BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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Myfembree® (relugolix, estradiol hemihydrate, norethindrone acetate) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Myfembree (relugolix, estradiol hemihydrate, norethindrone acetate) is considered ***medically necessary*** and will be approved when **ALL** of 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 woman 18 years of age or older

  3. A confirmed diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women diagnosed by ultrasound

  4. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Bone Mineral Density (BMD) assessment by dual-energy X-ray absorptiometry (DXA)
     b. Negative Pregnancy Test

  5. Documented failure, contraindication per FDA label, intolerance, or not a candidate to **BOTH** of the following:
     a. Hormone contraception (e.g., estrogen-progestin oral, vaginal ring or transdermal patch, or progestin-releasing intrauterine device)
     b. Tranexamic acid

  6. There are **NO** FDA-label contraindications, such as:
     a. High risk of arterial, venous thrombotic, or thromboembolic disorder (see Definition Section)
     b. Pregnancy
     c. Known osteoporosis
     d. Current or history of breast cancer or other hormone-sensitive malignancies
     e. Known hepatic impairment or disease
     f. Undiagnosed abnormal uterine bleeding

  7. Individual has not previously received 24 months or longer of any gonadotropin-releasing hormone (GnRH) antagonists (e.g., Myfembree, Oriahnn, Orilissa).

  8. Will not be used with hormonal contraceptives or other GnRH antagonists (e.g., Oriahnn, Orilissa).

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Myfembree (relugolix, estradiol hemihydrate, norethindrone acetate) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gynecologist

2. Individual's condition has responded
    a. Response is defined as
        i. Reduction of menstrual blood loss by at least 50%

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Uncontrolled blood pressure
        ii. Gall bladder disease or jaundice
        iii. Suicidal ideation

5. There are no significant interacting drugs

6. Individual has not previously received 24 months or longer of any GnRH antagonists (e.g., Myfembree, Oriahnn, Orilissa).

7. Will not be used with hormonal contraceptives or other GnRH antagonists (e.g., Oriahnn, Orilissa)

Renewal duration: 12 months
NOTE: Maximum total duration of approval is 24 months due to the risk of continued bone loss which may not be reversible

- 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 a Non-Cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

Description:

Uterine leiomyomas are noncancerous tumors that may arise in females of reproductive age. They are common in premenopausal women but are largely asymptomatic and often go undiagnosed. It is estimated that 25% of women with leiomyomas have symptoms clinically significant enough to require intervention. The most common presenting symptoms include prolonged or heavy bleeding, with or without anemia and menstrual cramping. Other bulk-related symptoms arise from an enlarged uterus, which may include feelings of fullness similar to pregnancy, urinary frequency, constipation, pressure and pain. Additionally, leiomyomas may cause reproductive dysfunction.

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Treatment of symptomatic uterine leiomyomas includes expectant (monitoring), medical, interventional, and surgical therapies. Medical treatments primarily address bleeding symptoms and procedural and surgical approaches decrease uterine or fibroid mass. Medical treatment options that address bleeding symptoms are GnRH antagonists, levonorgestrel-releasing intrauterine devices (IUDs), contraceptive steroids and tranexamic acid. GnRH agonists reduce both bleeding and leiomyoma size but are primarily used as a bridge to a procedure or surgery due to their risk of blood loss and regrowth of fibroids after drug cessation.

Myfembree is a combination of relugolix, a gonadotropin-releasing hormone (GnRH) receptor antagonist, estradiol, an estrogen, and norethindrone acetate, a progestin. It is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Myfembree use should be limited to 24 months due to the risk of continued bone loss which may not be reversible. The combination of a GnRH antagonist with an estrogen and progestin is considered “add-back” therapy which offsets the hypoestrogenic effects of the GnRH antagonist, minimizing hot flushes, increases in serum lipid levels and loss of bone mineral density.

Definitions:

Examples of women with high risk of arterial, venous thrombotic, or thromboembolic disorders:

- Over 35 years of age who smoke
- Current or history of deep vein thrombosis or pulmonary embolism
- Vascular disease (e.g., cerebrovascular disease, coronary artery disease, peripheral artery disease, peripheral vascular disease
- Thrombogenic valvular or thrombogenic rhythm diseases of the heart (e.g., subacute bacterial endocarditis with valvular disease, or atrial fibrillation)
- Inherited or acquired hypercoagulopathies
- Uncontrolled hypertension
- Headaches with focal neurological symptoms or migraine headaches with aura if over 35 years of age

Resources:

Myfembree product information, revised by Myovant Sciences, Inc. June 2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on July 30, 2021.

Stewart EA. Uterine fibroids (leiomyomas): Treatment Overview. In: UpToDate, Barbierie RL, Chakrabarti A (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on August 6, 2021.

Stewart EA, Laughlin-Tommaso SK. Uterine fibroids (leiomyomas): Epidemiology, clinical features, diagnosis, and natural history. In: UpToDate, Barbierie RL, Levine D, Chakrabarti A (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on August 10, 2021.

Management of symptomatic uterine leiomyomas. ACOG Practice Bulletin No. 228. American College of Obstetricians and Gynecologists. Obstet Gynecol 2021;137:e100-15.