Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Esomeprazole 20 mg gastro-resistant tablets

(esomeprazole)

Product Licence Number: PL 20416/0635

Crescent Pharma Limited

LAY SUMMARY

Esomeprazole 20 mg gastro-resistant tablets

(esomeprazole)

This is a summary of the Public Assessment Report (PAR) for Esomeprazole 20 mg gastro-resistant tablets. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Esomeprazole Tablets in this lay summary for ease of reading.

For practical information about using Esomeprazole Tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Esomeprazole Tablets and what are they used for?
This application is the same as Esomeprazole 20 mg Gastro-resistant tablets (PL 20416/0487), which is already authorised.

The Company responsible for Esomeprazole 20 mg Gastro-resistant tablets has agreed that its scientific data can be used as the basis for the grant of an identical licence for Esomeprazole Tablets.

Esomeprazole tablets are used to treat the following conditions:

Adults

- 'Gastroesophageal reflux disease' (GERD). This is where acid from the stomach escapes into the gullet (the tube which connects the throat to the stomach) causing pain, inflammation and heartburn.
- Ulcers in the stomach or upper part of the gut (intestine) that are infected with bacteria called '*Helicobacter pylori*'. If patients have this condition, a doctor may also prescribe antibiotics to treat the infection and allow the ulcer to heal.
- Stomach ulcers caused by medicines called NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). Esomeprazole gastro-resistant tablets can also be used to stop stomach ulcers from forming if patients are taking NSAIDs.
- Too much acid in the stomach caused by a growth in the pancreas (Zollinger-Ellison syndrome).
- Prolonged treatment after prevention of rebleeding of ulcers with intravenous esomeprazole.

Adolescents aged 12 years and above

- 'Gastroesophageal reflux disease' (GERD). This is where acid from the stomach escapes into the gullet (the tube which connects the throat to the stomach) causing pain, inflammation and heartburn.
- Ulcers in the stomach or upper part of the gut (intestine) that are infected with bacteria called 'Helicobacter pylori'. If patients have this condition, a doctor may also prescribe antibiotics to treat the infection and allow the ulcer to heal.

How do Esomeprazole Tablets work?
Esomeprazole Tablets contain the active ingredient esomeprazole. Esomeprazole tablets contain a medicine called esomeprazole. This belongs to a group of medicines called 'proton pump inhibitors'. This medicine works by reducing the amount of acid that the stomach produces.

How are Esomeprazole Tablets used?
The pharmaceutical form of this medicine is a tablet and the route of administration is oral (by mouth). The tablets should be swallowed whole with a drink of water. The tablets can be taken at any time of the day and should not be chewed or crushed. This is because the tablets contain coated pellets which stop the medicine from being broken down by the acid in the stomach. It is important not to damage the pellets.

Patients who have trouble swallowing the tablets should:
- Put them into a glass of still (non-fizzy) water. They should not use any other liquids.
- Stir until the tablets break up (the mixture will not be clear). Then drink the mixture straight away or within 30 minutes. Always stir the mixture just before drinking it.
- To make sure that patients have drunk all of the medicine, rinse the glass very well with half a glass of water and drink it. The solid pieces contain the medicine, patients should not chew or crush them.

If patients cannot swallow at all, the tablet can be mixed with some water and put into a syringe. It can then be given to patients through a tube directly into the stomach ('gastric tube').

Patients should always take this medicine exactly as a doctor or pharmacist has told them. Check with a doctor or pharmacist if patients are not sure.

If patients are taking this medicine for a long time, a doctor will want to monitor them (particularly if patients are taking it for more than a year).

If a doctor has told them to take this medicine as and when they need it, tell a doctor if the symptoms change.

How much to take
- A doctor will tell patients how many tablets to take and how long to take them for. This will depend on patient's condition, how old they are and how well their liver works.

- The recommended doses are given below.

Adults aged 18 and above
To treat heartburn caused by gastroesophageal reflux disease (GERD):
If a doctor has found that the food pipe (gullet) has been slightly damaged, the recommended dose is one Esomeprazole 40 mg gastro-resistant tablet once a day for 4 weeks. A doctor may tell patients to take the same dose for a further 4 weeks if the gullet has not yet healed.

