GEDEON RICHTER

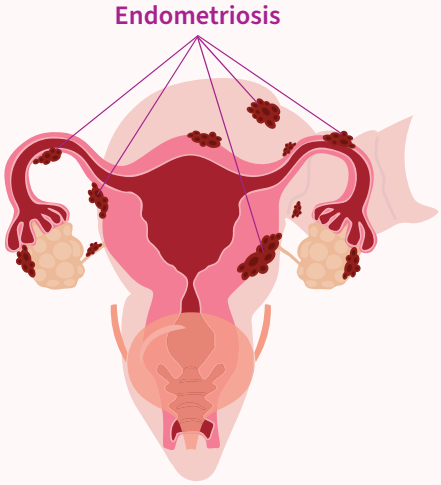
RYEQO® CONSULTATION GUIDE

SUPPORTING CONVERSATIONS WITH YOUR PATIENT ABOUT THEIR ENDOMETRIOSIS TREATMENT

Ryeqo®
relugolix, estradiol, and norethisterone acetate

WHAT IS ENDOMETRIOSIS?

Endometriosis is a condition in which **tissue** similar to the lining of the uterus **grows outside the uterus.** A hormone called **estrogen** contributes to the growth of these tissues. As the level of estrogen varies throughout the body's natural menstrual cycle, this causes the tissues to grow.[1]



SYMPTOMS[1,2]

Symptoms of endometriosis vary among women; some women don't experience any symptoms.

However, **many women** with endometriosis experience severe pain in the pelvis:

- During a period
- Between periods
- During or after sex
- When urinating or defecating between periods

Some women also experience:

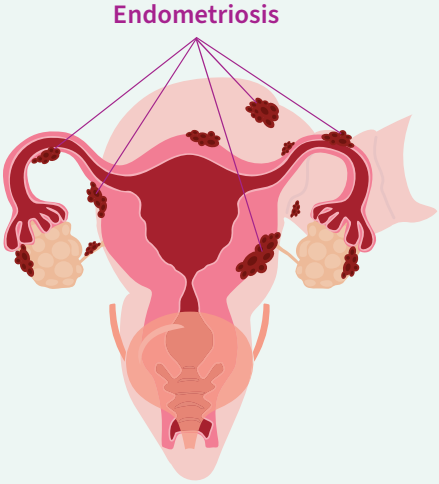
- Chronic pelvic pain
- Difficulty getting pregnant
- Heavy bleeding during periods or between periods
- Bloating or nausea
- Fatigue
- Depression or anxiety

Symptoms often improve after menopause, but not always.

References: 1. Zondervan KT, *et al. N Engl J Med*. 2020;382:1244–56. **2.** Tomassetti C, *et al. Hum Reprod Open.* 2021(4):1–10.

WHAT IS ENDOMETRIOSIS?

Endometriosis is an **estrogen-driven disease** characterised by the presence of endometrium-like epithelium and/or stroma **outside the endometrium** and **myometrium,** usually with an associated inflammatory process.[1,2]



SYMPTOMS[1,2]

Pain

- Severe dysmenorrhoea
- Recurring or persistent pelvic pain (menstrual and non-menstrual)
- Deep dyspareunia
- Ovulation pain
- Pain during internal examination
- Back or leg pain

Bowel and bladder symptoms

- Cyclic bladder or bowel symptoms
- Pain before or after opening bowels
- Pain before, during or after urination
- Bleeding from the bowel
- Blood in the urine
- Constipation, diarrhoea or colic

Bleeding

- Heavy, irregular, extended or post-coital bleeding with or without clots
- Dark or old blood being passed before or at the end of menses

Other symptoms

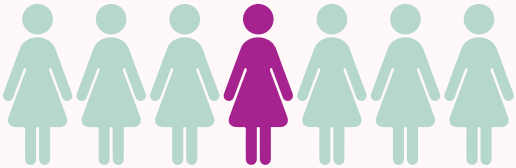
- Chronic fatigue, weariness, bloating or pain not during periods or ovulation
- Infertility
- Fainting during periods or feeling faint
- Nausea
- Depression

References: 1. Zondervan KT, *et al. N Engl J Med*. 2020;382:1244–56. **2.** Tomassetti C, *et al. Hum Reprod Open.* 2021(4):1–10.

ENDOMETRIOSIS KEY FACTS

HOW COMMON IS ENDOMETRIOSIS?

You are not alone.



In Australia, **1** in **7** women and those assigned female at birth are estimated to have endometriosis.[1]*

ENDOMETRIOSIS AND INFERTILITY[2]

There are many reasons why a couple may struggle to conceive a child, and **sometimes** endometriosis may be responsible. Studies estimate that between 30–50% of women with endometriosis experience infertility.[3]

In a minority of cases, scar tissue caused by the endometriosis can block the fallopian tubes. However, in most women it is **not clear why** endometriosis affects their fertility.[2,3]

Even so, many women with endometriosis **can still conceive** and **carry a pregnancy** to term.[2,3]

*Based on those diagnosed with the condition by age 44–49.

References: 1. Australian Institute of Health and Welfare (2023) Endometriosis, AIHW, Australian Government, accessed May 2024. **2.** Macer ML, *et al. Obstet Gynecol Clin North Am.* 2012;39(4):535–49. **3.** Bulletti C. *et al., J Assist Reprod Genet.* 2010;27(8):441–7.

ENDOMETRIOSIS FACTSHEET

PREVALENCE

Endometriosis impacts:

1 in 7 women
and those assigned female at birth in Australia.[1*]

Up to **75%** of women
with moderate to severe pelvic pain.[2]

BURDEN

Endometriosis is associated with a significant **disease burden** in Australia. Endometriosis was:

- Responsible for **8,213 years** of healthy life lost in 2023.[3]
- The **third leading cause** of non-fatal disease burden among females due to reproductive and maternal conditions.[3]
- Associated with **40,500 hospitalisations** in 2021–2022.[1]
- Associated with **poor mental health,** severe depression levels and moderate anxiety and stress levels.[4]

The estimated economic burden of endometriosis in Australia is:[1,5†]

PER PERSON	
Health cost	**$3,900**
Productivity cost	**$25,800**
Carer cost	**$1,100**
Total cost	**$30,900**

*Based on those diagnosed with the condition by age 44–49. †Estimates based on data from 2017.

