# Gonadotropin-Releasing Hormone Antagonists

**Goal(s):**

- Promote safe use of elagolix and relugolix/estradiol/norethindrone in people with endometriosis-associated pain
- Promote safe use of elagolix/estradiol/norethindrone and relugolix/estradiol/norethindrone for heavy menstrual bleeding associated with uterine fibroids (leiomyoma).
- Promote use that is consistent with medical evidence and product labeling.
- Allow case-by-case review for members covered under the EPSDT program.

**Length of Authorization:**

- Initial: Up to 6 months
- Elagolix renewal: Up to 6 months for 150 mg daily dose with total cumulative lifetime treatment period not to exceed 24 months in patients with normal hepatic function. For patients with moderate hepatic impairment receiving 150 mg once daily, duration of therapy should not exceed 6 months. In patients receiving high dose elagolix therapy (200 mg twice daily), maximum treatment duration is 6 months.
- Elagolix/estradiol/norethindrone renewal: Up to 6 months for elagolix 300 mg dosed twice daily with a total cumulative treatment period not to exceed 24 months
- Relugolix/estradiol/norethindrone renewal: Up to 6 months for relugolix component 40 mg dosed once daily with a total cumulative treatment period not to exceed 24 months

**Requires PA:**

- Elagolix (ORLISSA)
- Elagolix/estradiol/norethindrone (ORIAHNN)
- Relugolix/estradiol/norethindrone (MYFEMBREE)

**Covered Alternatives:**

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

| Approval Criteria | | |
|---|---|---|
| 1. What diagnosis is being treated? | Record ICD10 code. | |
| 2. Is the diagnosis funded by OHP? | **Yes:** Go to #4 | **No: :** Current age ≥ 21 years: Pass to RPh. Deny; not funded by the OHP<br><br>Current age < 21 years: Go to #3 |
| 3. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc)? | **Yes:** Go to #4 | **No:** Pass to RPh. Deny; medical necessity. |

| Approval Criteria | | |
|---|---|---|
| 4. Is this a request for continuation of therapy previously approved by the FFS program? | **Yes:** Go to **Renewal Criteria** | **No:** Go to #5 |
| 5. Is the patient pregnant or actively trying to conceive? | **Yes:** Pass to RPh. Deny; medical appropriateness | **No:** Go to #6 |
| 6. Is there documentation that the provider and patient have discussed the teratogenic risks of the drug if the patient were to become pregnant? | **Yes:** Go to #7 | **No:** Pass to RPh. Deny; medical appropriateness |
| 7. Is this request for management of moderate to severe pain associated with endometriosis in a premenopausal patient? | **Yes**: Go to #8 | **No:** Go to #14 |
| 8. Has the patient tried and failed an adequate trial of preferred first line endometriosis therapy options including administration of combined hormonal contraceptives or progestins (oral, depot injection, or intrauterine) alone?<br>-or-<br>Does the patient have a documented intolerance, FDA-labeled contraindication, or hypersensitivity the first-line therapy options? | **Yes:** Go to #9 | **No:** Pass to RPh. Deny; medical appropriateness<br><br>First-line therapy options such as combined hormonal contraceptives or progestins do not require PA |

| Approval Criteria | | |
|---|---|---|
| 9. Is the patient taking any concomitant medications that are strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine, gemfibrozil, etc.), combined P-glycoprotein inhibitor and moderate CYP3A inhibitor (e.g., erythromycin), combined P-glycoprotein inducer and strong CYP3A inducer (e.g., rifampin)?<br><br>Note: Elagolix levels are increased when co-administered with OATP1B1 inhibitors. Relugolix levels are increased when co-administered with inhibitors such as erythromycin and decreased when co-administered with inducers such as rifampin. Avoid combinations of these therapies due to drug interactions that can increase the risk of adverse reactions or decrease the efficacy of GnRH antagonists. | **Yes:** Deny; medical appropriateness | **No:** Go to #10 |
| 10. Does the patient have a diagnosis of osteoporosis or related bone-loss condition?<br><br>Note: In patients with major risk factors for decreased bone mineral density (BMD) such as chronic alcohol (> 3 units per day) or tobacco use, strong family history of osteoporosis, or chronic use of drugs that can decrease BMD, such as anticonvulsants or corticosteroids, use of GnRH antagonists may pose an additional risk, and the risks and benefits should be weighed carefully. | **Yes:** Pass to RPh. Deny; medical appropriateness | **No:** Go to #11 |
| 11. Does the patient have severe hepatic impairment as documented by Child-Pugh class C? | **Yes:** Pass to RPh. Deny; medical appropriateness | **No:** Go to #12 |