The recommended dose once the gullet has healed is one Esomeprazole 20 mg gastro-resistant tablet once a day.
If the gullet has not been damaged, the recommended dose is one Esomeprazole 20 mg gastro-resistant tablet each day. Once the condition has been controlled, a doctor may tell them to take the medicine as and when they need it, up to a maximum of one Esomeprazole 20 mg gastro-resistant tablet each day.

If patients have severe liver problems, a doctor may give them a lower dose.

To treat ulcers caused by Helicobacter pylori infection and to stop them coming back:
The recommended dose is one Esomeprazole 20 mg gastro-resistant tablet twice a day for one week.
A doctor will also tell patients to take antibiotics for example amoxicillin and clarithromycin.

To treat stomach ulcers caused by NSAIDs (Non-Steroidal Anti-Inflammatory Drugs):
The recommended dose is one Esomeprazole 20 mg gastro-resistant tablet once a day for 4 to 8 weeks.

To prevent stomach ulcers if patients are taking NSAIDs (Non-Steroidal Anti-Inflammatory Drugs):
The recommended dose is one Esomeprazole 20 mg gastro-resistant tablet once a day.

To treat too much acid in the stomach caused by a growth in the pancreas (Zollinger-Ellison syndrome):
The recommended dose is one esomeprazole 40 mg gastro-resistant tablet twice a day.

A doctor will adjust the dose depending on the needs and will also decide how long they need to take the medicine for. The maximum dose is 80 mg twice a day.

Prolonged treatment after prevention of rebleeding of ulcers with intravenous esomeprazole:
The recommended dose is one esomeprazole 40 mg gastro-resistant tablet once a day for 4 weeks.

Adolescents aged 12 or above
To treat heartburn caused by gastroesophageal reflux disease (GERD):

If a doctor has found that the food pipe (gullet) has been slightly damaged, the recommended dose is one esomeprazole 40 mg gastro-resistant tablet once a day for 4 weeks. A doctor may tell you to take the same dose for a further 4 weeks if the gullet has not yet healed.

The recommended dose once the gullet has healed is one Esomeprazole 20 mg gastro-resistant tablet once a day.

If the gullet has not been damaged, the recommended dose is one Esomeprazole 20 mg gastro-resistant tablet each day.

If patients have severe liver problems, a doctor may give them a lower dose.

To treat ulcers caused by *Helicobacter pylori* infection and to stop them coming back:

The recommended dose is one Esomeprazole 20 mg gastro-resistant tablet twice a day for one week.

A doctor will also tell them to take antibiotics for example amoxicillin and clarithromycin.

Children under the age of 12 years
Esomeprazole gastro-resistant tablets are not recommended for children less than 12 years old.

Older people
Dose adjustment is not required in the elderly.

For further information on how Esomeprazole Tablets are used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Esomeprazole Tablets have been shown in studies?
Esomeprazole Tablets are considered identical to the previously authorised product with the same benefits and risks. No new studies have been provided for Esomeprazole Tablets, however, reference is made to the data for Esomeprazole 20 mg Gastro-resistant tablets.

What are the possible side effects of Esomeprazole Tablets?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Esomeprazole Tablets are considered to be identical to the previously authorised product with the same benefits and risks.

Why was Esomeprazole Tablets approved?
The MHRA decided that the benefits of Esomeprazole Tablets are greater than the risks and recommended that this medicine is approved for use.

What measures are being taken to ensure the safe and effective use of Esomeprazole Tablets?
A Risk Management Plan (RMP) has been developed to ensure that Esomeprazole Tablets is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Esomeprazole Tablets
A Marketing Authorisation was granted in the United Kingdom on 03 August 2021.

The full PAR for Esomeprazole Tablets follows this summary.

This summary was last updated in October 2021.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Esomeprazole 20 mg gastro-resistant tablets (PL 20416/0635) could be approved.

The product is approved for the following indications:
Esomeprazole gastro-resistant tablets are indicated in adults for:

Gastroesophageal Reflux Disease (GERD)

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

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 intravenous (i.v). induced prevention of rebleeding of peptic ulcers.