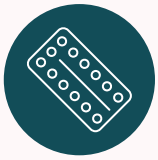
References: 1. Australian Institute of Health and Welfare (2023) Endometriosis, AIHW, Australian Government, accessed May 2024. **2.** Buck Louis GM, *et al. Fertil Steril.* 2011;96:360–65. **3.** Australian Institute of Health and Welfare, Australian Burden of Disease Study 2023, AIHW website, accessed May 2024. **4.** Rush G, *et al.* Monash University Behavioural Sciences Lab, 2018. **5.** Armour M, *et al. PLoS One.* 2019;10;14(10).

CURRENT TREATMENT OPTIONS

Traditionally treatment options for women with endometriosis have been limited, and no **new treatments** have been approved in Australia for **13 years.**[1-3] This means that patients have had to rely on:

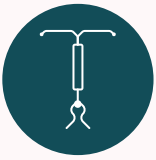
TREATMENTS OPTIONS[4]

ANALGESICS
Pain relievers



ORAL CONTRACEPTIVES
Birth control pills

PROGESTOGENS
Synthetic hormones similar to those used in birth control



HORMONAL IUDS
Devices inserted into the uterus which release a hormone to prevent pregnancy

GNRH AGONISTS
Hormone injections or nasal sprays

SURGERY
Surgical removal of tissue

Ryeqo has now been introduced to treat the symptoms of endometriosis.[5]

GnRH, gonadotropin-releasing hormone; IUD, intrauterine device.

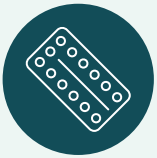
References: 1. Ellis K *et al. Front Glob Womens Health.* 2022;3:902371. **2.** Donnez J *et al. J Clin Med.* 2021;10:1085. **3.** First treatment for endometriosis* in 13 years in Australia approved by TGA (2024), Media Release, Gedeon Richter. **4.** Endometriosis. RANZCOG 2021. Available at: https://ranzcog.edu.au/wp-content/uploads/2022/06/Endometriosis_pamphlet.pdf, accessed May 2024. **5.** Ryeqo Approved Product Information. January 2024.

CURRENT TREATMENT OPTIONS

There have been no new treatment options for endometriosis approved in Australia for **13 years.**[1-3] Women need effective, long-term symptom control they can live with.[1,2]

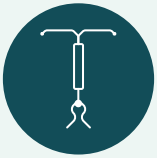
TREATMENTS OPTIONS[4]

ANALGESICS



ORAL CONTRACEPTIVES

PROGESTOGENS



HORMONAL IUDS

GNRH AGONISTS

SURGERY

Ryeqo, a GnRH antagonist with add-back therapy has now been introduced for the symptomatic treatment of endometriosis.[5]

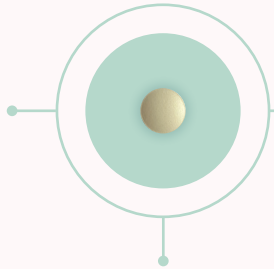
GnRH, gonadotropin-releasing hormone; IUD, intrauterine device.

References: 1. Ellis K *et al. Front Glob Womens Health*. 2022;3:902371. **2.** Donnez J *et al. J Clin Med.* 2021;10:1085. **3.** First treatment for endometriosis* in 13 years in Australia approved by TGA (2024), Media Release, Gedeon Richter. **4.** Australian clinical practice guideline for the diagnosis and management of endometriosis (2021). RANZCOG, Australia. **5.** Ryeqo Approved Product Information. January 2024.

WHAT IS RYEQO?

Ryeqo is a treatment for women who have already had other medical or surgical treatment for their endometriosis, this could include analgesics such as ibuprofen or paracetamol or hormonal treatments such as the oral contraceptive pill.[1]

Ryeqo contains relugolix, and the hormones, estradiol and norethisterone acetate. These active substances help **balance** the level of certain hormones in your body to help **reduce the symptoms** of endometriosis.[1]



RELUGOLIX

Reduces hormones such as estrogen, which reduces endometriosis pain.[1,2]

NORETHISTERONE ACETATE

May protect the uterus from the effect of estrogen alone.[1]

ESTRADIOL

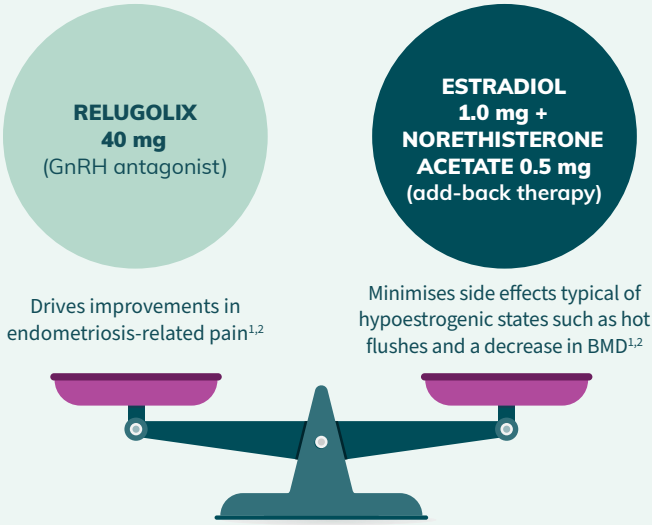
An estrogen to support hormonal balance.[1]

This means you can get relief from the pain of your endometriosis, while still benefiting from the positive impact of balanced hormones, such as on the health of your bones. At the same time this can also minimise any potential side effects, for example hot flushes.[1,2]

References: 1. Ryeqo Approved Product Information. January 2024. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279.

