BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

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

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 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. 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.

Criteria:

➢ **Criteria for therapy:** Orilissa (elagolix) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gynecologist
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of moderate to severe pain associated with endometriosis in a premenopausal woman
4. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **BOTH** of the following:

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

a. **ONE** non-steroidal anti-inflammatory agent such as ibuprofen, indomethacin, naproxen, meloxicam, and others
b. **ONE** hormonal product such as oral estrogen-progestin contraceptive or progestin (oral or depot (e.g. medroxyprogesterone or norethindrone acetate))

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
   a. Negative pregnancy test in a woman of childbearing potential
   b. Liver function tests
   c. Bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis

7. There are **NO** FDA-label contraindications such as:
   a. Pregnancy
   b. Known osteoporosis because of the risk of further bone loss
   c. Severe hepatic impairment (Child-Pugh Class C)
   d. Use with strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (i.e. cyclosporine, gemfibrozil)

8. Individual has not previously received 24 months or longer of therapy with Oriahnn (elagolix-estradiol-norethindrone) or Myfembree (relugolix, estradiol, & norethindrone) either alone or sequentially

Maximum approval durations:
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.
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

- 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**

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

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 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.

Definitions:

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

PHARMACY COVERAGE GUIDELINE

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

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.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.