Treatment of Zollinger Ellison Syndrome

Esomeprazole gastro-resistant tablets are indicated in adolescents from the age of 12 years for:

Gastroesophageal Reflux Disease (GERD)

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

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

Esomeprazole is the S-isomer of omeprazole and reduces gastric acid secretion through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Both the R- and S-isomer of omeprazole have similar pharmacodynamic activity.

Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme H^+K^+-ATPase – the acid pump and inhibits both basal and stimulated acid secretion.

This is a national application approved under Regulation 56 of The Human Medicines Regulations 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as an informed consent application. The application cross-refers to the reference product

Esomeprazole 20 mg Gastro-resistant tablets (PL 20416/0487), authorised to Crescent Pharma Limited on 22 June 2018.

No new non-clinical or clinical data have been supplied and none are required for this informed consent application.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the application is for an identical version of an already authorised product, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A national marketing authorisation was granted in the United Kingdom on 03 August 2021.

II. EXPERT REPORT

The applicant cross-refers to the data for Esomeprazole 20 mg Gastro-resistant tablets (PL 20416/0487; Crescent Pharma Limited), to which this application is claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with that for Esomeprazole 20 mg Gastro-resistant tablets (PL 20416/0487), dated 22 June 2018.

PATIENT INFORMATION LEAFLET (PIL)

A leaflet mock-up has been provided which has been aligned with that for Esomeprazole 20 mg Gastro-resistant tablets (PL 20416/0487), dated May 2018. The user test report submitted for DK/H/1725/001-002/DC has been provided.

LABEL

Label mock-ups have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specification

The source of the active substance is in line with the cross-reference product. The proposed drug substance specification is consistent with the details registered for the cross-reference product.

IV.2. Drug Product

Name

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Esomeprazole 20 mg Gastro-resistant tablets are available in polyethylene bottle with a tamper proof, polypropylene stock ribbed closure equipped with a desiccant canister, with a

pack size of 28 tablets. The product is also available in aluminium/aluminium blister package with cartons of 28 tablets.
The appearance of the product is identical to that of the cross-reference product.

The proposed shelf-life of the product is 2 years with a special storage condition 'Store below 25°C'. The medicine should be kept in the original packaged and the bottle tightly closed to protect from moisture.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

Legal status
Prescription only medicine (POM).

Manufacturers
The proposed manufacturing site are consistent with the details registered for the cross-reference product and evidence of GMP compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed product is consistent with the details registered for the cross-reference product.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference product and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference product.

TSE Compliance
The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. Confirmation has also been given that the magnesium oxide used in the tablets is of vegetable origin.

This product does not contain or consist of genetically modified organisms (GMO).

V. NON-CLINICAL ASPECTS

As this application is submitted under Regulation 56 of The Human Medicines Regulations 2012, as amended, (as an informed consent application) no new non-clinical data have been supplied and none are required.

VI. CLINICAL ASPECTS

As this application is submitted under Regulation 56 of The Human Medicines Regulations 2012, as amended, (as an informed consent application) no new clinical data have been supplied and none are required.

VII. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulations 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VIII. USER CONSULTATION

A full colour mock-up of the PIL has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Esomeprazole 20 mg gastro-resistant Tablets (DK/H/1725/001-02/DC). The bridging report submitted by the applicant is acceptable.

