LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Magnesium EQL Pharma
(magnesium hydroxide)

Asp no: 2017-0917

This module reflects the scientific discussion for the approval of Magnesium EQL Pharma. The procedure was finalised on 2018-08-24. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

EQL Pharma has applied for a marketing authorisation for Magnesium EQL Pharma, 250 mg, tablet. The active substance is magnesium hydroxide (Magnesium is the fourth most abundant essential mineral in the body. It is distributed approximately one half in the bone and one half in the muscle and other soft tissues. Magnesium is a cofactor for more than 300 metabolic reactions. Magnesium deficiencies are common in people with poor nutrition or who use certain medicinal products such as diuretics).

For approved indications, see the Summary of Product Characteristics.

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

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 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 Pharmacology

The pharmacology of magnesium hydroxide is well known. The Applicant provided literature based data on the pharmacology of magnesium hydroxide, since this application is based on well-established use of the substance. The non-clinical overview is dated April 11 2017, and 9 literature references up to year 2015 are provided.

III.2 Pharmacokinetics

The pharmacokinetics of magnesium hydroxide is well known. The Applicant provided literature based data on the pharmacokinetics of magnesium hydroxide, since this application is based on well-established use of the substance.

III.3 Toxicology

The toxicology of magnesium hydroxide is well known. The Applicant provided literature based data on the toxicology of magnesium hydroxide, since this application is based on well-established use of the substance. This is considered acceptable.

No separate Assessment report is prepared for the non-clinical module.

III.4 Ecotoxicity/environmental risk assessment

A justification for not submitting an environmental risk assessment has been provided by the Applicant. Since Magnesium EQL Pharma is intended for substitution, this will not lead to an increased exposure of magnesium hydroxide to the environment. Therefore, no additional environmental risks are expected for Magnesium EQL Pharma.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

An application according to Article 10(a), well established use, should be a complete, stand-alone application, meaning that literature data should be provided to cover all aspects of a complete application and support statements in the SmPC. In the response to question, the Applicant submitted an updated Overview which is considered adequate.

The absolute bioavailability of dietary magnesium is stated to be 40%, while the absolute bioavailability of magnesium hydroxide has been shown to be 15%. Other magnesium salts may have different solubility and might have different bioavailability. The Applicant has submitted some literature references with efficacy and safety data for magnesium hydroxide, supporting the use of magnesium hydroxide salt in the sought indications.

The pharmacokinetic documentation is considered sufficient.

IV.2 Pharmacodynamics

Magnesium is the fourth most abundant essential mineral in the body. It is distributed approximately one half in the bone and one half in the muscle and other soft tissues. Magnesium is a cofactor for more than 300 metabolic reactions. Magnesium deficiencies are common in people with poor nutrition or who use certain medicinal products such as diuretics.

The symptoms of magnesium deficiency of different aetiology can be easily treated with oral supplementation therapy. Such products have been marketed for decades in Sweden; also other products that contain magnesium hydroxide.

IV.3 Clinical efficacy and safety

The Clinical overview provided in support of the present application concerning clinical efficacy and clinical safety of magnesium hydroxide is considered adequate. Magnesium hydroxide is from a clinical point of view considered a well-known compound with well-known efficacy and safety profiles.

IV.4 Risk Management Plans

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Magnesium EQL Pharma.

Safety specification
The proposed safety concerns can be seen in the table below.

Summary of safety concerns	
Important identified risks	• Diarrhoea • Renal impairment • Renal stone disease with infection stones • Chronic UTIs • Hypersensitivity to the active substance or to any of the excipients

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

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

Summary of the RMP
The submitted Risk Management Plan, version 0.1 signed 2017-05-12 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

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was Swedish.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Magnesium EQL Pharma, 250 mg, tablet is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 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

Magnesium EQL Pharma, 250 mg, tablet was approved in the national procedure on 2018-08-24.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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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