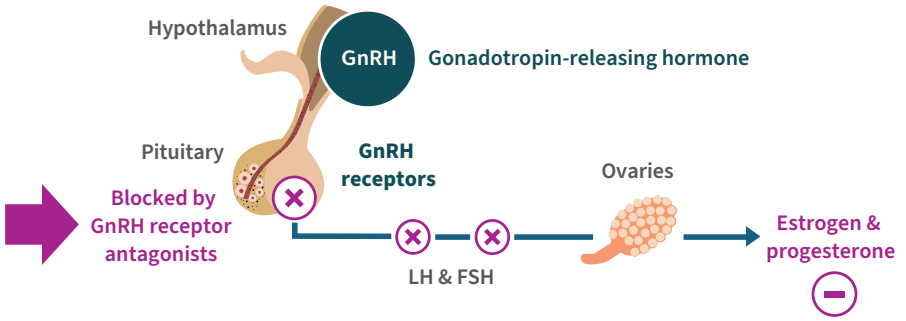
WHAT IS RYEQO?

Ryeqo is the **first and only oral GnRH receptor antagonist** combination therapy in Australia; representing a new class of treatments for endometriosis.[1] Ryeqo has been carefully designed to **delicately balance efficacy and safety.**[1,2]



MECHANISM OF ACTION

Unlike the GnRH agonists, GnRH antagonists are **administered orally** and **do not induce** an initial stimulation of gonadotropin release. Instead, they cause an **immediate and rapid, reversible suppression** of gonadotropin secretion, which results in **a reduction of estradiol.**[3]



BMD, bone mineral density; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinising hormone.

References: 1. Ryeqo Approved Product Information. January 2024. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279. **3.** Huirne JA, Lambalk CB. *Lancet.* 2001;358:1793–803.

RYEQO INFORMATION

RYEQO IN CLINICAL TRIALS

Ryeqo has been assessed via clinical trials which have evaluated the **long-term impact of Ryeqo** for patients with endometriosis.[1,2]

WILL RYEQO CURE MY ENDOMETRIOSIS?

There is currently **no cure for endometriosis,** but there are a number of treatments available to manage the symptoms of endometriosis.[1,3] Ryeqo is a non-surgical option that helps reduce the impact symptoms have on your life by offering **effective relief from your pain.**[4]

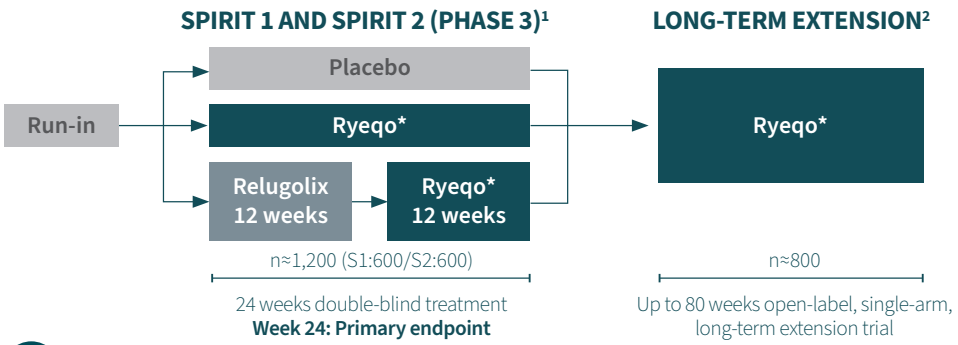
It has been shown that treatment with Ryeqo leads to substantial and sustained improvements in the **quality of life** for women with endometriosis. This is achieved by Ryeqo **reducing their symptoms** and the distress they cause.[1,2]

References: 1. Giudice LC *et al. Lancet.* 2022;399:2267–2279. **2.** Becker CM *et al. Human Reproduction.* 2024;39(3):526–537. **3.** Office on Women's Health in the U.S. Department of Health and Human Services. 2021. Endometriosis. Accessed May 2024. Available from: https://www.womenshealth.gov/a-z-topics/endometriosis. **4.** Ryeqo Approved Product Information. January 2024.

RYEQO CLINICAL STUDIES[1,2]

Ryeqo has been assessed across two replicate clinical trials and a long-term extension study.[1,2]

STUDY DESIGN



Objective: To evaluate the efficacy and safety of Ryeqo* once daily in women with endometriosis-associated pain[3]

STUDY ENDPOINTS

SPIRIT 1 and SPIRIT 2

CO-PRIMARY ENDPOINTS[1]

- Proportion of responders to Ryeqo vs placebo based on the dysmenorrhoea and NMPP NRS scores and analgesic use at Week 24

  Clinical responders were defined as those:

  - Achieving a mean reduction in NRS scores of ≥2.8 points for dysmenorrhoea OR ≥2.1 points for NMPP **AND**
  - No increase in use of analgesic medications

KEY SECONDARY ENDPOINTS[1]

- **Pain** (change in EHP-30 pain domain score)
- **Dysmenorrhoea** (change in average NRS score)
- **NMPP** (change in average NRS score)
- **Overall pelvic pain** (change in average NRS score)
- **Dyspareunia** (change in average NRS scores)
- % of patients not using opioids for endometriosis-associated pain
- % of patients not using analgesics for endometriosis-associated pain (SPIRIT 1) or change from baseline in analgesic use (based on average daily pill count; SPIRIT 2)

Scan the QR code for the SPIRIT 1 and 2 clinical trial results

Scan the QR code for the long-term extension study results

*Ryeqo contains 40 mg relugolix, 1 mg estradiol and 0.5 mg norethisterone acetate.[3]

NMPP, non-menstrual pelvic pain; NRS, Numerical Rating Scale; S1, SPIRIT 1; S2, SPIRIT 2.

