Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Ryeqo 40 mg/1 mg/0.5 mg film-coated tablets

(relugolix, estradiol and norethisterone acetate)

PLGB 04854/0186

Gedeon Richter Plc.

LAY SUMMARY

Ryeqo 40 mg/1 mg/0.5 mg film-coated tablets (relugolix, estradiol and norethisterone acetate)

This is a summary of the Public Assessment Report (PAR) for Ryeqo 40 mg/1 mg/0.5 mg film-coated 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 Ryeqo in this lay summary for ease of reading.

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

What is Ryeqo and what is it used for?

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 16 July 2021 (EMEA/H/C/005267/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Ryeqo is used to treat moderate to severe symptoms of uterine fibroids (commonly known as myomas), which are non-cancerous tumours of the uterus (womb). Ryeqo is used in adult women (over 18 years of age) before they reach menopause.

In some women, uterine fibroids may cause heavy menstrual bleeding (a woman's 'period') and pelvic pain (pain below the belly button). It is used for the treatment of fibroids to stop or reduce bleeding and to decrease pain and pelvic discomfort associated with uterine fibroids.

This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine are suitable for treating the specified indications.

How does Ryeqo work?

Ryeqo contains the active substances relugolix, estradiol and norethisterone acetate.

This medicine contains relugolix, which blocks certain receptors in the brain and this reduces the production of hormones that in turn stimulate the ovaries to produce estradiol and progesterone. When blocked, the levels of estrogen and progesterone circulating in the body are reduced. This medicine also contains two types of female hormones, estradiol which belongs to a group of medicines called estrogens and norethisterone which belongs to a group of medicines called progestogens. The inclusion of these hormones in Ryeqo maintains a hormonal state similar to the beginning of the menstrual cycle and thus relieves symptoms while helping to protect the strength of the bones.

How is Ryeqo used?

The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (via the mouth).

The recommended dose is one tablet per day.

The tablet must be taken orally every day, at about the same time, with or without food with a little liquid. It is recommended that the woman starts taking Ryeqo within the first 5 days after the start of bleeding due to their period. If they start at another time of their menstrual cycle, they may initially experience irregular or heavier bleeding.

For further information on how Ryeqo is 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 the 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 Ryeqo have been shown in studies?
Ryeqo has been shown to be effective in treating symptoms linked to uterine fibroids in two studies involving pre-menopausal women aged 18 to 50 with heavy menstrual bleeding. In both studies, around 500 women received either Ryeqo or placebo (a dummy treatment) for 24 weeks.

In the first study, 73% (94 out of 128) of women using Ryeqo reported monthly menstrual blood loss of fewer than 80 mL and at least 50% less blood loss than before the treatment, compared with 19% (24 out of 128) of those taking placebo. In the second study, 71% (89 out of 126) achieved this reduction in the volume of blood lost while using Ryeqo, compared with 15% (19 out of 129) of those given the placebo.

What are the possible side effects of Ryeqo?
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 or search for ‘MHRA Yellow Card’ online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was Ryeqo approved?
Symptoms linked to uterine fibroids can be serious and debilitating. Ryeqo was shown to be effective at reducing moderate to severe symptoms of uterine fibroids, such as heavy periods, with manageable side effects. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Ryeqo?
A Risk Management Plan (RMP) has been developed to ensure that Ryeqo 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 Ryeqo

A marketing authorisation was granted in Great Britain on 09 August 2021.

The full PAR for Ryeqo follows this summary.

This summary was last updated in October 2021.

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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 Ryeqo 40 mg/1 mg/0.5 mg film-coated tablets (PLGB 04854/0186) could be approved.

Ryeqo 40 mg/1 mg/0.5 mg film-coated tablets are indicated for treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

Relugolix is a non-peptide GnRH receptor antagonist that binds to and inhibits GnRH receptors in the anterior pituitary gland. In humans, inhibition of GnRH receptor results in a dose dependent decrease in the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary gland. As a result, circulating concentrations of LH and FSH are reduced. The reduction in FSH concentrations prevents follicular growth and development, thereby reducing the production of estrogen. Prevention of an LH surge inhibits ovulation and development of the corpus luteum, which precludes the production of progesterone. Therefore, Ryeqo provides adequate contraception when taken for at least 1 month (see section 4.2 of the SmPC).

