

## PHARMACY COVERAGE GUIDELINE

### ORILISSA™ (elagolix) oral Generic Equivalent (if available)

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
  - This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
  - Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
  - The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
  - The “Description” section describes the Service.
  - The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
  - The “Resources” section lists the information and materials we considered in developing this PCG
  - **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
  - Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).
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## Medical Necessity Requirements for ORILISSA (elagolix)

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### Criteria for Initial Therapy:

#### **Prescriber Qualifications**

- Prescribed is a Gynecologist or in consultation with one

#### **Indication**

- Moderate to severe pain associated with endometriosis in a premenopausal woman

#### **Age Requirement**

- 18 years of age or older

ORIGINAL EFFECTIVE DATE: 09/20/2018 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 08/21/2025

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#### Baseline Clinical Evaluation

- Negative pregnancy test in a woman of childbearing potential
- Liver function tests
- Bone mineral density in a woman with risk factors for bone loss or osteoporosis

#### Alternative Therapies

- Failure contraindication, intolerance, or is not a candidate for **BOTH** of the following:
  - **ONE** nonsteroidal anti inflammatory agent such as ibuprofen, indomethacin, naproxen, meloxicam, and others
  - **ONE** hormonal product such as oral estrogen progestin contraceptive or progestin (oral or depot, e.g. medroxyprogesterone or norethindrone acetate)

#### Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

#### Safety

- Does not have any of the following FDA label contraindications:
  - Pregnancy
  - Known osteoporosis
  - Severe hepatic impairment (Child Pugh Class C)
  - Concomitant use with strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g. cyclosporine, gemfibrozil)
- Has not previously received 24 months or longer of therapy with Oriahnn (elagolix estradiol norethindrone) or Myfembree (relugolix, estradiol, norethindrone) either alone or sequentially

#### Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (pregnancy test, liver function tests, bone mineral density)
  - Supporting clinical documentation

#### Approval Duration

- 24 months for patients with no coexisting conditions using 150 mg once daily
- 6 months for patients with moderate hepatic impairment (Child Pugh Class B) using 150 mg once daily
- 6 months for patients with dyspareunia using 200 mg twice daily
- OR end of plan year
- **Note:** Decreased bone mineral density (BMD) is related to dose and coexisting conditions that influence duration of use. Decreases in BMD may not be completely reversible after stopping treatment. Calculation of duration will consider any previous use and coexisting condition.

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#### Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
  2. Off-Label Use of Cancer Medications
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#### Description:

Orilissa (elagolix) is an oral gonadotropin-releasing hormone (GnRH) receptor antagonist that suppresses luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased blood concentrations of the ovarian sex hormones, estradiol and progesterone. It is indicated for the management of moderate to severe pain associated with endometriosis. GnRH regulates the anterior pituitary gland synthesis and secretion of FSH and LH.

Endometriosis is defined as endometrial glands and stroma that occur outside the uterine cavity. The lesions are usually located in the pelvis but can occur at other sites including the bowel, diaphragm, and pleural cavity. Endometriosis is an estrogen-dependent, benign, inflammatory disease that can affect a woman during their premenarcheal, reproductive, and postmenopausal hormonal stages. Ectopic endometrial tissue and inflammation may cause dysmenorrhea, dyspareunia, chronic pelvic pain, pelvic tenderness, pelvic induration, infertility and/or an ovarian mass. Less common symptoms include bowel and bladder dysfunction (e.g., dyschezia and dysuria), abnormal uterine bleeding, low back pain, or chronic fatigue. For some, the disease is asymptomatic and is an incidental finding at the time of surgery or imaging done for other indications.

The safety and efficacy of Orilissa were demonstrated in two controlled studies in premenopausal women with moderate to severe endometriosis pain. Patients received either Orilissa or placebo. The primary endpoints were the proportion of patients whose dysmenorrhea responded to treatment at month 3 and the proportion of patients whose non-menstrual pelvic pain responded to treatment at month 3. A higher proportion of women treated with Orilissa were responders for dysmenorrhea and non-menstrual pelvic pain.

A progestin, danazol, extended cycle combined oral contraceptive, nonsteroidal anti-inflammatory drug (NSAIDs), or GnRH agonist can be used for the initial treatment of pain in women with suspected endometriosis. In women with a history of endometriosis who wish to preserve their fertility, NSAIDs or combined oral contraceptive can be used to treat recurrent pain. Oral or depot medroxyprogesterone acetate is also an effective treatment option. If none of these therapies are successful, a progestin, GnRH agonist, or androgen may be used. If treatment with a GnRH agonist is successful, the use of an add-back regimen can reduce or eliminate bone mineral loss and provide symptomatic relief without reduction in pain.

Add-back therapy refers to the addition of hormone replacement therapy to GnRH agonists, in order to avoid adverse effects that are caused by GnRH agonist-induced hormone suppression. Evidence suggests that add-back therapy is more effective for symptomatic relief than use of a GnRH agonist alone, both immediately after treatment and at 6 months. Add-back therapy increases estrogen levels but does not reduce the efficacy of GnRH agonists for treating dysmenorrhea and dyspareunia. Add-back regimens have been used in women undergoing

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long-term therapy; they may include a progestin alone, low dose progestin, progestin plus bisphosphonate, or estrogen.

Lupron Depot 3.75 mg monthly and 11.25 mg every 3-month IM injections are indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions. Lupron Depot monthly with norethindrone acetate 5 mg daily is also indicated for initial management of endometriosis and for management of recurrence of symptoms.

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#### **Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

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#### **Resources:**

Orilissa (elagolix) product information, revised by AbbVie, Inc. 06-2023. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed May 12, 2025.

Schenken RS. Endometriosis: Pathogenesis, epidemiology, and clinical impact. In: UpToDate, Barbieri RL, Eckler K (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2025. Topic last updated December 03, 2024. Accessed June 16, 2025.

Schenken RS. Endometriosis: Treatment of pelvic pain. In: UpToDate, Barbieri RL, Eckler K (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2025. Topic last updated May 14, 2025. Accessed June 16, 2025.

Hornstein MD. Endometriosis: Long-term treatment gonadotropin-releasing hormone agonists. In: UpToDate, Barbieri RL, Eckler K (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2025. Topic last updated March 21, 2023. Accessed June 16, 2025.