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Section:	Prescription Drugs	Effective Date:	October 1, 2023
Subsection:	Endocrine and Metabolic Drugs	Original Policy Date:	June 18, 2021
Subject:	Myfembree	Page:	1 of 5

Last Review Date: September 8, 2023

Myfembree

Description

Myfembree (relugolix, estradiol, and norethindrone acetate)

Background

Myfembree combines relugolix, estradiol (E2), and norethindrone acetate (NETA). Relugolix is a GnRH receptor antagonist that binds competitively to pituitary GnRH receptors, thereby reducing the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased serum concentrations of the ovarian sex hormones estradiol and progesterone and reduced bleeding associated with uterine fibroids (1).

Estradiol acts by binding to nuclear receptors that are expressed in estrogen-responsive tissues. As a component of Myfembree, the addition of exogenous estradiol may reduce the increase in bone resorption and resultant bone loss that can occur due to a decrease in circulating estrogen from relugolix alone (1).

Progestins such as norethindrone act by binding to nuclear receptors that are expressed in progesterone-responsive tissues. As a component of Myfembree, norethindrone may protect the uterus from the potential adverse endometrial effects of unopposed estrogen (1).

Regulatory Status

FDA-approved indications: Myfembree is indicated in premenopausal women for the: (1)

- management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids).
- management of moderate to severe pain associated with endometriosis.

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Limitations of Use: Use of Myfembree should be limited to 24 months due to the risk of continued bone loss, which may not be reversible (1).

Myfembree has a boxed warning regarding the increased risk of thromboembolic disorders and vascular events, especially in women at increased risk for these events. Myfembree is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke or women with uncontrolled hypertension (1).

Pregnancy should be excluded before starting Myfembree. The recommended total duration of treatment with Myfembree is 24 months (1).

Myfembree is contraindicated in women with known osteoporosis. Myfembree may cause a decrease in bone mineral density (BMD) in some patients. BMD loss may be greater with increasing duration of use and may not be completely reversibly after stopping treatment. The duration of use should be limited to 24 months to reduce the extent of bone loss (1).

Myfembree also has a warning regarding depression, mood disorders, and suicidal ideation. Promptly evaluate patients with mood changes and depressive symptoms to determine whether the risks of continued therapy outweigh the benefits. Advise patients to seek immediate medical attention for suicidal ideation and behavior. Reevaluate the benefits and risks of continuing Myfembree if such events occur (1).

Myfembree is contraindicated in patients with known hepatic impairment or disease (1).

The safety and effectiveness of Myfembree in pediatric patients less than 18 years of age have not been established (1).

Related policies

Oriahnn, Orilissa

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Myfembree may be considered **medically necessary** if the conditions indicated below are met.

Myfembree may be considered **investigational** for all other indications.

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Prior-Approval Requirements

Age 18 years of age and older

Gender Female

Diagnoses

Patient must have **ONE** of the following:

1. Heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
2. Moderate to severe pain associated with endometriosis

AND ALL of the following:

1. Patient is premenopausal
2. Pregnancy has been excluded
3. Medication is being prescribed by or in consultation with an obstetrician-gynecologist (OB-GYN)
4. Patient has **NOT** already used Myfembree or Oriahnn cumulatively for 24 months
5. **NOT** used in combination with Oriahnn
6. Patient does **NOT** have current, or history of thrombotic or thromboembolic disorders **AND** patient is not at increased risk for these events (e.g., women over 35 years of age who smoke or women with uncontrolled hypertension)
7. **NO** known liver impairment or disease (e.g., clinically significant elevated transaminases > 2-3 times upper limit of normal, fibrosis F1-F4, etc.)
8. **NO** known osteoporosis
9. Prescriber agrees to monitor for suicidal ideation and mood disorders

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Gender Female

Diagnoses

Patient must have **ONE** of the following:

1. Heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
2. Moderate to severe pain associated with endometriosis

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AND ALL of the following:

1. Documented improvement in patient's condition
2. Medication is being prescribed by or in consultation with an obstetrician-gynecologist (OB-GYN)
3. Patient has **NOT** already used Myfembree or Oriahnn cumulatively for 24 months
4. **NOT** used in combination with Oriahnn
5. Patient does **NOT** have current, or history of thrombotic or thromboembolic disorders **AND** patient is not at increased risk for these events (e.g., women over 35 years of age who smoke or women with uncontrolled hypertension)
6. **NO** known liver impairment or disease (e.g., clinically significant elevated transaminases > 2-3 times upper limit of normal, fibrosis F1-F4, etc.)
7. **NO** known osteoporosis
8. Prescriber agrees to monitor for suicidal ideation and mood disorders

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 84 tablets per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 84 tablets per 84 days

Duration 12 months – **One renewal ONLY**

Rationale

Summary

Myfembree combines relugolix, estradiol, and norethindrone acetate. Myfembree is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) or for moderate to severe pain associated with endometriosis. The duration of use should be

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limited to 24 months to reduce the extent of bone loss. The safety and effectiveness of Myfembree in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Myfembree while maintaining optimal therapeutic outcomes.

References

1. Myfembree [package insert]. Brisbane, CA: Myovant Sciences, Inc.; January 2023.

Policy History

Date	Action
June 2021	Addition to PA
September 2021	Annual review. Added "> 2-3 times upper limit of normal" to define clinically significant elevated transaminases per SME
March 2022	Annual editorial review. Added requirement "not used in combination with Oriahnn"
August 2022	Per PI update, addition of indication: moderate to severe pain associated with endometriosis
December 2022	Annual review and reference update
June 2023	Annual review and reference update
September 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 8, 2023 and is effective on October 1, 2023.