References: 1. Giudice LC *et al. Lancet.* 2022;399:2267–2279. **2.** Becker CM *et al. Human Reproduction.* 2024;39(3):526–537. **3.** Ryeqo Approved Product Information. January 2024.

WHAT SHOULD I EXPECT FROM TREATMENT WITH RYEQO?

For many patients, Ryeqo offers relief from endometriosis symptoms from **4 weeks** of treatment.[1]

If it takes a little longer for you to see improvements, this is completely normal. It is important that you continue to take the tablets even if symptoms persist.[1]

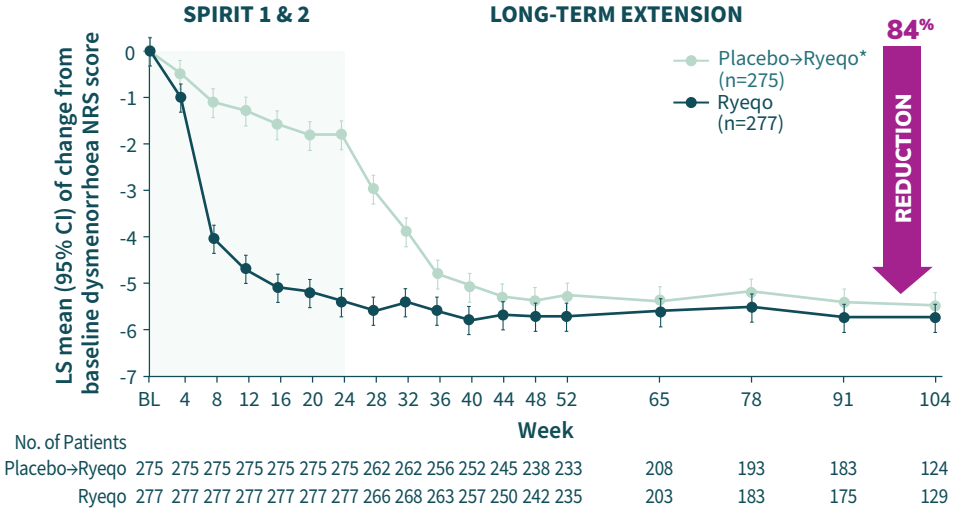
Ryeqo works on your hormone levels and this may disrupt your usual menstrual cycle. In most cases, Ryeqo will reduce menstrual bleeding within the first 2 months of treatment, and many patients may eventually experience no menstrual bleeding at all.[2]

References: 1. Giudice LC *et al. Lancet*. 2022;399:2267–2279. **2.** Ryeqo Approved Product Information. January 2024.

RYEQO EFFICACY

Ryeqo offers pain relief to the majority of women with endometriosis.[1,2]

RYEQO OFFERS SIGNIFICANT REDUCTION IN DYSMENORRHOEA.[1,2]



Adapted from Becker *et al.* 2024.[1]
Error bars show upper and lower limit of 95% confidence intervals.*Placebo for 24 weeks and Ryeqo for 80 weeks.

Ryeqo achieved **73-75% dysmenorrhoea reduction** from baseline at **24 weeks** (significant vs placebo).[2]

This reduction was sustained, with an **84% reduction in dysmenorrhoea** score from baseline to **2 years.**[1]

LS, least squares; NRS, Numerical Rating Scale

References: 1. Becker CM *et al. Human Reproduction,* 2024;39(3):526–537. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279.

DOES RYEQO WORK?

DURING PERIODS

84% less pain during periods.[1*]

*At two years, compared with the amount of pain experienced before treatment started.

BETWEEN PERIODS

69% less pain between periods.[1†]

†At two years, compared with the amount of pain experienced before treatment started.

DURING SEX

59% less pain during sex.[1‡§]

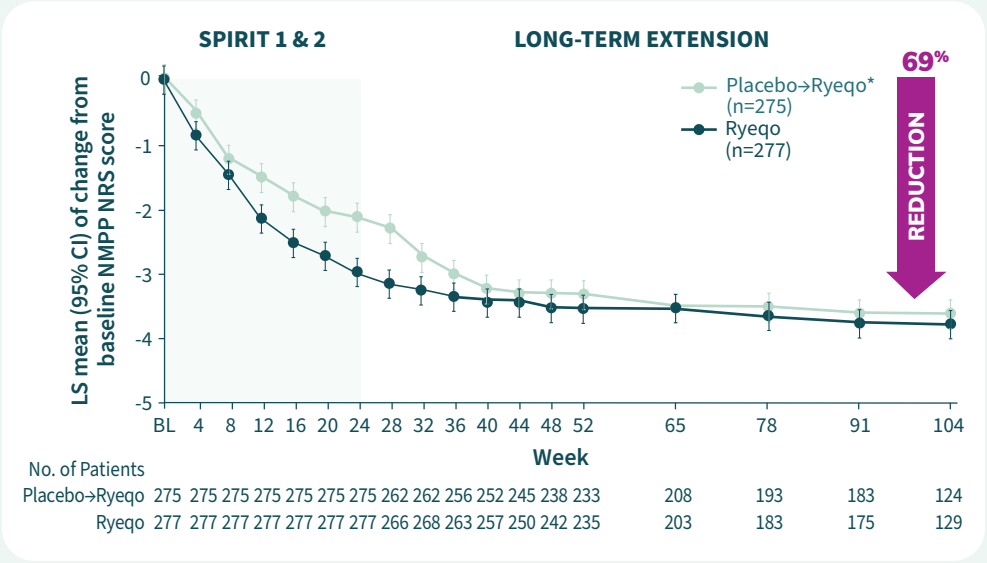
‡At two years, compared with the amount of pain experienced before treatment started.

§Based on those women who were engaging in sex at the start of and during the clinical trials.

Reference: 1. Becker CM *et al. Human Reproduction*. 2024;39(3):526–537.

