For premenopausal women with moderate to severe endometriosis pain
The recommended total duration of treatment is 24 months.

Myfembree®
(relugolix, estradiol, and norethindrone acetate) tablets
40 mg, 1 mg, 0.5 mg

Myfembree is proven to relieve 3 types of endometriosis pain[1]

PERIOD PAIN

Co-primary endpoint at Week 24[1]: **7 out of 10** women felt less period pain over the last 35 days of treatment[2,*]

Compared with **3 out of 10** women on placebo (74.8% vs 28.6%).[3,†]

PAIN BETWEEN PERIODS

Co-primary endpoint at Week 24[1]: **6 out of 10** women felt less pain between periods over the last 35 days of treatment[2,*]

Compared with **4 out of 10** women on placebo (62.1% vs 41.0%).[2,‡]

PAIN DURING SEX

Key secondary endpoint at Week 24[1]: **43%** less pain during sex[1,2,§,‖,¶,#]

Compared with placebo at **29%** (43.4% vs 28.9%).[2,§]

[#]Pain with sex associated with endometriosis was evaluated in a subgroup of women who engaged in sexual activity with vaginal intercourse at baseline and during treatment (68% of enrolled women).[1]

*Co-primary endpoints were the proportion of women who achieved a reduction from baseline in period pain 0-10 NRS scores of ≥2.8 points and the proportion of women who achieved a reduction from baseline in pain between periods 0-10 NRS scores of ≥2.1 points over the last 35 days of treatment, both without an increase in analgesic use (nonsteroidal anti-inflammatory drug or opioid) for endometriosis-associated pain. Period pain and pain between periods were evaluated daily by women asked to rate their pain severity during the prior 24 hours as a score of 0 ("no pain") to 10 ("pain as bad as you can imagine").[1,3]

†Data shown represent results from a pooled post hoc analysis of SPIRIT 1 and 2; this endpoint at Week 24 was statistically significant in each study (SPIRIT 1: $P \leq 0.0001$, SPIRIT 2: $P \leq 0.0001$).[1]

‡Data shown represent results from a pooled post hoc analysis of SPIRIT 1 and 2; this endpoint at Week 24 was statistically significant in each study (SPIRIT 1: $P \leq 0.0001$, SPIRIT 2: $P \leq 0.0001$).[1]

§Data shown represent results from a pooled post hoc analysis of SPIRIT 1 and 2; this endpoint at Week 24 was statistically significant in each study (SPIRIT 1: $P = 0.0149$, SPIRIT 2: $P = 0.0371$).[3]

‖LS mean percent change in NRS score: 43.4%. LS mean change in NRS score for Myfembree vs placebo from baseline (5.8 vs 5.7) to Week 24: -2.4 vs -1.8.[2]

¶Women rated their pain during sexual intercourse daily using an 11-point NRS score ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine").[1]

LS = least squares; NRS = numerical rating scale; $P = P$ value.

Not an actual patient.

INDICATION

Myfembree is indicated for the management of moderate to severe pain associated with endometriosis in premenopausal women.
Limitations of Use: Use of Myfembree should be limited to 24 months due to the risk of continued bone loss which may not be reversible.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: THROMBOEMBOLIC DISORDERS AND VASCULAR EVENTS

- Estrogen and progestin combination products, including Myfembree, increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism, deep vein thrombosis, stroke and myocardial infarction, especially in women at increased risk for these events.
- Myfembree is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and those at increased risk for these events, including women >35 years of age who smoke or with uncontrolled hypertension.

CONTRAINDICATIONS

Myfembree is contraindicated in women with: high risk of arterial, venous thrombotic, or thromboembolic disorder; pregnancy; known osteoporosis; current or history of breast- or other hormone-sensitive cancers; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known hypersensitivity to components of Myfembree.

Please scroll for additional Important Safety Information and click for full Prescribing Information, including BOXED WARNING

POWERFUL REDUCTIONS IN PERIOD PAIN AT WEEK 24[2]