| Approval Criteria | | |
|---|---|---|
| 12. Does the patient have moderate hepatic impairment as documented by Child-Pugh class B? | **Yes:** Go to #13 | **No:** Approve for 6 months<br><br>* FDA approved elagolix dosing for patients with normal liver function or mild liver impairment: 150 mg once daily for up to 24 months or 200 mg twice daily for up to 6 months |
| 13. Is the dose for elagolix 150 mg once daily or relugolix 40 mg /estradiol 1 mg/norethindrone 0.5 mg? | **Yes:** Approve for 6 months (cumulative lifetime treatment)<br><br>* FDA approved elagolix dosing for moderate hepatic impairment: 150 mg once daily for up to 6 months. | **No:** Pass to RPh. Deny; medical appropriateness |
| 14. Is the request for elagolix/estradiol/norethindrone or relugolix/estradiol/norethindrone for management of heavy menstrual bleeding associated with uterine fibroids (leiomyomas)? | **Yes:** Go to #15 | **No:** Pass to RPh. Deny; medical appropriateness |

| Approval Criteria | | |
|---|---|---|
| 15. Has the patient tried and failed a trial of first line therapy options including at least 1 of the following for at least 3 months:<br>a) hormone-releasing IUD OR<br>b) continuous administration of combined hormonal contraceptives OR<br>c) cyclic progestins OR<br>d) tranexamic acid?<br>OR<br>Does the patient have a documented intolerance, FDA-labeled contraindication, or hypersensitivity to the first-line therapy options? | **Yes**: Go to #16 | **No:** Pass to RPh. Deny; medical appropriateness<br><br>First-line therapy options such as hormonal contraceptives, progestins, or tranexamic acid do not require PA |
| 16. Does the patient have a diagnosis of osteoporosis or related bone-loss condition?<br><br>Note: In patients with major risk factors for decreased bone mineral density (BMD) such as chronic alcohol (> 3 units per day) or tobacco use, strong family history of osteoporosis, or chronic use of drugs that can decrease BMD, such as anticonvulsants or corticosteroids, use of GnRH antagonists may pose an additional risk, and the risks and benefits should be weighed carefully. | **Yes:** Pass to RPh. Deny; medical appropriateness | **No:** Approve for 6 months (cumulative, lifetime treatment) |

| Renewal Criteria | | |
|---|---|---|
| 1. Has the patient been receiving elagolix/estradiol/norethindrone for management of uterine fibroids or relugolix/estradiol/norethindrone for management of uterine fibroids or pain associated with endometriosis? | **Yes:** Go to #4 | **No:** Go to #2 |
| 2. Has the patient been receiving therapy with elagolix 150 mg once daily for management of endometriosis? | **Yes:** Go to #3 | **No:** Pass to RPh; Deny; medical appropriateness.<br><br>(Elagolix 200 mg twice daily is limited to 6-month maximum treatment duration per FDA labeling) |

| Renewal Criteria | | |
|---|---|---|
| 3. Does the patient have moderate hepatic impairment as documented by Child-Pugh Class B? | **Yes:** Pass to RPh; Deny; medical appropriateness.<br><br>(Elagolix 150 mg once daily is limited to 6-month maximum treatment duration in patients with moderate hepatic impairment per FDA labeling) | **No:** Go to #4 |
| 4. Has the patient's condition* improved as assessed and documented by the prescriber?<br><br>*For endometriosis: has pain associated with endometriosis improved?<br>For uterine fibroids: has patient experienced at least a 50% reduction in menstrual blood loss from baseline? | **Yes:** Approve for up to 18 months<br><br>Document physician attestation received.<br><br>Total cumulative treatment period not to exceed 24 months. | **No:** Pass to RPh; Deny; medical appropriateness. |

*P&T/DUR Review: 2/23(DM); 12/21, 3/19 (DM),11/18 (DE)*
*Implementation: 4/1/23; 1/1/22; 5/1/19*