RYEQO EFFICACY

RYEQO OFFERS SIGNIFICANT REDUCTION IN NON-MENSTRUAL PELVIC PAIN (NMPP).[1,2]



Adapted from Becker *et al.* 2024.[1]
Error bars show upper and lower limit of 95% confidence intervals.*Placebo for 24 weeks and Ryeqo for 80 weeks.

Patients on Ryeqo achieved a reduction of **~50% in their NMPP score** from baseline at **24 weeks** (significant vs placebo).[2]

This reduction was sustained, with a **69% reduction in NMPP score** from baseline to **2 years**.[1]

LS, least squares; NMPP, non-menstrual pelvic pain; NRS, Numerical Rating Scale.
References: 1. Becker CM *et al. Human Reproduction.* 2024;39(3):526–537. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279.

CAN RYEQO HELP TO IMPROVE YOUR QUALITY OF LIFE?

USE OF PAIN KILLERS

Less women used pain killers (including opioids) on Ryeqo compared with a group who received a placebo.[1]

After 24 weeks, up to **31% more women did not take pain killers** while being treated with Ryeqo compared to those in the placebo group.[1]

After two years of Ryeqo treatment, a long-term study showed that **75.1% of women were analgesic-free**.[2]

References: 1. Giudice LC *et al. Lancet.* 2022;399:2267–2279. **2.** Becker CM *et al. Human Reproduction.* 2024; 39(3):526–537.

QUALITY OF LIFE WITH RYEQO

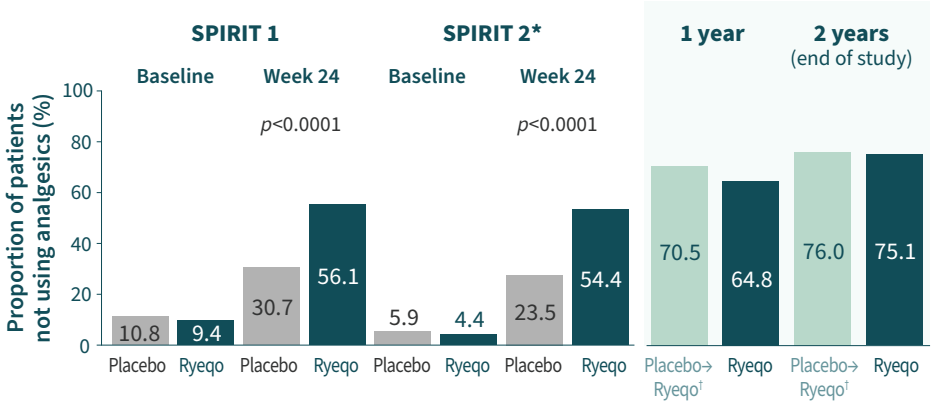
ANALGESIC USE

Less women used analgesics on Ryeqo (including opioids) vs placebo.[1]

25.5% more women
were analgesic free at **week 24** during SPIRIT 1 with Ryeqo[1]
(56% vs 31% with placebo; p<0.0001)

30.8% more women
were analgesic free at **week 24** during SPIRIT 2 with Ryeqo[1]
(54% vs 24% with placebo; p<0.0001; post-hoc exploratory analysis)

For women originally randomised to Ryeqo in SPIRIT 1 and SPIRIT 2, the percentage of women not using analgesics (including opioids) **continued to rise to week 104** in an 80-week long-term extension study.[2]



*SPIRIT 2 data for patients not using analgesics for endometriosis-associated pain were from a post-hoc exploratory analysis.[1]
†Placebo for 24 weeks and Ryeqo for 80 weeks.

References: 1. Giudice LC *et al. Lancet*. 2022;399:2267–2279. **2.** Becker CM *et al. Human Reproduction*. 2024; 39(3):526–537.

CAN RYEQO HELP TO IMPROVE YOUR QUALITY OF LIFE?

DAILY ACTIVITY

Ryeqo has been shown to reduce the overall impact endometriosis pain had on daily activities such as:[1]

Sitting, standing, walking, or exercising

Sleeping

Participating in leisure activities

Coping with pain

Attending social events

MENSTRUAL BLEEDING

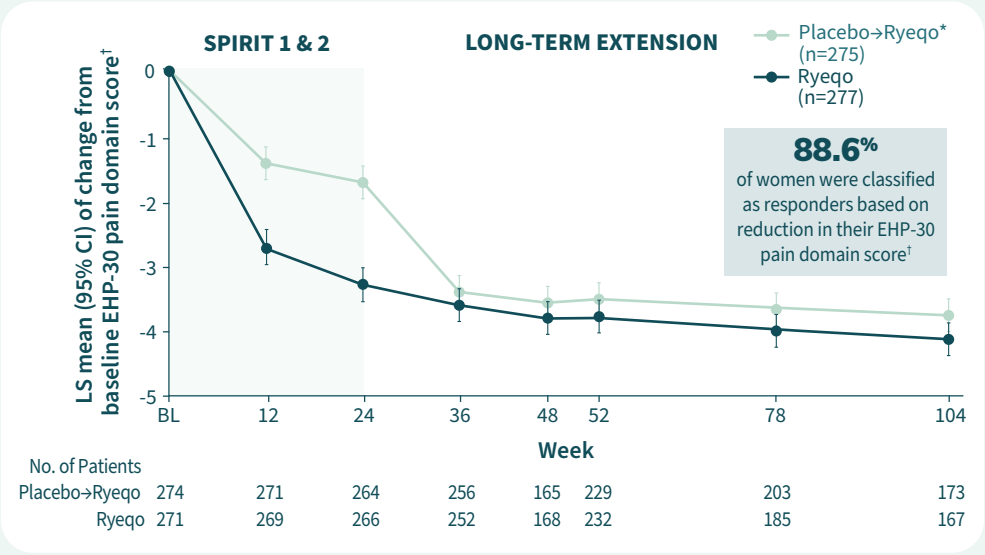
After two years of treatment with Ryeqo **76.9%** of women had **no menstrual bleeding.**[2]

References: 1. Giudice LC *et al. Lancet*. 2022;399:2267–2279 (including Supplementary Appendix). **2.** Becker CM *et al. Human Reproduction.* 2024; 39(3):526–537.

