



elagolix (Orilissa™, Oriahnn™)

EOCCO POLICY



Policy Type: PA

Pharmacy Coverage Policy: EOCCO021

Description

Elagolix (Orilissa) and elagolix/estradiol/norethindrone acetate (Oriahnn) are oral gonadotropin-releasing hormone (GnRH) antagonists.

Length of Authorization

- Initial: Three months
- Renewal:
 - i. Elagolix (Orilissa) 150 mg: Up to 12 months; maximum total (lifetime) fills should not exceed #24 30-day fills
 - ii. Elagolix (Orilissa) 200 mg: Up to three months; maximum total (lifetime)fills should not exceed #6 30-day fills
 - iii. Elagolix/estradiol/norethindrone acetate (Oriahnn): Up to 12 months; maximum total (lifetime) fills should not exceed #24 28-day fills

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
elagolix (Orilissa)	150 mg tablets	Moderate to severe pain associated with endometriosis	30 tablets/30 days
	200 mg tablets		60 tablets/30 days
elagolix/estradiol/norethindrone acetate (Oriahnn)	300 mg/1 mg/0.5 mg tablets	Treatment of heavy menstrual bleeding associated with uterine fibroids	56 tablets/28 days

Initial Evaluation

- I. **Elagolix (Orilissa) and elagolix/estradiol/norethindrone acetate (Oriahnn)** may be considered medically necessary when the following criteria below are met:
 - A. Member is 18 years of age or older; **AND**
 - B. Member must be premenopausal; **AND**
 - C. Member does not have history of osteoporosis (defined as a T-score less than or equal to -2.5 or Z-score less than -1.5 at the lumbar spine, femoral neck or total hip); **AND**
 - D. Provider attests the member is not pregnant and does not have plans to become pregnant; **AND**
 - E. A diagnosis of one of the following:
 1. **Moderate-to-severe pain associated with endometriosis; AND**

- i. Request is for elagolix (Orilissa); **AND**
 - ii. Treatment with one of the following has been ineffective, contraindicated, or not tolerated:
 - a. Nonsteroidal anti-inflammatory drugs (NSAIDs); **OR**
 - b. Hormonal contraceptives (oral, IUD, implant, etc.); **AND**
 - iii. If continued use of estrogen containing contraceptives is planned in combination with elagolix (Orilissa), the provider acknowledges that the efficacy of both the contraceptive and elagolix (Orilissa) may be decreased (use of non-hormonal contraceptives is recommended); **OR**
2. **Heavy menstrual bleeding associated with uterine fibroids; AND**
- i. Request is for elagolix/estradiol/norethindrone acetate (Oriahnn); **AND**
 - ii. Treatment with hormonal contraceptives (oral, IUD, implant, etc.) has been ineffective, contraindicated, or not tolerated

Renewal Evaluation

- I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
- II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
- III. Absence of unacceptable toxicity from the drug, such as, fractures due to loss of bone mineral density; **AND**
- IV. Provider attests the member is not pregnant and does not have plans to become pregnant; **AND**
- V. **Elagolix (Orilissa):**
 - A. Member has experienced a clinical improvement in pain symptoms relating to endometriosis; **AND**
 1. If the request is for elagolix (Orilissa) 150 mg; the member has not received treatment with elagolix (Orilissa) 150 mg for more than 24 months; **OR**
 2. If the request is for elagolix (Orilissa) 200 mg; the member has not received treatment with elagolix (Orilissa) 200 mg for more than 6 months; **OR**
- II. **Elagolix/estradiol/norethindrone acetate (Oriahnn):**
 - A. Member has exhibited improvement of disease symptoms (significant/sustained reduction in menstrual blood loss per cycle, improved quality of life, etc.); **AND**
 1. The member has not received treatment for more than 24 months

Supporting Evidence

- I. Elagolix (Orilissa) is an oral GnRH antagonist for the management of moderate to severe pain associated with endometriosis. The drug was studied in two randomized, double-blind, placebo-controlled, Phase 3, trials (Study EM-1 and Study EM-2; Elaris Endometriosis I and II).
 - At three months, both elagolix (Orilissa) 150 mg and 200 mg regimens showed a higher proportion of responders compared to placebo. Both treatment arms showed statistically significant differences in greater mean decreases in non-menstrual pelvic pain scores from baseline at six months.
- II. The FDA-approved maximum duration of use for 150 mg tablets is 24 months, though clinical trials only studied up to 12 months. The FDA-approved maximum duration of use for 200 mg tablets is six months. These FDA maximum durations of treatment are recommended due to loss of bone marrow density as seen in clinical trials. Bone loss of more than 5% was seen in lumbar spine, total hip, and femoral neck within six months of treatment. Studies have not yet been completed to evaluate in combination with bone loss prevention treatments.
- III. For the treatment of pain associated with endometriosis there are no studies supporting one treatment, or treatment combination, over another. Treatment choice is based upon symptom severity, patient preferences, medication side effects, treatment efficacy, contraceptive needs, costs, and availability. Treatments commonly used first-line are NSAIDs and continuous hormonal contraceptives because these therapies are low-risk, have few side effects, and provide relief of symptoms for many women. Second-line treatments include GnRH agonists (leuprolide depot (Lupron), nafarelin acetate (Synarel), goserelin acetate (Zoladex), etc.), progestins, and danazol.
- IV. Due to the mechanism of action, use of estrogen containing contraceptives are expected to reduce the efficacy of elagolix (Orilissa); likewise, use of elagolix (Orilissa) will reduce efficacy of estrogen containing oral contraceptives. To avoid drug interactions, use of non-hormonal contraceptives during treatment with elagolix (Orilissa) is recommended.
- V. For the treatment of heavy menstrual bleeding associated with uterine fibroids there is a lack of randomized trial data demonstrating the effectiveness of medical therapies. Treatment options include hormonal contraceptives (oral, IUD, implant, etc.), ulipristal acetate (Ella), mifepristone (Korlym, Mifeprex), GnRH agonists (leuprolide depot (Lupron), nafarelin acetate (Synarel), goserelin acetate (Zoladex), etc.), raloxifene (Evista), and danazol. GnRH agonists are the most effective medical therapy but due to side effects are primarily used selectively as preoperative therapy. Surgical treatment options are available, but often cause patients to become incapable of reproduction.
- VI. Elagolix/estradiol/norethindrone acetate (Oriahnn) was evaluated in two six-month, randomized, double-blind, placebo-controlled, Phase 3 trials (Elaris UF-1 and Elaris UF-2) and one six-month, extension trial (Elaris UF-EXTEND). The primary efficacy outcome was the percentage of women who had menstrual blood loss (MBL) volume <80 mL during the final

