relugolix–estradiol–norethindrone acetate
Myfembree

**Pharmaceutical company:** Myovant Sciences GmbH and Pfizer

**Pharmacologic classification:** Gonadotropin-releasing hormone receptor antagonist/estrogen/progestin

**Therapeutic classification:** Hormonal agent

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**AVAILABLE FORMS**
Tablets: relugolix 40 mg, estradiol 1 mg, norethindrone acetate 0.5 mg

**INDICATIONS AND DOSAGES**
Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women

*Adults:* One tablet PO daily for up to 24 months.

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**CONTRAINDICATIONS AND CAUTIONS**

- **Black Box Warning:** This drug increases the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and MI, especially in women at increased risk for these events.

- **Black Box Warning:** This drug is contraindicated in women with current or a history of thrombotic or thromboembolic disorders, and in women at increased risk for these events, including women over age 35 who smoke, or women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.

- Contraindicated in women at high risk for arterial, venous thrombotic, or thromboembolic disorder (cerebrovascular disease, coronary artery disease, peripheral vascular disease, thrombogenic valvular or thrombogenic rhythm diseases of the heart, inherited or acquired hypercoagulopathies, or headaches with focal neurologic symptoms or migraine headaches with aura if over age 35).

- Contraindicated for use in patients with known osteoporosis, current or history of breast cancer or other hormone-sensitive malignancies, increased risk for hormone-sensitive malignancies, known hepatic impairment or disease, undiagnosed abnormal uterine bleeding, or hypersensitivity to any of the drugs in the product.

- Discontinue the drug immediately if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs, or if a hormone-sensitive malignancy is diagnosed.

- Stop the drug if sudden unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions occurs, and evaluate for retinal vein thrombosis immediately.

- Treatment duration is limited to 24 months. This drug may cause decreases in bone mineral density (BMD) that may not be completely reversible. Baseline and periodic BMD assessments are recommended. Assess risk-benefit for women with additional risk factors for bone loss.

- This drug may contribute to depression, mood disorders, or suicidal ideation.

- Use cautiously in women with well-controlled hypertension; continue to monitor blood pressure and stop the drug if blood pressure rises significantly.

- Use cautiously in women with a history of cholestatic jaundice related to past estrogen use or pregnancy.

- Use cautiously in patients with prediabetes, diabetes, and hypertriglyceridermia. This drug may decrease glucose tolerance and increase cholesterol and triglyceride levels.

- This drug may cause uterine fibroid prolapse or expulsion; advise patients to seek medical attention for severe uterine bleeding.

- This drug may cause alopecia; discontinue the drug if hair loss becomes a concern.

- Safety and effectiveness in children have not been established.

**Dialyzable drug:** Unknown.

**Overdose S&S:** Nausea, vomiting, breast tenderness, abdominal pain, drowsiness, fatigue, and withdrawal bleeding.
PREGNANCY-LACTATION-REPRODUCTION
- This drug is contraindicated in pregnancy. Females who are pregnant and exposed to the drug are encouraged to call the Myfembree Pregnancy Exposure Registry at 1-(855)-428-0707.
- This drug can cause early pregnancy loss; exclude pregnancy before initiating treatment.
- This drug may delay the ability to recognize pregnancy because it alters menstrual bleeding. Perform testing if pregnancy is suspected and discontinue the drug if pregnancy is confirmed.
- Advise women of reproductive potential to use effective non-hormonal contraception during treatment with the drug and for 1 week after the final dose. Avoid concomitant use of hormonal contraceptives.
- This drug is likely to be present in human milk. Weigh the benefits against the risk of adverse effects to the breastfed child.

INTERACTIONS
Drug-drug. Combined P-glycoprotein (P-gp) and strong CYP3A inducers (rifampin): May decrease concentrations of relugolix, estradiol, or norethindrone; avoid concurrent use.
Estrogen-containing contraception: May increase estrogen levels, risk of estrogen-associated adverse events, and decrease efficacy of relugolix, estradiol, and norethindrone. Avoid concurrent use.
P-gp inhibitors (erythromycin): May increase relugolix concentrations; avoid concurrent use or if cannot discontinue P-gp inhibitor, separate doses by 6 hours and monitor for adverse reactions.
Drug-herb. St. John’s wort: May decrease concentrations of relugolix, estradiol, or norethindrone. Discourage use together.
Drug-lifestyle. Black Box Warning: Smoking: Smoking increases the risk of thromboembolic disorders and vascular events, especially in those over age 35. Discourage smoking.

ADVERSE REACTIONS
CNS: depression, mood disorders, irritability, anxiety.
CV: hypertension, hot flush.
GI: dyspepsia.
GU: abnormal uterine bleeding, loss of libido.
Musculoskeletal: bone loss.
Skin: alopecia, hyperhidrosis or night sweats.
Other: hypersensitivity, breast cyst.

Reactions in bold italics are life-threatening.

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