Pharmacy Policy Bulletin: J-0278 Elagolix and Relugolix-Containing Products – Commercial and Healthcare Reform	
Number: J-0278	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0278-008	**Original Date:** 08/05/2020
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Oriahnn (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) • Myfembree (relugolix, estradiol, norethindrone acetate) • Orilissa (elagolix)

FDA-Approved Indication(s):	• Oriahnn
	  ○ Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women
	• Myfembree
	  ○ Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women
	  ○ Management of moderate to severe pain associated with endometriosis in premenopausal women
	• Orilissa
	  ○ Management of moderate to severe pain associated with endometriosis

Background:	• Elagolix and relugolix are gonadotropin-releasing hormone (GnRH) receptor antagonists that lead to the suppression of luteinizing hormone and follicle-stimulating hormone resulting in decreased bleeding. Estradiol reduces the increase in bone resorption and bone loss while norethindrone acetate protects the uterus from the adverse endometrial effects of estradiol. **<u>Uterine Leiomyomas (Fibroids)</u>** • Uterine fibroids are the most common tumors present in premenopausal women affecting between 20% and 80% of women in the United States (U.S.) by the age of 50. Fibroids are benign muscle tumors that usually resolve after menopause; however, fibroids are a leading reason for hysterectomy in the U.S. as they cause severe symptoms such as heavy menstrual bleeding and pain. • The American Family Physician (AFP) guidelines recommend GnRH agonists, Mirena, nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, selective progesterone receptor modulators, or tranexamic acid as treatment options for the reduction of blood loss associated with uterine leiomyomas.

Surgical therapies include hysterectomy, magnetic resonance-guided focused ultrasound surgery, myomectomy, or uterine artery embolization.

Endometriosis

- Endometriosis is a disease characterized by the presence of endometrium-like epithelium and/or stroma outside the endometrium and myometrium, usually with an associated inflammatory process. Endometriosis is primarily characterized by symptoms, like pain and infertility. The disease's prevalence is estimated to between 2%-10% in females, and up to 50% in infertile females.
- The 2022 European Society of Human Reproduction and Embryology Endometriosis Guidelines provide the following recommendations for the treatment of endometriosis-related pain:
  - NSAIDs or other analgesics are recommended as an option to reduce endometriosis-associated pain. The recommendation is graded as a weak recommendation since it is limited to one small randomized-controlled trial.
  - Combined hormonal contraceptives, progestogens, or GnRH antagonists are recommended as a strong recommendation.
  - GnRH agonists such as leuprolide are recommended as a strong recommendation for second line therapy if hormonal contraceptives or progestogens have not been effective.
  - GnRH antagonists such as elagolix and relugolix should be used as second line treatment options due to limited evidence when combined hormonal contraceptives or progestogens have not been effective.
  - Danazol may be used for the treatment of endometriosis-associated pain only if no other medical therapy is available due to the side effect profile of Danazol.
  - Aromatase inhibitors are only recommended in patients who are refractory to other medical or surgical treatments.
  - Nafarelin was included in the guidelines as an option for recurrent endometriosis.
- Prescribing considerations
  - Total duration of Oriahnn, Orilissa, or Myfembree should be limited to 24 months in patients due to the risk of bone loss.
  - Oriahnn and Myfembree are contraindicated in patients with liver impairment, osteoporosis, high risk of thromboembolic disorder, current or history of breast cancer, undiagnosed uterine bleeding, hypersensitivity to the ingredients of Oriahnn or Myfembree, and in pregnant patients.
  - Orilissa is contraindicated in patients with osteoporosis, severe hepatic impairment, organic anion transporting polypeptide (OATP) 1B1 inhibitors that significantly increase elagolix plasma concentrations, hypersensitivity to Orilissa or any of its inactive components, and in pregnant patients.
  - Assessment of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter for patients treated with Oriahnn or Myfembree. BMD assessments should be considered in patients taking Orilissa with a history of bone fracture or other osteoporosis or bone loss risk factors.

