IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Rennie Dual Action Chewable Tablets Calcium carbonate 625mg Magnesium carbonate 73.5mg Alginic acid 150mg
Alginic acid
Calcium carbonate
Magnesium carbonate
PA1410/052/003

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.

CONTENTS

I. INTRODUCTION

This application for a repeat use, MRP for Rennie Dual Action Chewable Tablets was submitted in accordance with Article 10a of Directive 2001/83/EC as amended, a well-established use application.

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

Name of the product	Rennie Dual Action Chewable Tablets Calcium carbonate 625mg Magnesium carbonate 73.5mg Alginic acid 150mg
Name(s) of the active substance(s) (INN)	Alginic acid, Calcium carbonate, Magnesium carbonate
Pharmacotherapeutic classification (ATC code)	A02AX
Pharmaceutical form and strength(s)	Chewable Tablets Calcium carbonate 625mg Magnesium carbonate 73.5mg Alginic acid 150mg
Marketing Authorisation Number(s) in Ireland (PA)	PA1410/052/003
Marketing Authorisation Holder	Bayer Limited
MRP/DCP No.	IE/H/0588/001/E/001
Reference Member State	IE
Concerned Member State	AT BE CY CZ EL FI HU LU MT PL PT SK NL

II. QUALITY ASPECTS

II.1. Introduction

This application is for Rennie Dual Action Chewable Tablets Calcium carbonate 625mg Magnesium carbonate 73.5mg Alginic acid 150mg.

II.2 Drug substance

The active substance are Calcium carbonate, Magnesium carbonate and Alginic acid 150mg, all established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substances specifications are considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with the specifications have been provided.

II.3 Medicinal product

P.1 Composition

*Each c*hewable tablet contain 625 mg of Calcium carbonate, 73.5 mg of Magnesium carbonate and 150 mg Alginic acid.

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

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 guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary 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 Tablets/chewable 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 have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with Ph. Eur. requirements and EU legislation for use with foodstuffs.

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 and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

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 Rennie Dual Action Chewable Tablets Calcium carbonate 625mg Magnesium carbonate 73.5mg Alginic acid 150mg.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This application for a repeat use, MRP for Rennie Dual Action Chewable Tablets was submitted in accordance with Article 10a of Directive 2001/83/EC as amended, a well-established use application.

III.2 Pharmacology

Calcium carbonate and magnesium carbonate have antacid properties which have been demonstrated in *in vitro* studies.

They react with hydrochloric acid to form sodium chloride or magnesium chloride and carbon dioxide:

$$CaCO_3 + 2HCl \leftrightarrow CaCl_2 + H_2O + CO_2$$
$$MgCO_3 + 2HCl \leftrightarrow MgCl_2 + H_2O + CO_2$$

Thus, they cause rapid and relatively irreversible neutralisation of hydrochloric acid.

Alginic acid is a polyuronic acid mixture [$(C_6H_8O_6)n$] made up of D-mannuronic acid and L-guluronic acid residues. Sodium alginate is the sodium salt of alginic acid.

In vivo, after oral administration, alginates form a viscous gel in the stomach in the presence of acid. After incorporating carbon dioxide, the gel floats on the top of the food bolus, hence the term "raft". It offers partially mechanical relief to gastro-oesophageal reflux.

III.3 Pharmacokinetics

Calcium carbonate
Insoluble calcium carbonate is converted into soluble calcium chloride in the stomach. Ionized calcium is absorbed in the intestine or converted into insoluble salts (carbonate, stearate) and eliminated in the faeces. The absorbed fraction, approximately 15%, is primarily excreted in the urine, as a function of creatinine clearance.

Magnesium carbonate
Insoluble magnesium carbonate is converted into soluble magnesium chloride in the stomach. Approximately 5-10% ionized magnesium is absorbed and then rapidly excreted in urine or converted into insoluble salts (carbonate, stearate) and eliminated in the faeces.

Alginic acid
Due to its structure and rheological properties, very little alginate is absorbed in the gut. Distribution studies in animals have shown that the percentage of alginic acid that is absorbed is extremely low. Thus approximately 99 % of the dose is excreted in 48 h; 97 % in the faeces and 2 % in the urine.

III.4 Toxicology

The vast majority of the safety information on the Rennie® products is based on published data as well as the extensive marketing experience gained over the many decades of commercialization of the products worldwide. The pre-clinical sub-acute toxicity study conducted in rats confirms the well-known safety profile of the product.

Alginic acid is extensively used as a food additive in the food industry. Furthermore, it has been used for many years for the treatment of gastrooesophageal reflux. For this reason, it is not necessary to carry out further toxicological studies.

III.5 Ecotoxicity/environmental risk assessment

Since Rennie Dual Action Chewable Tablets is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Alginic acid, calcium carbonate and magnesium carbonate are well known active substance with established efficacy and tolerability. No new nonclinical data have been supplied with this application and none are required for an application of this type.
The available preclinical data on each of the activities based on conventional studies of repeated dose toxicity, genotoxicity and or carcinogenic potential, and toxicity to reproduction revealed no specific hazard at therapeutic doses for humans.

IV. CLINICAL ASPECTS

IV.1 Introduction

Alginic acid 150mg, calcium carbonate 625mg and heavy magnesium carbonate
73.50mg are well known active substance with established efficacy and tolerability.

The content of the SmPC approved during the MR RUP procedure is in accordance with that accepted in the original procedure.

No new clinical data have been supplied with this application and none are required
for an application of this type.

No new or unexpected safety concerns arise from this application.
The SPC, PIL and labelling are satisfactory and consistent with that for Rennie Duo ® chewable tablets.

V. OVERALL CONCLUSIONS

There is Extensive clinical experience with calcium carbonate, magnesium carbonate and

alginic acid is considered to have demonstrated the therapeutic value of the compounds. The risk benefit is, therefore, considered to be positive.
The Applicant has committed to updates to the product information after the procedure.

VI. REVISION DATE

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