Estradiol is the same as the endogenously produced hormone and is a potent agonist of the nuclear estrogen receptor (ER) subtypes. Exogenously administered estradiol alleviates symptoms associated with a hypoestrogenic state, such as vasomotor symptoms and bone mineral density loss.

Norethisterone acetate is a synthetic progestogen. As estrogens promote the growth of the endometrium, unopposed estrogens increase the risk of endometrial hyperplasia and cancer. The addition of a progestogen reduces the estrogen-induced risk of endometrial hyperplasia in non-hysterectomised women.

This product have been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 16 July 2021 (EMEA/H/C/005267/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of The Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended), a full-dossier application.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a full product specific waiver P/0108/2019.

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 Marketing Authorisation was granted on 09 August 2021.

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

V. CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional risks and safety measures have been proposed:

Study Status	Summary of objectives	Safety concerns addressed	Milestones	Due dates
Category 1 - Imposed mandatory additional pharmacovigilance activities which are conditions of the marketing authorisation *(key to benefit risk)*				
None				

Study Status	Summary of objectives	Safety concerns addressed	Milestones	Due dates
Category 2 – Imposed mandatory additional pharmacovigilance activities which are Specific Obligations in the context of a conditional marketing authorisation or a marketing authorisation under exceptional circumstances *(key to benefit risk)*				
None				
Category 3 - Required additional pharmacovigilance activities *(by the competent authority)*				
MVT-601-035: An international Phase III double-blind, placebo-controlled, randomised withdrawal study of relugolix co-administered with E2+NETA in women with heavy menstrual bleeding associated with uterine fibroids *Ongoing*	To evaluate the efficacy and safety of long-term use of relugolix	Loss of BMD Long-term use beyond 12 months	Final study report	Q4 2021

This is acceptable.

VII. USER CONSULTATION

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

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL 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.

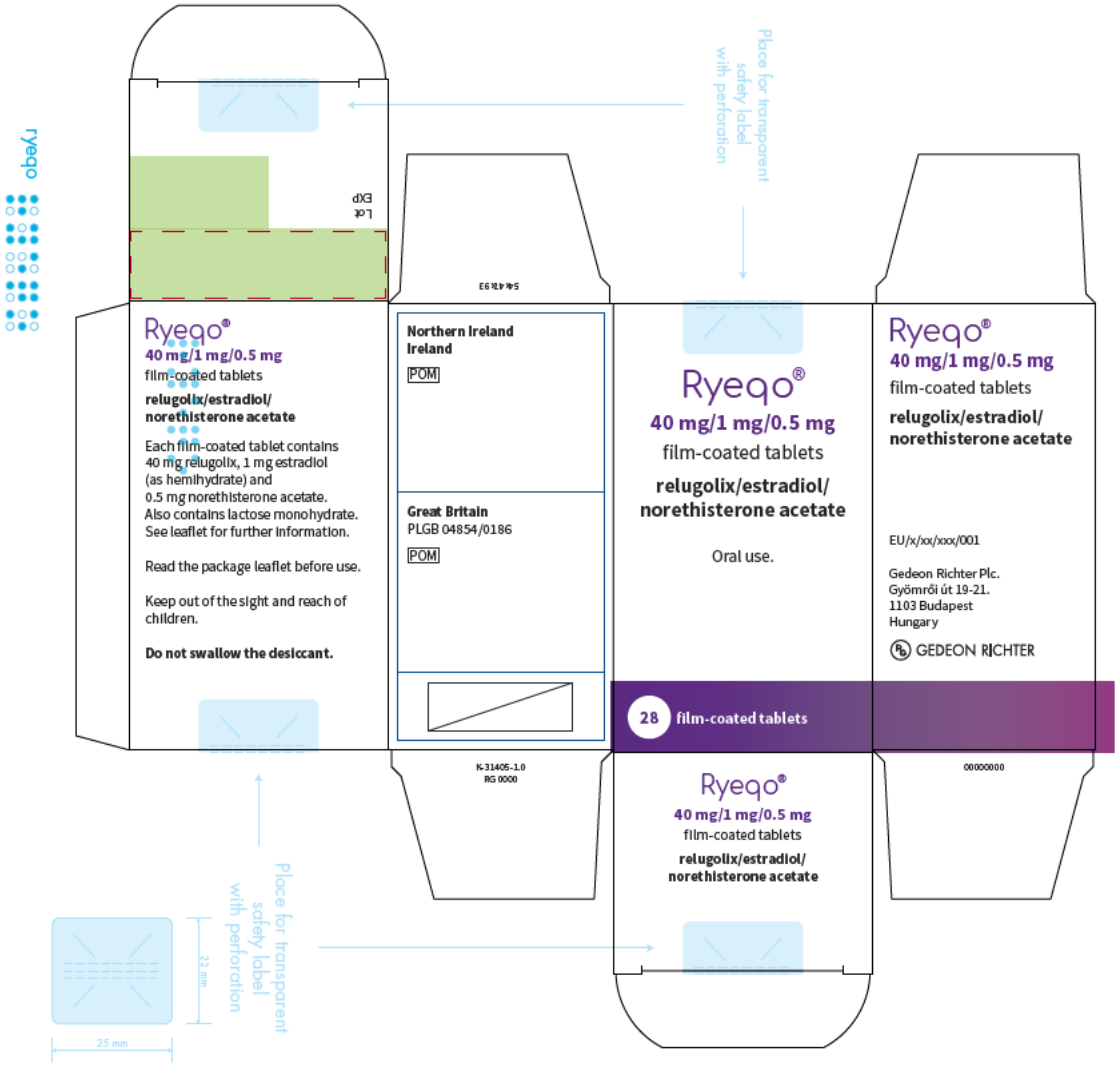
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