QUALITY OF LIFE WITH RYEQO

EFFECT OF PAIN ON DAILY ACTIVITY

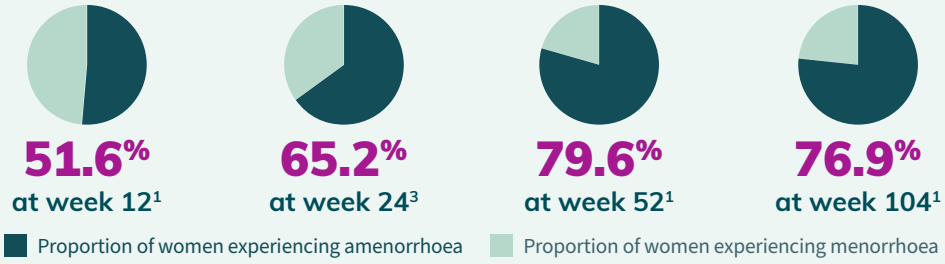
Over two years, Ryeqo has been demonstrated to reduce the effect of pain on daily activity.[1]



Adapted from Becker *et al.* 2024.[1]
Error bars show upper and lower limit of 95% confidence intervals.

AMENORRHOEA

Rates of amenorrhoea achieved with Ryeqo:



*Placebo for 24 weeks and Ryeqo for 80 weeks.
†EHP-30 is a survey designed from the patient's perspective to assess the effect of endo-related pain on daily function and health-related quality of life. It assesses the effect of pain on normal daily activity including the ability to stand, sit, walk, exercise, sleep, to participate in social events and jobs, and the effect on appetite.[2]
BL, baseline; EHP-30, Endometriosis Health Profile-30; LS, least squares.

References: 1. Becker CM *et al. Human Reproduction.* 2024;39(3):526–537. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279. **3.** Ryeqo Approved Product Information. January 2024.

WILL I EXPERIENCE ANY SIDE EFFECTS WITH RYEQO?

As with any treatment, side effects are a possibility – however, when Ryeqo patients were compared to those who did not receive any medical treatment for endometriosis, there were no significant side effects experienced.[1,2]

The most common side effects[1,2] of taking Ryeqo for endometriosis pain were headache and hot flushes.

Less common side effects[1,2] include sweating, or night sweats; mood changes, including worsening depression; abnormal vaginal bleeding (bleeding that lasts too long, that is too heavy, or is unexpected); nausea; toothache; back pain; decreased interest in sex; joint pain; tiredness; and dizziness.

Serious side effects[1,2] were reported in 2.9% of women on Ryeqo and 2.2% of women on placebo.

These are not all the possible side effects of Ryeqo. You should talk to your healthcare professional if you experience any side effects while taking Ryeqo.

References: 1. Ryeqo Consumer Medicine Information. January 2024. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279.

RYEQO SAFETY

RYEQO IS A WELL TOLERATED TREATMENT THAT GOES BEYOND THE SHORT TERM[1,2]

Reported **adverse events** were **similar** in the Ryeqo and placebo arms of SPIRIT 1, 2 and the long-term extension study:[1,2]

	SPIRIT 1 (24 weeks)[1]		SPIRIT 2 (24 weeks)[1]		LONG-TERM EXTENSION (2 years)[2]	
	Placebo (n=212)	Ryeqo (n=212)	Placebo (n=204)	Ryeqo (n=206)	Placebo→ Ryeqo* (n=275)	Ryeqo (n=277)
Adverse events Death	140 (66%) 0	151 (71%) 0	153 (75%) 0	166 (81%) 0	215 (78.2) 0	204 (73.6) 0
Adverse events (≥Grade 3)	12 (6%)	10 (5%)	7 (3%)	14 (7%)	30 (10.9%)	15 (5.4%)
Serious adverse events	5 (2%)	3 (1%)	4 (2%)	9 (4%)	18 (6.5%)	7 (2.5%)
Adverse events leading to trial-drug discontinuation	4 (2%)	8 (4%)	8 (4%)	11 (5%)	22 (8.0%)	15 (5.4%)

Ryeqo was generally **well tolerated:**[1,2]

	SPIRIT 1 (24 weeks)[1]		SPIRIT 2 (24 weeks)[1]		LONG-TERM EXTENSION (2 years)[2]	
Adverse events reported in >5% of patients in any group	Placebo (n=212)	Ryeqo (n=212)	Placebo (n=204)	Ryeqo (n=206)	Placebo→ Ryeqo* (n=275)	Ryeqo (n=277)
Headache	46 (22%)	57 (27%)	64 (31%)	81 (39%)	38 (13.8%)	38 (13.7%)
Nasopharyngitis	12 (6%)	13 (6%)	17 (8%)	29 (14%)	22 (8.0%)	24 (8.7%)
Hot flush	21 (10%)	22 (10%)	7 (3%)	28 (14%)	22 (8.0%)	9 (3.2%)
Toothache	3 (1%)	5 (2%)	7 (3%)	18 (9%)	5 (1.8%)	10 (3.6%)
Back pain	5 (2%)	8 (4%)	7 (3%)	12 (6%)	15 (5.5%)	11 (4.0%)
Nausea	11 (5%)	13 (6%)	6 (3%)	12 (6%)	10 (3.6%)	8 (2.9%)
Arthralgia	2 (1%)	4 (2%)	7 (3%)	11 (5%)	NR	NR
Bone density decreased	4 (2%)	5 (2%)	5 (2%)	11 (5%)	NR	NR
Libido decreased	1 (<1%)	5 (2%)	4 (2%)	11 (5%)	NR	NR
Urinary tract infection	6 (3%)	4 (2%)	5 (2%)	11 (5%)	18 (6.5%)	12 (4.9%)
Acne	13 (6%)	2 (1%)	11 (5%)	7 (3%)	NR	NR
Vitamin D decreased	15 (7%)	4 (2%)	3 (1%)	1 (1%)	NR	NR
Vulvovaginal mycotic infection	NR	NR	NR	NR	15 (5.5%)	28 (10.1%)

*Placebo for 24 weeks and Ryeqo for 80 weeks.
NR, not reported.

