IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

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

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Emazole Control 20mg Gastro-resistant Tablets, from IQ Pharmatek Ltd, Tipperary, Ireland on 18/10/2019 for the following indications:

Adults
Gastro-Oesophageal Reflux Disease (GORD)
-treatment of erosive reflux oesophagitis
-long-term management of patients with healed oesophagitis to prevent relapse
-symptomatic treatment of gastro-oesophageal reflux disease (GORD)

In combination with appropriate antibacterial therapeutic regimens for the eradication of *Helicobacter pylori* and
-healing of *Helicobacter pylori* associated duodenal ulcer and
-prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers.

Patients requiring continued NSAID therapy
-healing of gastric ulcers associated with NSAID therapy
-prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk.

Prolonged treatment after i.v. induced prevention of rebleeding of peptic ulcers

Treatment of Zollinger Ellison Syndrome

Adolescents from the age of 12 years

Gastroesophageal Reflux Disease (GORD)
-treatment of erosive reflux esophagitis
-long-term management of patients with healed esophagitis to prevent relapse
-symptomatic treatment of gastroesophageal reflux disease (GORD)

In combination with antibiotics in treatment of duodenal ulcer caused by *Helicobacter pylori*.

This national application for a marketing authorisation for Emazole Control 20mg Gastro-resistant tablets is a duplicate application of Emazole 20mg gastro-resistant tablets PA0711/158/001 which was submitted to HPRA in accordance with Article 10.1 of Directive 2001/83/EC.

The product is authorised for pharmacy only supply as prescription only medicinal product which may be renewed.

Name of the product	Emazole Control 20mg Gastro-resistant Tablets
Name(s) of the active substance(s) (INN)	ESOMEPRAZOLE MAGNESIUM DIHYDRATE
Pharmacotherapeutic classification (ATC code)	A02BC02 Proton pump inhibitors
Pharmaceutical form and strength(s)	Tablets Gastro-Resistant 20mg
Marketing Authorisation Number(s) in Ireland (PA)	PA0711/355/001
Marketing Authorisation Holder	Rowex Ltd, Newtown, Bantry, Co. Cork, Ireland

II. QUALITY ASPECTS

This application is for Emazole Control 20mg Gastro-resistant Tablets

This national application for a marketing authorisation for Emazole Control 20mg Gastro-resistant tablets is a duplicate application of Emazole 20mg gastro-resistant tablets PA0711/158/001 which was submitted to HPRA in accordance with Article 10.1 of Directive 2001/83/EC

The product is deemed to be manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites. The manufacturing sites of both the drug substance and the drug product have been approved in line with that of the duplicate licence PA0711/158/001.

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 for Emazole Control 20mg Gastro-resistant Tablets.

III. NON-CLINICAL ASPECTS

No new preclinical data have been submitted with this application. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

An Environmental Risk Assessment has not been performed as this product is intended for generic substitution and therefore will not result in an increase of risk to the environment during use, storage and disposal.

IV. CLINICAL ASPECTS

Esomeprazole is a well-known active substance with established efficacy and tolerability.

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The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Nexium 20mg gastro-resistant tablets marketed by MAH Astra Zeneca.

IV.2 Pharmacokinetics
The pharmacokinetics of esomeprazole are well established. No new data has been submitted.

IV.3 Pharmacodynamics
Not applicable. The applicant has not submitted any new pharmacodynamic data in accordance with EC article 10.1 (a) (iii) of directive 2001/83/EEC.

IV.4 Clinical Efficacy
No additional clinical efficacy studies were conducted for this procedure which is acceptable for this application type.

This is a duplicate application of Emazole 20mg gastro-resistant tablets PA0711/158/001 which was submitted to HPRA in accordance with Article 10.1 of Directive 2001/83/EC.
In the original application, the applicant provided 3 bioequivalence studies, one pilot and two pivotal, comparing the Emazole 20mg gastro-resistant tablets product with originator product Nexium MUPS from Astra Zeneca which was used as the European reference product for the generic application for Emazole 20mg gastro-resistant tablets.

The pilot study (2006-48-MDT-1) was performed as a single dose cross-over study under fasting conditions with the 20 mg and was performed at the clinical facility of Algorithme Pharma Inc., Mount-Royal, Quebec, Canada with Eric Sicard, M.D. as clinical investigator. 10 subjects were recruited and completed the study. The pharmacokinetic variables evaluated were standard and were evaluated for esomeprazole. Bioequivalence was determined based on AUC0-t, AUC0-∞ and Cmax as primary variables.

Study 2007-02-MDT-1 was performed under fed (high fat) conditions with the 40 mg tablets. The study was a single dose, two-way, cross-over study performed at the clinical facility of Algorithme Pharma Inc., Mount-Royal, Quebec, Canada with Eric Sicard, M.D. as clinical investigator. 101 subjects participated in the study and 95 completed. The pharmacokinetic variables evaluated were standard and were evaluated for esomeprazole. Bioequivalence was determined based on AUC0-t, AUC0-∞ and Cmax as primary variables.

Study 2007-04-MDT-3 was performed as a single and multiple dose study with the 40 mg tablets. The study was 2-way cross-over and conducted under fasting conditions. A single dose of 1x40mg was administered on the mornings of days 1 to 7 in each period. The last dose of period 1 and the first dose of period 2 were separated by a wash out period of 7 days. The study was performed at MDS Pharma Services, St. Laurent (Montreal), Quebec, Canada with Gaetano Morelli, M.D., and Marika Pasternyl Di Marco, MSc., PhD, MDS as investigators. 104 subjects participated in the study with 94 completing the single dose portion and 92 the multiple dose portion. The pharmacokinetic variables evaluated were standard and were evaluated for

esomeprazole. Bioequivalence was determined based on AUC0-t and Cmax for the single dose portion and on AUCtss and Cmaxss for the steady state phase.