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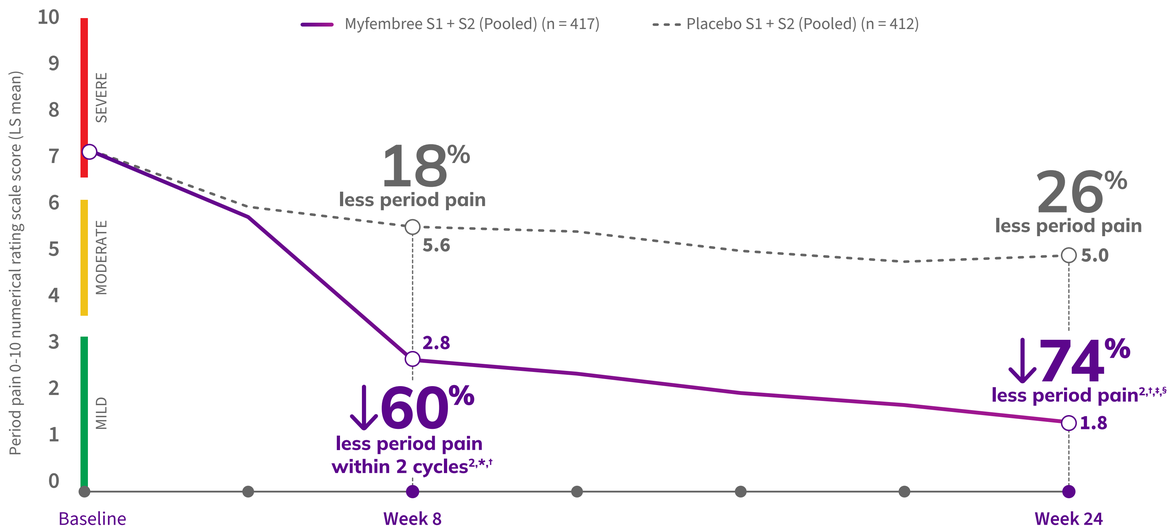
KEY SECONDARY ENDPOINT



*Pain assessment at Week 8 was a prespecified key secondary endpoint, but was not adjusted for multiplicity.[3]

KEY SECONDARY ENDPOINT AT WEEK 24: 50% LESS PAIN BETWEEN PERIODS, COMPARED TO 36% WITH PLACEBO (LS MEAN PERCENT CHANGE IN NRS SCORE, 49.7% COMPARED WITH PLACEBO AT 36.0%).[1,2,‖,¶,#]

Trial Design: Myfembree was studied in two 24-week, randomized, double-blind, placebo-controlled trials (SPIRIT 1 and 2), evaluating 1251 premenopausal women with moderate to severe pain associated with endometriosis.[1,3]

IMPORTANT SAFETY INFORMATION *(Cont'd)*
WARNINGS AND PRECAUTIONS

Thromboembolic Disorders: Discontinue immediately if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs or is suspected; or if there is sudden unexplained partial or complete loss of vision, proptosis, diplopia, papilledema or retinal vascular lesions and evaluate for retinal vein thrombosis. Discontinue ≥4 to 6 weeks before surgery associated with an increased risk of thromboembolism or during prolonged immobilization.

Bone Loss: Myfembree may decrease bone mineral density (BMD) in some patients, which may be greater with longer use and may not be completely reversible. Consider the benefits and risks in patients with a history of low trauma fracture or risk factors for osteoporosis or bone loss. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and annually thereafter.

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[†]LS mean change in NRS score for Myfembree vs placebo from baseline (7.2 vs 7.2) to Week 8: -4.1 vs -1.3; to Week 24: -5.1 vs -1.9.[2]
[‡]Women rated their period pain daily using an 11-point NRS score ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine").[1]
[§]Data shown represent results from a pooled post hoc analysis of SPIRIT 1 and 2; this endpoint at Week 24 was statistically significant in each study (SPIRIT 1: *P*<0.0001, SPIRIT 2: *P*<0.0001).[3]
[‖]LS mean change in NRS score for Myfembree vs placebo from baseline (5.9 vs 5.7) to Week 24: -2.8 vs -2.0.[2]
[¶]Women rated their pain between periods daily using an 11-point NRS score ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine").[1]
[#]Data shown represent results from a pooled post hoc analysis of SPIRIT 1 and 2; this endpoint at Week 24 was statistically significant in each study (SPIRIT 1: *P*=0.0002, SPIRIT 2: *P*=0.0017).[2]

LS = least squares; NRS = numerical rating scale; *P* = *P* value.

MYFEMBREE IS *PURPOSEFULLY* DESIGNED TO RELIEVE ENDOMETRIOSIS PAIN WHILE *MITIGATING* SIDE EFFECTS

like bone loss, associated with relugolix alone[1,3-5]

Not actual pill size.[2]

Myfembree is the *only* once daily pill that combines[1,4,5]

GnRH antagonist	Purposeful low-dose add-back therapy (ABT)	
Relugolix (40 mg)	**E2** (1 mg)	**NETA** (0.5 mg)
Reduces hormones like estradiol, decreasing endo pain	Could offset potential bone loss due to low estradiol from relugolix alone[3]	Protects the uterus from the effect of estrogen alone[1]

Adverse Reactions

Most common adverse reactions (incidence of ≥3% and greater than placebo) include headache, vasomotor symptoms, mood disorders, abnormal uterine bleeding, nausea, toothache, back pain, decreased sexual desire and arousal, arthralgia, fatigue, and dizziness. These are not all the possible side effects.[1]

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IMPORTANT SAFETY INFORMATION *(Cont'd)*
WARNINGS AND PRECAUTIONS *(Cont'd)*

Hormone-Sensitive Malignancies: Discontinue Myfembree if a hormone-sensitive malignancy is diagnosed. Breast exams and mammography are recommended. Use of estrogen alone or estrogen plus progestin has resulted in abnormal mammograms requiring further evaluation.