References: 1. Giudice LC *et al. Lancet.* 2022;399:2267–2279. **2.** Becker CM *et al. Hum Reprod* 2024;39(3):526–537.

WHY MEASURE BONE MINERAL DENSITY (BMD)?

BONE LOSS OR DECREASED BMD[1,2]

BMD is a measure of the amount of minerals contained in your bones. Measuring this can help to indicate the strength and health of your bones.[3]

The estradiol and norethisterone acetate component of Ryeqo is designed to mitigate the risk of BMD loss. Clinical trials show no significant BMD loss over 2 years of treatment. However, some patients may still experience BMD loss.[1,2]

Your doctor may order an X-ray test called a DXA scan to check your BMD when you start Ryeqo and then monitor it with a DXA scan each year after that. If your DXA scan shows that you have existing bone health issues, you should not take Ryeqo.[1]

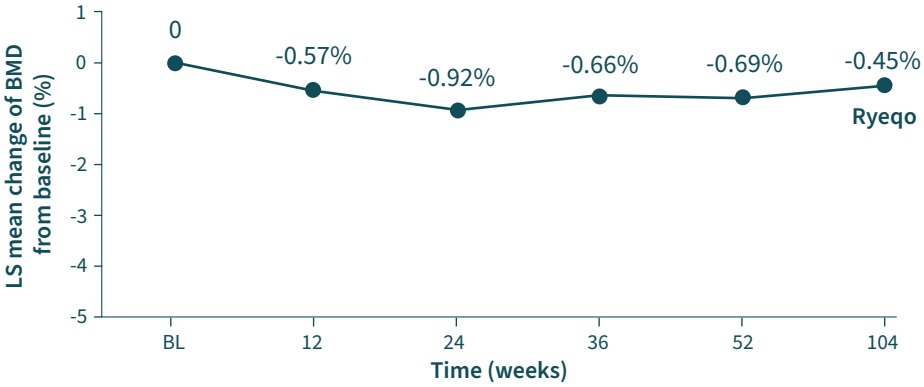
BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry.

References: 1. Ryeqo Approved Product Information. January 2024. **2.** Becker CM *et al. Hum Reprod* 2024;39(3):526–537. **3.** Cefalu CA. *Curr Med Res Opin.* 2004;20(3):341–349.

RYEQO SAFETY

BONE MINERAL DENSITY[1]

BMD was preserved with Ryeqo over **104 weeks.[1]***
Minimal change from baseline in BMD over the 104-week treatment period (<1%).[1]



RECOMMENDATIONS[1,2]

- Assessment of BMD via DXA is recommended at baseline, 12 months and annually after starting treatment.
- Use of Ryeqo is recommended to be limited to 24 months, with extension of therapy conditional on stability of DXA and reassessment of risk/benefit in the individual patient by the treating physician.
- Ryeqo is contraindicated in women with known osteoporosis.

*BMD of lumbar spine.
BL, baseline; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; LS, least squares.
References: 1. Becker CM *et al. Human Reproduction.* 2024;39(3):526–537. **2.** Ryeqo Approved Product Information. January 2024.

WHAT ABOUT RYEQO AND CONTRACEPTION?

CONTRACEPTION[1]

Firstly, you should not take Ryeqo if you are pregnant or breastfeeding.

It is also important to remember that Ryeqo has a contraceptive effect (will stop you becoming pregnant) after one month of continuous use. You therefore should not take oral contraceptive pills while taking Ryeqo, and you are unlikely to become pregnant while you take Ryeqo as recommended.

Non-hormonal birth control (e.g. condoms) should be used **during the first month** after starting Ryeqo.

FERTILITY[1]

However, **should you want to become pregnant** in the near future, don't worry: your fertility will r**eturn rapidly after you stop taking Ryeqo.**[1]

Reference: 1. Ryeqo Consumer Medicine Information. January 2024.

RYEQO AND CONTRACEPTION/FERTILITY

CONTRACEPTION[1]

In healthy premenopausal women, Ryeqo has:

- Demonstrated adequate contraception after 1 month of use.
- Inhibited ovulation in 100% of patients (Hoogland-Skouby score), during an 84-day treatment period.

Ensure patients are aware of the need for non-hormonal birth control during this first month of Ryeqo treatment.

FERTILITY[1]

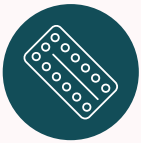
After discontinuation of Ryeqo, all women assessed (66 of 67) returned to ovulation within 43 days (mean 23.5 days).

Reference: 1. Ryeqo Approved Product Information. January 2024.

HOW DO I TAKE RYEQO?

It's simple. Ryeqo is a small tablet that only needs to be taken once a day.[1]

IT IS RECOMMENDED THAT YOU:[1]



Start taking Ryeqo within the **first 5 days** after the start of bleeding due to your period.

Keep taking it daily at the same time of day.

Take Ryeqo with or without food.

Store at room temperature (below 30°C).

Your healthcare professional is the best person to talk to if you have any questions about your treatment.

Reference: 1. Ryeqo Consumer Medicine Information. January 2024.

STARTING RYEQO

Please refer to the prescribing information found on the back page of this consultation tool for detailed prescribing guidance.