Based on the submitted bioequivalence studies Emazole 20mg gastro-resistant tablets were considered bioequivalent with the European reference medicinal product, Nexium Mups gastro-resistant tablets by Astra Zeneca, under single dose fasting and fed conditions and under multiple dosing.

This application for Emazole Control 20mg gastro-resistant tablets is a duplicate of Emazole 20mg gastro-resistant tablets submitted in accordance with Article 10.1 of Directive 2001/83/EC.

IV.5 Clinical Safety

No new safety findings were noted during the original bioequivalence studies and no additional safety studies were conducted for this procedure which is acceptable for this application type.

Risk Management Plan

The applicant 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 Emazole control 20mg gastro-resistant tablets. The revised RMP (version 1.1 dated final sign off 16/02/2018) is acceptable. Routine risk minimization activities are considered sufficient. The applicant is requested to ensure it maintains the RMP in line with the latest SmPC updates and maintains regular reviews.

Summary table of safety concerns as approved in RMP

Important identified risks	• Agranulocytosis; • Hypersensitivity reactions; • Hypomagnesemia; • Depression; • Hepatic reactions; • SCARs; • Interstitial nephritis; • Fracture of the hip, wrist or spine; • Gastrointestinal infections; • Interaction with warfarin or other coumarin derivatives; • Interaction with phenytoin; • Interaction with atazanavir; • Interaction with nelfinavir; • Interaction with digoxin; • Interaction with methotrexate; • Interaction with tacrolimus; • Interaction with clopidrogel;
Important potential risks	• Convulsion/seizure; • Pneumonia;
Missing information	• Use in pregnant and lactating women; • Use in patients with renal impairment;

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

For this marketing authorisation, reference is made to the clinical studies and experience with the innovator product Nexium 20mg gastro-resistant tablets marketed by MAH Astra Zeneca.
This national application for a marketing authorisation is a duplicate application of Emazole 20mg gastro-resistant tablets PA0711/158/001 which was submitted to HPRA in accordance with Article 10.1 of Directive 2001/83/EC.
The reference product used is Nexium 20mg gastro-resistant tablets, MAH Astra Zeneca.

In this national duplicate application for Emazole Control 20mg Gastro-resistant tablets, no new clinical or non-clinical studies were conducted which is acceptable for this type of application.
The MAH demonstrated through the original bioequivalence studies for Emazole 20mg Gastro-resistant tablets that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product.
Bioequivalence was demonstrated between the Emazole 20mg gastro-resistant tablets test product and the European reference product Nexium Mups gastro-resistant tablets by Astra Zeneca, as outlined above.

The safety and efficacy profiles for the active substance in this medicinal product are well-established over many years.

There were no new or unexpected safety concerns noted during assessment of this procedure.

There is extensive clinical experience with esomeprazole in the treatment of the authorised indications for this product which has demonstrated a positive benefit risk profile in the management of the following indications in adults and adolescents, as follows:

Adults

Gastro-Oesophageal Reflux Disease (GORD)
-treatment of erosive reflux oesophagitis
-long-term management of patients with healed oesophagitis to prevent relapse
-symptomatic treatment of gastro-oesophageal reflux disease (GORD)

In combination with appropriate antibacterial therapeutic regimens for the eradication of *Helicobacter pylori* and
-healing of *Helicobacter pylori* associated duodenal ulcer and
-prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers.

Patients requiring continued NSAID therapy
-healing of gastric ulcers associated with NSAID therapy
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Prolonged treatment after i.v. induced prevention of rebleeding of peptic ulcers

Treatment of Zollinger Ellison Syndrome

Adolescents from the age of 12 years

Gastroesophageal Reflux Disease (GORD)
-treatment of erosive reflux esophagitis
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In combination with antibiotics in treatment of duodenal ulcer caused by *Helicobacter pylori*.

V. OVERALL CONCLUSIONS

Emazole Control 20mg Gastro-resistant tablets are a generic formulation of Nexium 20mg gastro-resistant tablets.

The active substance, esomeprazole, is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

This national application for a marketing authorisation for Emazole Control 20mg Gastro-resistant tablets is a duplicate application of Emazole 20mg gastro-resistant tablets PA0711/158/001 which was submitted to HPRA in accordance with Article 10.1 of Directive 2001/83/EC.

For this marketing authorisation, reference is made to the clinical studies and experience with the innovator product Nexium 20mg gastro-resistant tablets marketed by MAH Astra Zeneca.

Bioequivalence has been demonstrated to the European reference product in the original generic application for Emazole 20mg gastro-resistant tablets PA0711/158/001.

No new non clinical or clinical safety concerns have been identified.

The SmPC for Emazole Control 20mg Gastro-resistant tablets is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted, considered that Emazole Control 20mg Gastro-resistant tablets demonstrated adequate evidence of efficacy for the approved indications, as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

May 2025

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
MA Transfer	CRN00F593	SmPC section 7, 8, 10 Package Leaflet New MA Holder: Rowa Pharmaceuticals Limited New PA number: PA0074/100/001	N/A	31/05/2024
MA Transfer	CRN00G72V	SmPC section 7, 8, 10 Package Leaflet New MA Holder: Rowex Ltd New PA number: PA0711/355/001	N/A	16/05/2025