of the knee).

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10a of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Glucosamine is a naturally occurring compound in animals and humans where it is included in the synthesis of glycosaminoglycan (GAG) which is a main part of all connective tissue. The pharmacodynamic, pharmacokinetic and toxicological properties of glucosamine are well-known. Since this well-established product has been shown to be essentially similar and refer to a product approved based on a full application with regard to non-clinical data, no further such data have been submitted or are considered necessary.

III.2 Ecotoxicity/environmental risk assessment

Glucosamine hydrochloride is a salt of a natural amino-monosaccharide, glucosamine, which is physiologically present in the human body. A complete Environmental Risk Assessment (ERA) is, therefore, not considered necessary.

III.3 Discussion on the non-clinical aspects

The non-clinical overview has been written by an appropriately qualified person and the overview is considered acceptable. In conclusion, this application is approvable from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Introduction

Glucosamine is an endogenous substance, an essential component of glucosaminoglycans required for the formation of proteoglycans (PGs) found in joint cartilage and other organs. Glucosamine has been widely available as a prescription medicinal product in EU countries for many years (since 1974) to relieve symptoms of mild to moderate osteoarthritis of the knee. Glamin contain 625 mg glucosamine (750 mg glucosamine hydrochloride) per capsule.

IV.2 Pharmacokinetics

The pharmacokinetic documentation for Glucosamine is based mainly on small, published studies. The mean baseline endogenous plasma level is approximately 50-60 ng/mL. The MAH has provided limited, but sufficient data from the literature on the pharmacokinetics of glucosamine. There are no objections to the approval of Glamin from a pharmacokinetic point of view.

IV.3 Pharmacodynamics

The MAH provided data from the literature on the pharmacodynamics of glucosamine. The submitted literature references consisted of in vitro studies where glucosamine was added to chondrocytes isolated from human articular healthy and OA cartilage. The results of the

studies suggest that glucosamine may have some chondroprotective effects.

However, the mechanism of action of glucosamine relevant its clinical use in humans remains unknown.

IV.4 Clinical efficacy

A number of individual studies published in the literature were submitted to support efficacy. Overall, although not all studies were supportive, it is considered that the MAH provided sufficient bibliographic data to support the efficacy of glucosamine for the applied for indication and dosing regimen from a clinical point of view.

IV.5 Clinical safety

Glucosamine has been available as a medicinal product for many years in Europe. The MAH provided literature data to support the safety of the proposed product, including individual studies and meta-analyses.

The overall extent of exposure in the individual clinical efficacy studies was 3014 patients, with durations of exposure between 3 weeks and 3 years. Two hundred and seven of those patients were treated with glucosamine for a duration of at least 2 years. The most common AEs reported in those clinical efficacy studies in which safety information was also recorded, were GI in nature (e.g. epigastralgia, nausea) and have generally been reported to be mild. Overall, the MAH provided sufficient bibliographic data to support the safety of glucosamine for the applied for indication and dosing regimen from a clinical point of view.

IV.6 Risk Management Plans

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, (Version 1.0, DLP 31 May 2016, signed 28 November 2017) describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Glamin 625 mg, hard capsule.

Safety specification

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Important missing information	• None

The MAH's proposal for not including any identified or potential risks in the safety specification of the RMP is endorsed. Some edits and restructuring of the RMP have been made as previously requested.

Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the MAH, which is endorsed.

Risk minimisation measures

Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the MAH, which is endorsed.

Summary of the RMP
The MAH has satisfactory responded to the questions raised and updated the RMP accordingly.

The submitted Risk Management Plan, version 1 signed 16 May 2018 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the MPA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Glukosamin Apofri 625 mg capsule, hard, UK/H/3497/01/DC, and Ranitidin Apofri 150 mg film-coated tablet, Dnr. 111:2012/79828. The bridging report submitted by the MAH has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application for Glamin is submitted according to Article 10a of Directive 2001/83/EC, WEU. The MAH has shown that the active substance of the medicinal product has been in well-established medicinal use for the claimed therapeutic indication within the Union for at least ten years, with recognised efficacy and an acceptable level of safety. The MAH has provided sufficient bibliographic data to support the efficacy and safety of glucosamine for the applied for indication and dosing regimen.

From the bibliographic data submitted, the benefit-risk of Glamin 625 mg in the proposed indication is thus considered to be positive (section VI).

The quality of Glamin is found adequate. There are no objections to approval of Glamin, from a non-clinical and clinical point of view. The product information is acceptable. The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Glamin Capsules, hard; 625 mg, were approved in the national procedure on 2018-06-25.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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