Drug Coverage Policy

Effective Date 7/15/2025
Coverage Policy Number.....IP0205
Policy Title.....Myfembree

Gonadotropin-Releasing Hormone Antagonists – Myfembree

- Myfembree® (relugolix, estradiol, and norethindrone acetate tablets – Sumitomo Pharma)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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). 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]

Coverage Policy

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 requires Myfembree to be prescribed by a physician who has consulted with or who specializes in the condition.

Myfembree is considered medically necessary when ONE of the following is met:

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).

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Myfembree for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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]

References

1. Myfembree® tablets [prescribing information]. Marlborough, MA: Sumitomo; July 2024.
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 18, 2025.
5. Global Forum. Endometriosis.org. Available at: http://endometriosis.org/endometriosis/. Accessed on April 18, 2025.
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 18, 2025.
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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Uterine Fibroids (Leiomyomas).** **Updated** 'Uterine fibroids have been confirmed by imaging' TO 'Uterine fibroids have been confirmed by a pelvic ultrasound, including transvaginal ultrasonography or sonohysterography; hysteroscopy; or magnetic resonance imaging' **Uterine Fibroids (Leiomyomas), Endometriosis.** **Updated** authorization duration from 12 months to 24 months	8/1/2024
Annual Revision	No criteria changes.	7/15/2025

The policy effective date is in force until updated or retired.