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:	12/1/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

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 uterine leiomyoma (fibroids) confirmed by ultrasound;
2. Prescribed by or in consultation with an obstetrician/gynecologist;
3. Member has experienced heavy menstrual bleeding for at least 2 consecutive cycles;
4. Member is premenopausal
5. Member has not already received ≥ 24 cumulative months of Myfembree® therapy;
6. Member meets one of the following (a or b):
   a. Trial and failure of a 30-day trial of any of the following unless contraindicated or clinically significant adverse effects are experienced (i, ii or iii):
      i. Combination estrogen-progestin contraceptive agent;
      ii. Progestin;
      iii. Tranexamic acid;
   b. Member has had a previous interventional therapy to reduce bleeding;
7. Member has not received more than 24 cumulative months of Myfembree® therapy.

Approval Duration

All Lines of Business (except Medicare): 12 months

B. Endometriosis (must meet all):

1. Diagnosis of moderate to severe pain due to endometriosis;
2. Prescribed by or in consultation with a gynecologist or reproductive endocrinologist;
3. Member is premenopausal
4. Member meets one of the following criteria (a or b);
   a. Trial and failure of a 30-day trail agent from one of the following unless clinically significant adverse effects are experienced, or all are contraindicated (i or ii):
      i. Danazol
      ii. Combination progestin-containing contraceptive
   b. Member has had surgical ablation to prevent recurrence;
5. Member has not received more than 24 cumulative months of Myfembree® therapy

Approval Duration
All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication, excluding manufacturer samples;
2. Member has not received more than 24 cumulative months of Myfembree® therapy;

Approval Duration
All Lines of Business (except Medicare): 12 months

References

1. Acog practice bulletin no. 96: alternatives to hysterectomy in the management of leiomyomas. Obstetrics & Gynecology. 2008;112(2):387-400. Available at: https://journals.lww.com/greenjournal/Fulltext/2008/08000/ACOG_Practice_Bulletin_No__96__Alternatives_to.38.aspx. Accessed March 02, 2023.
2. American College of Obstetricians and Gynecologists. Practice bulletin: clinical management guidelines for obstetrician-gynecologist: management of endometriosis. Am J Obstet Gynecol 2010 Jul (reaffirmed 2016); 116(1):223-236. 5. Available at: https://journals.lww.com/greenjournal/Citation/2010/07000/Practice_Bulletin_No__114__Management_of.41.aspx . Accessed March 02, 2023.
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins– Gynecology. Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228. Obstet Gynecol. 2021 Jun 1;137(6):e100-e115. Available at: https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2021/06/management-of-symptomatic-uterine-leiomyomas. Accessed March 02, 2023.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	8/17/2021	09/14/2021
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated indication from Diagnosis of uterine leiomyoma (fibroids) to Diagnosis of uterine leiomyoma (fibroids) confirmed by ultrasound. 2. Initial Approval Criteria, I.A.4: Updated (a and b): a. updated to remove "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 ≥ 130 cm^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	4/26/2022	07/18/2022

method; c. Women has hemoglobin ≥ 8 g/dL;" b. and updated to include new diagnostic criteria Member has experienced heavy menstrual bleeding for at least 2 consecutive cycles. 3. Initial Approval Criteria, I.A.5: Updated trial and failure criteria from 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.) to Trial and failure of a 3 month trial of a combination estrogen-progestin contraceptive agent. 4. Appendix B, Drug Name: Updated to include new therapeutic alternative a. Oriahnn® b. Lupron Depot® c. NSAIDs: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclofenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam. d. Progestin-containing oral contraceptives: norethindrone, ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone. e. Depot injection progestin contraceptives: medroxyprogesterone acetate (DepoProvera®, Depo-SubQ Provera 104®). f. Combination estrogen-progestin contraceptive agent: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone. 5. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 6. References were reviewed and updated.		
Policy was reviewed: 1. Background: Updated to include new drug usage, management of moderate to severe pain associated with endometriosis. 2. Dosing Information, Indication: Updated to include	03/24/2023	04/13/2023

new indication Moderate to severe pain associated with endometriosis. 3. Initial Approval Criteria, I.A.5: Updated to include new criteria pertaining to indication Heavy menstrual bleeding associated with uterine leiomyomas (fibroids), Member has not already received ≥ 24 cumulative months of Myfembree® therapy. 4. Initial Approval Duration for Heavy Menstrual Bleeding associated with Uterine Fibroids was updated from 6 months to 12 months. 5. Initial Approval Criteria, I.B: Updated to include approval criteria for indication, Moderate to severe pain associated with endometriosis. 6. Continued Therapy Approval Criteria, II.A.3: Updated to include new criteria pertaining to indication Heavy Menstrual Bleeding associated with Uterine Fibroids and Moderate to severe pain associated with endometriosis, Member has not already received ≥ 24 cumulative months of Myfembree® therapy. 7. Continued Approval Duration for both indications updated from 24 months to 12 months. *8.* Added "*Total duration of therapy should not exceed 24 months"* verbiage after each approval duration section to reinforce 24-month utilization limit. 9. References were reviewed and updated.		
Policy was reviewed.	12/1/2023	12/1/2023