Novel Medications for the Treatment of Uterine Fibroids

Policy # 00730
Original Effective Date: 02/08/2021
Current Effective Date: 04/11/2022

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Oriahnn™‡ (elagolix/estradiol/norethindrone) or Myfembree®‡ (relugolix/estradiol/norethindrone) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Oriahnn (elagolix/estradiol/norethindrone) or Myfembree (relugolix/estradiol/norethindrone) will be considered when the following criteria are met:

- Patient has a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids); AND
- Patient is premenopausal; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE other therapy to treat the condition unless there is clinical evidence or patient history that suggests the use of the alternative products will be ineffective or cause an adverse reaction to the patient. Alternative therapies include estrogen/progesterone combination oral contraceptives (e.g., afirmelle, apri, aviane, desogestrel-ethinyl estradiol, drospirenone-ethinyl estradiol, junel, larin, larissia, levonorgestrel-ethinyl estradiol, norethindrone acetate-ethinyl estradiol, nortrel, zarah), oral progesterone, levonorgestrel-releasing intrauterine systems (e.g., Mirena®, Liletta®)‡ and depo-medroxyprogesterone injection; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Oriahnn and/or Myfembree will not be used for longer than 24 months (alone or in combination).

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Oriahnn (elagolix/estradiol/norethindrone) or Myfembree (relugolix/estradiol/norethindrone) when the patient has not tried and failed at least one other therapy used to treat the condition to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Oriahnn (elagolix/estradiol/norethindrone) or Myfembree (relugolix/estradiol/norethindrone) when patient selection criteria are not me (except those noted above as **not medically necessary****) to be **investigational.***

Background/Overview

Oriahnn contains elagolix, a gonadotropin-releasing hormone (GnRH) receptor antagonist that binds to GnRH receptors in the pituitary gland and results in suppression of luteinizing hormone (LH) and follicle stimulating hormone (FSH). Myfembree contains relugolix which is also a GnRH receptor antagonist. Both of these compounds decrease the blood concentrations of estradiol and progesterone. Oriahnn and Myfembree also contain estradiol and norethindrone which are considered "add back" therapy to attenuate the side effects of GnRH therapy. This combination is indicated to manage heavy menstrual bleeding associated with uterine fibroids in premenopausal women. The recommended dose of Oriahnn is one capsule in the morning (containing elagolix 300 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg) and one capsule in the evening (containing elagolix 300 mg). Myfembree is dosed once daily with once capsule taken at approximately the same time each day. Similar to other estrogen-containing products, these products have boxed warnings for an increased risk of thrombotic or thromboembolic disorders and are contraindicated in women with a current history of thrombotic or thromboembolic disorders or at increased risk for these events. Additionally, the use of these products (alone or in combination with each other) should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

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Uterine leiomyomas (fibroids) are benign tumors that are thought to affect up to 80% of women by the age of 50 years. In most cases, these fibroids are asymptomatic, but they can cause the symptoms of abnormal (heavy) uterine bleeding and pelvic pain or pressure. The clinical diagnosis of uterine fibroids is typically made based upon pelvic examination and pelvic ultrasound. Surgical interventions including hysterectomy and myomectomy still represent the main strategies for uterine fibroid management. Medical management for symptomatic fibroids includes combination oral contraceptives, progestins, and GnRH agonists. The goal of medical therapy is to help with symptomatic bleeding and/or pain.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Both Oriahnn and Myfembree are approved for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Oriahnn
The efficacy of Oriahnn in the management of heavy menstrual bleeding associated with uterine fibroids was demonstrated in two identical randomized, double-blind, placebo-controlled studies (Study UF-1 and Study UF-2) in which 790 premenopausal women with heavy menstrual bleeding received Oriahnn or placebo for 6 months. Heavy menstrual bleeding at baseline was defined as having at least 2 menstrual cycles with greater than 80 mL of menstrual blood loss (MBL) as assessed by alkaline hematin (AH) method (an objective, validated measure to quantify MBL volume on sanitary products).

The primary endpoint in both studies was the proportion of responders, defined as women who achieved both 1) MBL volume less than 80 mL at the final month and 2) 50% or greater reduction in MBL volume from baseline to the final month. The final month was defined as the last 29 days

before and including the last treatment visit date or last dose date. A higher proportion of Oriahnn-treated women were responders compared to placebo-treated women. In Study UF-1, 68.5% met the primary endpoint in the Oriahnn group vs 8.7% in the placebo group ($p<0.001$). In Study UF-2, 76.5% met the primary endpoint in the Oriahnn group vs 10.5% in the placebo group ($p<0.001$).

Myfembree
The efficacy and safety of Myfembree were evaluated in two replicate, 24-week, multinational, randomized, double-blind, placebo-controlled studies in a total of 768 premenopausal women with heavy menstrual bleeding associated with uterine fibroids in Study L1 and Study L2. For study inclusion, women had to have uterine fibroids confirmed by ultrasound examination in which at least one fibroid met at least one of the following criteria:

- Subserosal, intramural, or <50% intracavitary submucosal fibroid with a diameter ≥2 cm, or
- Multiple small fibroids with a total uterine volume of ≥130 cm^3.

Women also had to have MBL volume of ≥80 mL per cycle for 2 menstrual cycles or ≥160 mL during one cycle quantified by the alkaline hematin method. Women with hemoglobin <8 g/dL were excluded from the study. Iron therapy was required for women with hemoglobin ≤10 g/dL.women were allowed, but not required, to take calcium and vitamin D during the study.

In both studies, women were randomized 1:1:1 to receive a once daily relugolix 40 mg tablet plus an over encapsulated tablet of estradiol 1 mg and norethindrone 0.5 mg for 24 weeks, placebo for 24 weeks, or relugolix 40 mg monotherapy for 12 weeks followed by Myfembree for 12 weeks. Treatment was initiated within the first seven days after the onset of menses.

The primary endpoint was the proportion of women in the Myfembree group compared with women in the placebo group who achieved MBL volume of <80 mL and at least a 50% reduction from baseline MBL volume over the last 35 days of treatment, as measured by the alkaline hematin method. In both studies, a statistically higher proportion of women treated with Myfembree achieved the primary endpoint with 72.1% achieving it in study L1 compared to 16.8% in the placebo arm and 71.2% achieving it in study L2 compared to 14.7% in the placebo arm.

References

1. Oriahnn [package insert]. AbbVie Inc. North Chicago, IL. Updated May 2020.

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2. Oriahnn Drug Evaluation. Express Scripts. Updated June 2020.
3. Myfembree [package insert]. Myovant Sciences, Inc. Brisbane, CA. Updated October 2021.

Policy History

Original Effective Date: 02/08/2021
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01/07/2021	Medical Policy Committee review
01/13/2021	Medical Policy Implementation Committee approval. New policy.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. No change to coverage.
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Added new product, Myfembree, to policy with relevant criteria and background information. Changed title from "Oriahnn (elagolix/estradiol/norethindrone)" to "Novel Medications for the Treatment of Uterine Fibroids."

Next Scheduled Review Date: 03/2023

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or

3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.