Clinical Policy Title:	relugolix, estradiol, and norethindrone acetate
Policy Number:	RxA.696
Drug(s) Applied:	Myfembree®
Original Policy Date:	08/17/2021
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Relugolix, estradiol, and norethindrone acetate (Myfembree®) is a combination of relugolix, a gonadotropin-releasing hormone (GnRH) receptor antagonist, estradiol, an estrogen, and norethindrone acetate, a progestin, indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
relugolix, estradiol, and norethindrone acetate (Myfembree®)	Heavy menstrual bleeding associated with uterine leiomyomas (fibroids)	Take relugolix 40 mg/day; estradiol 1 mg/day; norethindrone acetate 0.5 mg/day (one tablet) orally once daily.	relugolix 40 mg/day; estradiol 1 mg/day; norethindrone acetate 0.5 mg/day

Dosage Forms

- Tablets: fixed-dose combination containing relugolix 40 mg, estradiol 1 mg and norethindrone acetate 0.5 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Heavy menstrual bleeding associated with uterine leiomyomas (fibroids) (must meet all):

1. Diagnosis of heavy menstrual bleeding associated with uterine leiomyoma (fibroids);
2. Prescribed by or in consultation with Obstetricians/gynecologists;
3. Member must be ≥ 18 years of age and premenopausal;
4. Member must meet all the following (a, b, and c):
   a. Uterine fibroids confirmed by ultrasound examination in which at least one fibroid met at least one

of the following criteria (i or ii);
   i. Subserosal, intramural, or < 50% intracavitary submucosal fibroid with a diameter ≥ 2 cm;
   ii. Multiple small fibroids with a total uterine volume of ≥ 130cm^3;
b. Women has menstrual blood loss (MBL) volume of ≥ 80 mL per cycle for two menstrual cycles or ≥ 160 mL during one cycle quantified by the alkaline hematin method;
c. Women has hemoglobin ≥ 8 g/dL;

5. Documentation of failure, intolerance, or contraindication to one or more prior treatments to reduce menstrual bleeding (oral contraceptives, levonorgestrel-releasing intrauterine systems, oral progesterone, etc.)
6. Dose does not exceed relugolix 40 mg/day; estradiol 1 mg/day; norethindrone acetate 0.5 mg/day orally.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Heavy menstrual bleeding associated with uterine leiomyomas (fibroids) (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, dose does not exceed relugolix 40 mg/day; estradiol 1 mg/day; norethindrone acetate 0.5 mg/day orally.

Approval Duration
Commercial: 24 months
Medicaid: 24 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
MBL: menstrual blood loss
GnRH: gonadotropin-releasing hormone

APPENDIX B: Therapeutic Alternatives
N/A

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - High risk of arterial, venous thrombotic, or thromboembolic disorder.
  - Pregnancy.
  - Known osteoporosis.
  - Current or history of breast cancer or other hormone-sensitive malignancies.
  - Known hepatic impairment or disease.
  - Undiagnosed abnormal uterine bleeding.
  - Known hypersensitivity to components of Myfembree®.

- Boxed Warning(s):
  - Thromboembolic disorders and vascular events.

APPENDIX D: General Information

- Discontinue Myfembree® if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. Discontinue Myfembree® if there is sudden unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- Do not use in women with uncontrolled hypertension. For women with well-controlled hypertension, continue to monitor blood pressure and stop Myfembree® if blood pressure rises significantly.
- Immediately discontinue Myfembree® if a hypersensitivity reaction occurs.
- Can cause early pregnancy loss. Advise women to use effective non-hormonal contraception.

References

1. Myfembree® Prescribing Information. Myovant Sciences, Inc. May 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214846s000lbl.pdf. Accessed August 17, 2021.
2. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Updated May 28, 2021. Accessed August 17, 2021.
3. IPD Analytics Rx Insights_New Drug Approval Review_ Myfembree® _05 2021. Accessed with subscription at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q= Myfembree. Accessed August 17, 2021.
4. Myfembree®. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at https://online.lexi.com. Accessed August 17, 2021.
5. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas. *Obstet Gynecol*. 2008;112(2 Pt 1):387-400. doi:10.1097/AOG.0b013e318183fbab

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	8/17/2021	09/14/2021