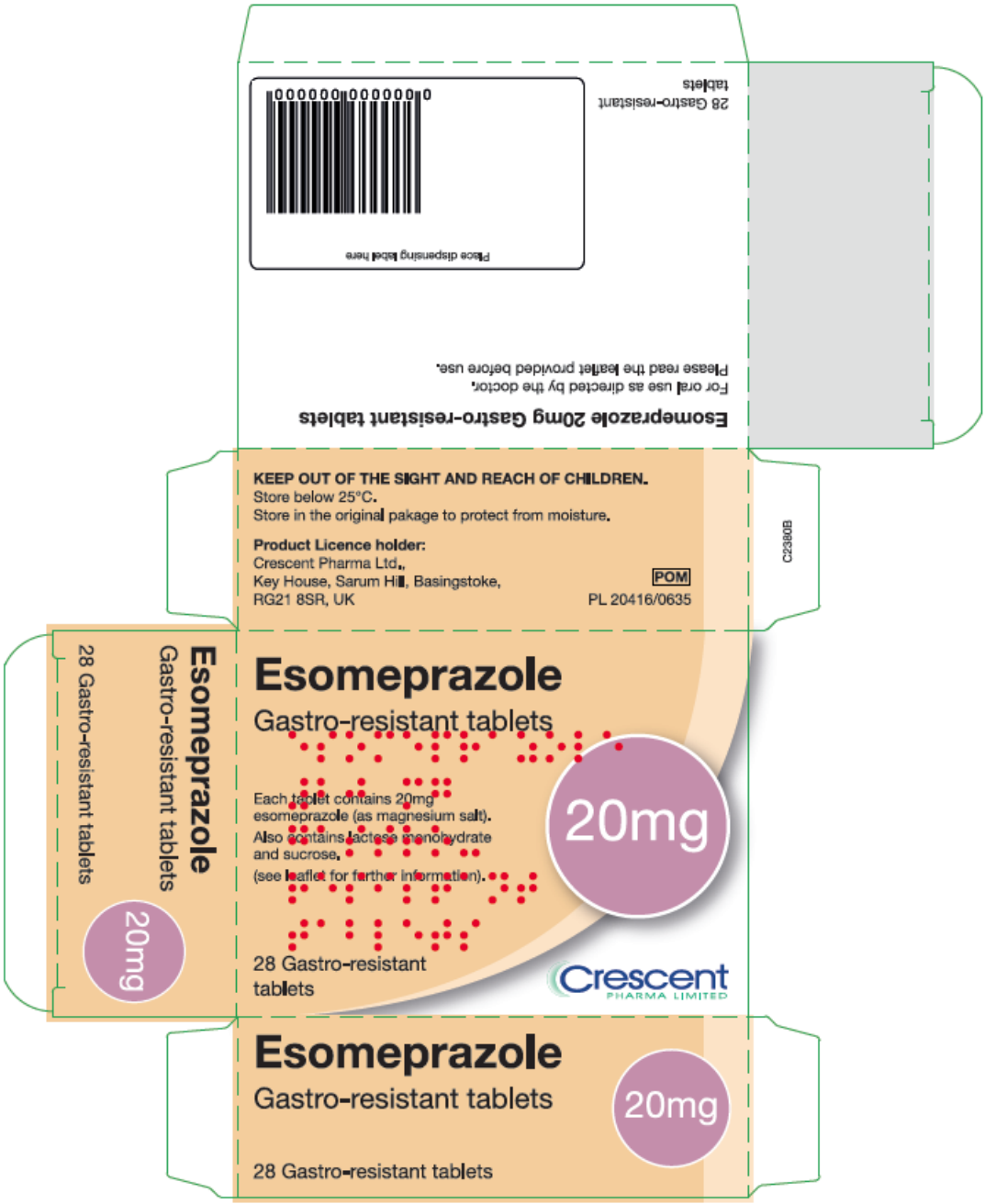
IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference product and positive.

The SmPC, PIL and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of licensing are provided below.


Esomeprazole 20mg Gastro-resistant tablets
For oral use as directed by the doctor.
Please read the leaflet provided before use.
28 Gastro-resistant tablets
Please dispensing label here
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.
Store below 25°C.
Store in the original pakage to protect from moisture.
Product Licence holder:
Crescent Pharma Ltd.,
Key House, Sarum Hill, Basingstoke,
RG21 8SR, UK
POM
PL 20416/0635
C2380B
Esomeprazole
Gastro-resistant tablets
20mg
28 Gastro-resistant tablets
Each tablet contains 20mg esomeprazole (as magnesium salt).
Also contains lactose monohydrate and sucrose.
(see leaflet for further information).
28 Gastro-resistant tablets
Crescent PHARMA LIMITED
Esomeprazole
Gastro-resistant tablets
20mg
28 Gastro-resistant tablets


Crescent Pharma Ltd
ESOMEPRAZOLE 20mg Gastro-resistant tablets
Crescent Pharma Ltd
ESOMEPRAZOLE 20mg Gastro-resistant tablets

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**