PRIOR AUTHORIZATION POLICY

POLICY: Gonadotropin-Releasing Hormone Antagonists – Myfembree Prior Authorization Policy
- Myfembree® (relugolix, estradiol, and norethindrone acetate tablets – Sumitomo Pharma)

REVIEW DATE: 04/19/2024

OVERVIEW

Myfembree, an oral gonadotropin-releasing hormone (GnRH) receptor antagonist with added estrogen and progestin therapy, is indicated for the following uses:[1]

- 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.

Limitation of Use. Use should be limited to 24 months due to the risk of continued bone loss which may not be reversible.[1]

Disease Overview

Uterine fibroids (leiomyomas) are benign tumors. They are the most frequent gynecologic benign disease.[2] Fibroids can be asymptomatic or cause symptoms; symptoms generally present as abnormal (heavy) uterine bleeding or pelvic pain/pressure. Heavy menstrual bleeding can cause associated problems, such as iron deficiency anemia. The actual prevalence of uterine fibroids is difficult to ascertain since many patients are asymptomatic, but it is estimated that fibroids can be detected in up to 80% of women by 50 years of age.[3]

Endometriosis is a condition where the tissues similar to the lining of the uterus (or endometrium) migrate outside of the womb to other body sites.[4,5] The migrated tissues are generally found in the pelvic cavity (e.g., peritoneum, uterosacral ligaments, rectal-vaginal septum, or any spaces between the bladder, uterus, vagina, and rectum) and can attach to any of the female reproductive organs (e.g., ovaries, fallopian tubes). The migrated tissue is less commonly found outside the pelvic cavity or on the intestines, colon, appendix or rectum. Endometriosis impacts up to 10% of patients of reproductive age in the US.[5]

Guidelines

Abnormal Uterine Bleeding/Uterine Leiomyomata (Fibroids)

Myfembree is addressed in the American College of Obstetrician and Gynecologists (ACOG) guidelines on the management of symptomatic uterine leiomyomas (2021) as a medication under clinical study (prior to FDA approval).[6] Medical treatment options for uterine leiomyomas include agents that address only bleeding symptoms, such as GnRH antagonists, levonorgestrel-releasing intrauterine devices, contraceptive steroids, and tranexamic acid. Agents that reduce both bleeding and leiomyoma size include GnRH agonists and selective progesterone receptor modulators (SPRMs). SPRMs are not approved in the US for the treatment of uterine leiomyomas. An oral GnRH antagonist, such as Oriahnn or Myfembree, can be considered for the treatment of abnormal uterine bleeding related to leiomyomas for up to 2 years. The hormonal add-back therapy is indicated to offset the hypoestrogenic effects of the product.

Endometriosis

According to the ACOG practice bulletin on the management of endometriosis (2010, reaffirmed 2018), empiric therapy with a 3-month course of a GnRH agonist is appropriate after an appropriate pretreatment

evaluation (to exclude other causes of chronic pelvic pain) and failure of initial treatment with oral contraceptives and nonsteroidal anti-inflammatory drugs (NSAIDs).[7]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Myfembree. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Myfembree as well as the monitoring required for adverse events and long-term efficacy, approval for certain diagnoses requires Myfembree to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Myfembree is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Uterine Fibroids (Leiomyomas).** Approve for up to 24 months if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   Note: Approve for **up to** 24 months. For example, a patient who has already received 6 months of treatment with Myfembree should be approved for a duration of 18 months.
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient is PREmenopausal (before menopause); AND
   - **C)** Patient is experiencing heavy menstrual bleeding associated with the uterine fibroids; AND
   - **D)** Uterine fibroids have been confirmed by a pelvic ultrasound, including transvaginal ultrasonography or sonohysterography; hysteroscopy; or magnetic resonance imaging; AND
   - **E)** Patient has tried at least one other therapy for the medical management of heavy menstrual bleeding; AND
     Note: Examples of therapy for the medical management of heavy menstrual bleeding include combination estrogen-progestin contraceptives (oral tablets, vaginal ring, transdermal patch), levonorgestrel-releasing intrauterine systems (e.g., Mirena, Liletta), oral progesterone (e.g., medroxyprogesterone acetate), depo-medroxyprogesterone injection, tranexamic acid tablets.
   - **F)** Patient has not previously received a continuous regimen of 24 months or longer of therapy with Myfembree or Oriahnn; AND
   - **G)** The medication is prescribed by or in consultation with an obstetrician-gynecologist or a health care practitioner who specializes in the treatment of women's health.

2. **Endometriosis.** Approve for up to 24 months if the patient meets ALL of the following criteria (A, B, and C):
   Note: Approve for **up to** 24 months. For example, a patient who has already received 6 months of treatment with Myfembree should be approved for a duration of 18 months.
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient is PREmenopausal (before menopause); AND
   - **C)** Patient has previously tried ONE of the following, unless contraindicated (i or ii):
     Note: An exception to this requirement can be made if the patient has previously used a gonadotropin-releasing hormone agonist (e.g., Lupron Depot [leuprolide depot injection]) or Orilissa (elagolix tablets).

i. A contraceptive (e.g., combination oral contraceptives, levonorgestrel-releasing intrauterine systems [e.g., Mirena {levonorgestrel intrauterine system}, Liletta {levonorgestrel intrauterine system}], depo-medroxyprogesterone injection); OR
ii. An oral progesterone (e.g., norethindrone tablets).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Myfembree is not recommended in the following situations:

1. **Heavy Menstrual Bleeding not associated with Uterine Fibroids.** Myfembree has shown efficacy in reducing heavy menstrual bleeding only in women with uterine fibroids.[1]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Myfembree® tablets [prescribing information]. Marlborough, MA: Sumitomo Pharma; August 2023.
2. Neri M, Melis G, Giancane E, et al. Clinical utility of elagolix as an oral treatment for women with uterine fibroids: A short report on the emerging efficacy data. *Int J Womens Health*. 2019;11:535-546.
3. De La Cruz MS, Buchanan EM. Uterine Fibroids: Diagnosis and Treatment. *Am Fam Physician.* 2017;95(2):100-107.
4. Endometriosis. Endometriosis Foundation of America. Updated 9/28/2022. Available at: https://www.endofound.org/endometriosis. Accessed on April 5, 2024.
5. Global Forum. Endometriosis.org. Available at: http://endometriosis.org/endometriosis/. Accessed on April 5, 2024.
6. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin. Management of Symptomatic Uterine Leiomyomas. No. 228. June 2021. Available at: https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2021/06/management-of-symptomatic-uterine-leiomyomas. Accessed on April 5, 2024.
7. Management of Endometriosis. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists. Number 114. 2010 (reaffirmed 2018). *Obstet & Gynecol*. 2010;116(1):223-236.