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

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


ryeqo
Lot
EXP
Place for transparent safety label with perforation
Ryeqo®
40 mg/1 mg/0.5 mg
film-coated tablets
relugolix/estradiol/
norethisterone acetate
Each film-coated tablet contains
40 mg relugolix, 1 mg estradiol
(as hemihydrate) and
0.5 mg norethisterone acetate.
Also contains lactose monohydrate.
See leaflet for further information.
Read the package leaflet before use.
Keep out of the sight and reach of children.
Do not swallow the desiccant.
Northern Ireland
Ireland
POM
Great Britain
PLGB 04854/0186
POM
K-31405-1.0
RG 0000
Ryeqo®
40 mg/1 mg/0.5 mg
film-coated tablets
relugolix/estradiol/
norethisterone acetate
Oral use.
28 film-coated tablets
Ryeqo®
40 mg/1 mg/0.5 mg
film-coated tablets
relugolix/estradiol/
norethisterone acetate
Ryeqo®
40 mg/1 mg/0.5 mg
film-coated tablets
relugolix/estradiol/
norethisterone acetate
EU/x/xx/xxx/001
Gedeon Richter Plc.
Gyömrői út 19-21.
1103 Budapest
Hungary
GEDEON RICHTER
00000000
Place for transparent safety label with perforation
22 mm
25 mm

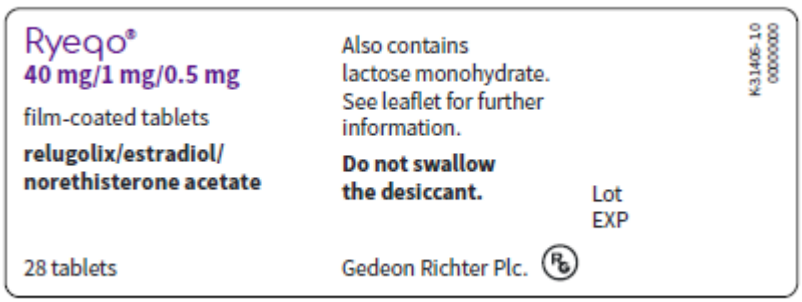

Ryeqo®
40 mg/1 mg/0.5 mg
film-coated tablets
relugolix/estradiol/
norethisterone acetate
28 tablets
Also contains
lactose monohydrate.
See leaflet for further
information.
Do not swallow
the desiccant.
Lot
EXP
Gedeon Richter Plc.
K-31405-1.0
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TABLE 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 SmPCs and/or PIL available on the MHRA website.

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