Approval Criteria

I. Initial Authorization

A. Uterine Leiomyomas (Fibroids)

When a benefit, coverage of Oriahnn or Myfembree may be approved when all of the following criteria are met **(1. through 8.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of uterine leiomyomas (ICD-10: D25).
3. The member is a premenopausal woman.
4. For females of childbearing age, the prescriber attests that the member is not pregnant.
5. The member is experiencing heavy menstrual bleeding.
6. The member does not have a diagnosis of osteoporosis.
7. The member has experienced therapeutic failure or intolerance to at least one (1) prior treatment to reduce menstrual bleeding (for example, IUD, oral contraceptives, tranexamic acid), or contraindication to all.
8. The total combined treatment duration with Oriahnn, Orilissa, and Myfembree has not exceeded 24 months.

B. Endometriosis

When a benefit, coverage of Orilissa or Myfembree may be approved when all of the following criteria are met **(1. through 7.)**:

1. The member is 18 years of age or older.
2. The member has a diagnosis of endometriosis (ICD-10: N80) with documentation of moderate to severe pain.
3. The member is a premenopausal woman.
4. For females of childbearing age, the prescriber attests that the member is not pregnant.
5. The member does not have a diagnosis of osteoporosis.
6. The member has experienced therapeutic failure, contraindication, or intolerance to at least two (2) of the following standard of care treatments **(a. through d.)**:
   a. Generic NSAID
   b. Combined hormonal contraceptive
   c. Progestin (specifically, medroxyprogesterone injection)
   d. GnRH agonist (for example, leuprolide)
7. The total combined treatment duration with Oriahnn, Orilissa, and Myfembree has not exceeded 24 months.

II. Reauthorization

A. Uterine Leiomyomas

When a benefit, reauthorization of Oriahnn or Myfembree may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member continues to experience heavy menstrual bleeding.
2. The prescriber attests that there has been a decrease in menstrual blood loss from baseline.
3. The prescriber attests that the benefit of treatment exceeds the risk of bone loss.
4. The total combined treatment duration with Oriahnn, Orilissa, and Myfembree has not exceeded 24 months.
5. For females of childbearing age, the prescriber attests that the member is not pregnant.

B. Endometriosis

When a benefit, reauthorization of Orilissa or Myfembree may be approved when all of the following criteria are met **(1. through 4.)**:

1. The prescriber attests that the member has experienced a reduction in pain associated with endometriosis.
2. The prescriber attests that the benefit of treatment exceeds the risk of bone loss.
3. The total combined treatment duration with Oriahnn, Orilissa, and Myfembree has not exceeded 24 months.
4. For females of childbearing age, the prescriber attests that the member is not pregnant.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Oriahnn, Orilissa, and Myfembree should not be used in severe hepatic impairment.
II. Coverage of drug(s) addressed in this policy for disease states outside of their FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
III. For Commercial and HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization:

- Commercial and HCR Plans: If approved, up to a 6 month authorization may be granted for Oriahnn, Orilissa, and Myfembree.
    - The total combined treatment duration with Oriahnn, Orilissa, and Myfembree should not exceed 24 months
    - Total cumulative treatment duration with Orilissa 200 mg should not exceed 6 months.

Reauthorization:

- Commercial and HCR Plans: If approved, up to an 18 month authorization may be granted.
    - The total combined treatment duration with Oriahnn, Orilissa, and Myfembree should not exceed 24 months
    - Total cumulative treatment duration with Orilissa 200 mg should not exceed 6 months.

Automatic Approval Criteria

None

References:

1. Oriahnn [package insert]. North Chicago, IL: AbbVie Inc; June 2023.
2. Myfembree [package insert]. Mississauga, Ontario: Myovant Sciences; January 2023.
3. Orilissa [package insert]. North Chicago, IL: AbbVie Inc.; June 2023.
4. U.S. Food & Drug Administration. FDA News Release. FDA Approves New Option to Treat Heavy Menstrual Bleeding Associated with Fibroids in Women. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-option-treat-heavy-menstrual-bleeding-associated-fibroids-women. Accessed August 15, 2022.
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8. 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.
9. Falcone T, Lebovic DI. Clinical management of endometriosis. *Obstetrics & Gynecology*. 2011;118(3):691-7
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