month and $\geq 50\%$ reduction in MBL volume from baseline to the final month. In Elaris UF-1, the primary outcome was 68.5%, 84.1%, and 8.7% ($p < 0.001$) for elagolix/estradiol/norethindrone acetate (Oriahnn) plus hormonal therapy, elagolix alone, and placebo, respectively. In Elaris UF-2, the primary outcome was 76.5%, 76.9%, 10.5% ($p < 0.001$) for elagolix/estradiol/norethindrone acetate (Oriahnn), elagolix alone, and placebo, respectively. In Elaris UF-EXTEND, the primary outcome was 87.9% for elagolix/estradiol/norethindrone acetate (Oriahnn). The hormonal therapy that was used in combination with elagolix was estradiol/norethidone (Activella, Amabelz, Combipatch, Lopreeza, Mimvey Lo, and Mimvey).

- VII. The most common adverse events noted for elagolix/estradiol/norethindrone acetate (Oriahnn) were hot flashes, night sweats, nausea, and headache; however, elagolix/estradiol/norethindrone acetate (Oriahnn) had lower rates of hot flashes and night sweats compared to elagolix (Orilissa). Elagolix/estradiol/norethindrone acetate (Oriahnn) also had a reduced change from baseline in bone mineral density compared to elagolix (Orilissa). Elaris UF-1 had similar rates of discontinuation due to adverse events across all treatment arms; however, in Elaris UF-2, elagolix (Orilissa) had a discontinuation rate of 12.6% compared to 8.5% and 5.3% for elagolix/estradiol/norethindrone acetate (Oriahnn) and placebo, respectively. Elaris UF-EXTEND had lower rates of adverse events in the final six months compared to Elaris UF-1 and UF-2.
- VIII. Clinical trials excluded patients with a Z-score less than -1.5 at the lumbar spine, femoral neck or total hip. Bone loss of more than 5% was seen in lumbar spine, total hip, and femoral neck within six months of treatment. Studies have not yet been completed to evaluate elagolix (Orilissa) and elagolix/estradiol/norethindrone acetate (Oriahnn) in combination with bone loss prevention treatments.
- IX. Elagolix (Orilissa) and elagolix/estradiol/norethindrone acetate (Oriahnn) are contraindicated in pregnant patients due to an increased risk of early pregnancy loss.

References

1. Orilissa [Prescribing Information]. North Chicago, IL: AbbVie Inc.; July 2018.
2. Oriahnn [Prescribing Information]. North Chicago, IL: AbbVie Inc.; May 2020.
3. UpToDate, Inc. Endometriosis: Treatment of pelvic pain. UpToDate [database online]. Waltham, MA. Updated July 29, 2019.
4. UpToDate, Inc. Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women. UpToDate [database online]. Waltham, MA. Updated July 11, 2019.
5. Taylor HS, Giudice LC, Lessey BA et al. Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. *N Engl J Med*. 2017;377:28-40. doi: 10.1056/NEJMoa1700089.
6. UpToDate, Inc. Overview of treatment of uterine leiomyomas (fibroids). UpToDate [database online]. Waltham, MA. Updated November 11, 2019.
7. Gillispie V, Muneyyirci-Delale O, Kim J, Liu R, et al. Up to 12 months of efficacy and safety of elagolix treatment in women with heavy menstrual bleeding associated with uterine fibroids. Presented at the American Association of Gynecologic Laparoscopists, November 9-13, 2019; Vancouver, Canada.

8. Schlaff W, Al-Hendy A, Barnhart K, et al. Elagolix Reduced Heavy Menstrual Bleeding with Uterine Fibroids: Primary, 6-month, Phase 3 Results. Presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists, May 3-6, 2019; Nashville, Tennessee, USA.
9. Bradley L, Feinberg E, Liu R, et al. Elagolix Treatment in Women with Uterine Fibroids: Secondary, 6-Month, Phase 3 Efficacy Results. Presented at the 2019 American College of Obstetricians and Gynecologists Annual Clinical and Scientific Meeting, May 3-6, 2019; Nashville, Tennessee, USA.

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed criteria: "Must be used in combination with a estradiol/norethindrone acetate product (Activella, Combipatch, Mimvey Lo, etc.)" from the indication heavy menstrual bleeding associated with uterine fibroids	12/2020
Added criteria for treatment of heavy menstrual bleeding associated with uterine fibroids, added requirements for premenopause and confirmation member is not pregnant. Also added NSAIDS as an option for trial and failure for pain associated with endometriosis.	12/2019
Transition from criteria to policy	09/2019
Criteria created	10/2018