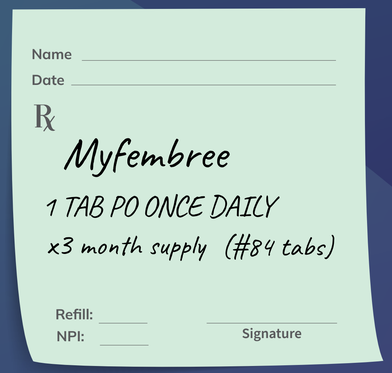
Suicidal Ideation and Mood Disorders (Including Depression): Evaluate patients with a history of suicidal ideation, depression, and mood disorders before starting treatment. Monitor for these symptoms including shortly after initiating treatment. Advise patients to seek medical care for new or worsening depression, anxiety, other mood changes, or suicidal ideation and behavior. Gonadotropin-releasing hormone receptor antagonists, including Myfembree, have been associated with mood disorders (including depression) and suicidal ideation.

Please scroll for additional Important Safety Information and click for full Prescribing Information, including BOXED WARNING

E2 = estradiol; GnRH = gonadotropin-releasing hormone; NETA = norethindrone acetate.

Help your patients get started on Myfembree

Learn More About Copay Coverage



Example Myfembree script for three-month supply

IMPORTANT SAFETY INFORMATION *(Cont'd)*
WARNINGS AND PRECAUTIONS *(Cont'd)*

Hepatic Impairment and Transaminase Elevations: Due to poor metabolism of steroid hormones, instruct these patients to promptly seek medical care for symptoms/signs of liver injury, e.g., jaundice or right upper abdominal pain. Acute liver test abnormalities may require discontinuing Myfembree until tests return to normal and Myfembree causation is excluded.

Gallbladder Disease or History of Cholestatic Jaundice: Discontinue Myfembree if signs/symptoms of gallbladder disease or jaundice occur. Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease.

Elevated Blood Pressure: In women with well-controlled hypertension, monitor blood pressure and stop Myfembree if it rises significantly.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy: Advise women to use non-hormonal contraception during and for one week after discontinuing Myfembree. Avoid use with hormonal contraceptives. Myfembree may delay recognition of pregnancy because it alters menstrual bleeding. Test for pregnancy if suspected and discontinue Myfembree if confirmed.

Risk of Early Pregnancy Loss: Myfembree can cause early pregnancy loss. Exclude pregnancy before initiating and advise women to use non-hormonal contraception.

Uterine Fibroid Prolapse or Expulsion: Advise women with known or suspected submucosal uterine fibroids about the risk of uterine fibroid prolapse or expulsion and instruct them to contact their physician if severe bleeding/cramping occurs.

Alopecia: Alopecia, hair loss, and hair thinning were reported in phase 3 trials in women with heavy menstrual bleeding associated with uterine fibroids with Myfembree. Whether hair loss is reversible is unknown.

Effects on Carbohydrate and Lipid Metabolism: More frequent monitoring in women with prediabetes and diabetes may be necessary. Myfembree may decrease glucose tolerance and increase blood glucose concentrations. Monitor lipid levels and consider discontinuing if hypercholesterolemia or hypertriglyceridemia worsens. In women with pre-existing hypertriglyceridemia, estrogen therapy may increase triglycerides levels leading to pancreatitis. Myfembree is associated with increases in total cholesterol and LDL-C.

Effect on Other Laboratory Results: Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy. Combined estrogen and progestin may raise serum concentrations of binding proteins, which may reduce free thyroid or corticosteroid hormone levels. Estrogen and progestin may also affect the levels of sex hormone-binding globulin and coagulation factors.

Hypersensitivity Reactions: Immediately discontinue Myfembree if a hypersensitivity reaction occurs.

ADVERSE REACTIONS: Most common adverse reactions (incidence ≥3% and greater than placebo) were headache, vasomotor symptoms, mood disorders, abnormal uterine bleeding, nausea, toothache, back pain, decreased sexual desire and arousal, arthralgia, fatigue, and dizziness. These are not all the possible side effects.

LACTATION: Advise women not to breastfeed while taking Myfembree.

Please see full Prescribing Information, including BOXED WARNING

References: 1. Myfembree [Prescribing Information]. Sumitomo Pharma America, Inc. July 2024. **2.** Data on file. Sumitomo Pharma America, Inc. **3.** Giudice LC, As-Sanie S, Arjona Ferreira JC, et al. Once daily oral relugolix combination therapy versus placebo in patients with endometriosis-associated pain: two replicate phase 3, randomised, double-blind, studies (SPIRIT 1 and 2). *Lancet*. 2022;399(10343):2267-2279. **4.** Arjona Ferreira JC, Migoya E. Development of relugolix combination therapy as a medical treatment option for women with uterine fibroids or endometriosis. *F S Rep*. 2022;4(2S):73-82. **5.** Barbieri RL. Hormone treatment of endometriosis: the estrogen threshold hypothesis. *Am J Obstet Gynecol*. 1992;166(2):740-745.

Sumitomo Pharma

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