When initiating a patient on Ryeqo, it is important to consider the following:[1]

- Ryeqo's **one tablet per day** dosing regimen is similar to that of an oral contraceptive, a dosing frequency which may already be familiar to your patients. However, note that Ryeqo must be taken continuously with no break in treatment.
- It is recommended that patients **start Ryeqo within the first 5 days of menstrual bleeding** to avoid any initial irregular or heavy bleeding.
- Ensure patients take Ryeqo at the **same time daily,** with or without food.
- If a patient misses a dose of Ryeqo, ensure they **take it as soon as possible** on the same day, and resume regular dosing the next day.
- If a patient misses 2 or more consecutive days of treatment, they should use non-hormonal contraceptives for 7 days.
- **DXA scans** are recommended **before treatment initiation** and **annually** thereafter for patients on Ryeqo.
- Patients should take Ryeqo at least 6 hours before taking a P-gp inhibitor and avoid use with combined P-gp and strong CYP3A inducers.
- Whilst many patients will start to see symptom improvements in as little as 4 weeks,[2] if it takes a little longer for some patients to see symptom improvements on Ryeqo, this is completely normal. It is important that your patients continue to take Ryeqo even if symptoms persist.

DXA, dual-energy X-ray absorptiometry; P-gp, P-glycoprotein.

References: 1. Ryeqo Approved Product Information. January 2024. **2.** Giudice LC *et al. Lancet.* 2022;399:2267–2279.

FURTHER INFORMATION FOR PATIENTS

Tell your healthcare professional as soon as possible if you experience any side effects using Ryeqo®.

If you have any concerns or questions about endometriosis or Ryeqo, please speak to your healthcare professional.

Alternatively, please contact Gedeon Richter at:

Phone: 1300 GEDEON (1300 433 033)

e-mail: medinfo@gedeonrichter.com.au

GEDEON RICHTER

FURTHER INFORMATION FOR HEALTHCARE PROFESSIONALS

For further information on Ryeqo and endometriosis, please visit the Ryeqo website
www.ryeqo.com.au

Alternatively, please contact Gedeon Richter at:

Phone: 1300 GEDEON (1300 433 033)

e-mail: medinfo@gedeonrichter.com.au

GEDEON RICHTER

PBS INFORMATION: Ryeqo® is PBS listed for the symptomatic treatment of endometriosis– Authority required (STREAMLINED) for endometriosis. Refer to PBS schedule for full authority information. This product is not PBS listed for Uterine Fibroids.

Please review the full Product Information (PI) before prescribing. Full Product Information is available from the TGA using this QR code.

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems

MINIMUM PRODUCT INFORMATION RYEQO® FILM-COATED TABLETS 40 mg relugolix, 1 mg estradiol (as hemihydrate) and 0.5 mg norethisterone acetate. **Indications:** Treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. Symptomatic treatment of endometriosis in adult women of reproductive age, with a history of previous medical or surgical treatment for their endometriosis. **Contraindications:** Hypersensitivity to the active substance(s) or to any of the excipients, venous thromboembolic disorder, arterial thromboembolic cardiovascular disease, known thrombophilic disorders, known osteoporosis, headaches with focal neurological symptoms or migraine headaches with aura, known or suspected sex steroid influenced malignancies, presence or history of liver tumours (benign or malignant), presence or history of severe hepatic disease as long as liver function values have not returned to normal, pregnancy or suspected pregnancy and breastfeeding, genital bleeding of unknown aetiology, concomitant use of hormonal contraceptives. pregnancy, depression, hypertension, galactose intolerance. **Precautions:** A dual X-ray absorptiometry (DXA) is recommended at baseline, after the first 52 weeks of treatment, and annually thereafter; risk of thromboembolic disorders; risk factors for venous thromboembolism (VTE) and risk factors for arterial thromboembolism (ATE), bone loss, liver tumours or liver disease, change in menstrual bleeding pattern, uterine fibroid prolapse or expulsion, reduced ability to recognise. **Use in pregnancy:** Category D contraindicated during pregnancy. Discontinue use of treatment if pregnancy occurs. **Use in lactation:** Breastfeeding is contraindicated during and for 2 weeks following discontinuation. **Use in renal impairment:** Exposure to relugolix is increased in patients with moderate or severe renal, no dose adjustment is required. **Interactions:** Concomitant use of Ryeqo with oral P-gp inhibitors is not recommended, co administration of Ryeqo with strong CYP3A4 and/or P-gp inducers is not recommended, medicinal products that inhibit the activity of hepatic drug-metabolising enzymes may increase circulating concentrations of the estrogen and norethisterone, the metabolism of estrogens and progestogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, Ritonavir and nelfinavir may decrease the exposure of estrogens and progestogens, St John's Wort (Hypericum perforatum) may induce the metabolism of estrogens and progestogens leading to decreased effectiveness of estrogens with regard to protection of bone loss. Long term concomitant use of liver enzyme inducers with Ryeqo is not recommended. Estrogen and progestogen medicinal products may affect the metabolism of other active substances, such that plasma concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine). **Adverse effects:** In patients with uterine fibroids: common – irritability, hot flush, dyspepsia, alopecia, hyperhidrosis, night sweats, uterine bleeding, breast cyst, libido decreased. In patients with endometriosis: very common – headache, hot flush; common – libido decreased, hyperhidrosis, night sweats, back pain, arthralgia, uterine bleeding, vulvovaginal dryness. **Dosage:** One tablet once daily, at about the same time with or without food. When starting treatment, the first tablet must be taken within 5 days of the onset of menstrual bleeding. If treatment is initiated on another day of the menstrual cycle, irregular and/or heavy bleeding may initially occur. Use is recommended to be limited to 24 months, with extension of therapy conditional on stability of DXA and reassessment of risk/benefit in the individual patient by the treating physician.

For further information, please visit the Ryeqo website: **www.ryeqo.com.au**.