

Clinical Policy: Relugolix (Orgovyx), Relugolix/Estradiol/Norethinedrone (Myfembree)

Reference Number: ERX.SPA.433

Effective Date: 06.01.21

Last Review Date: 05.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Relugolix (Orgovyx[™]) is a gonadotropin-releasing hormone (GnRH) receptor antagonist.

Relugolix/estradiol/norethinedrone (Myfembree[®]) is a combination of a GnRH receptor antagonist with an estrogen and progestin.

FDA Approved Indication(s)

Orgovyx is indicated for treatment of adult patients with advanced prostate cancer.

Myfembree is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that Orgovyx and Myfembree is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prostate Cancer (must meet all):

1. Diagnosis of advanced prostate cancer defined as one of the following (a, b, or c):
 - a. Evidence of biochemical (PSA) or clinical relapse following local primary intervention with curative intent;
 - b. Newly diagnosed castration-sensitive metastatic disease;
 - c. Advanced localized disease unlikely to be cured by local primary intervention with curative intent;
2. Request is for Orgovyx;
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a, b, or c):*
 - a. Initial dose does not exceed 360 mg (3 tablets) given on the first day of treatment as a loading dose;
 - b. Maintenance dose does not exceed (i or ii):
 - i. 120 mg (1 tablet) per day;
 - ii. 240 mg (2 tablets) per day if combined with rifampin and combination use is unavoidable;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:

Commercial – Length of Benefit

Medicaid – 12 months

B. Heavy Menstrual Bleeding Associated with Uterine Fibroids (must meet all):

1. Diagnosis of uterine leiomyomas (fibroids) confirmed by ultrasound;
2. Request is for Myfembree;
3. Prescribed by or in consultation with a gynecologist;
4. Age \geq 18 years;
5. Member has experienced heavy menstrual bleeding for at least 2 consecutive cycles;
6. Failure of a 3 month trial of a combination estrogen-progestin contraceptive agent (see *Appendix B for examples*);
7. Dose does not exceed 40 mg of relugolix (1 tablet) per day.

Approval duration: 12 months

Total duration of therapy should not exceed 24 months.

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Prostate Cancer (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Orgovyx for a covered indication and has received this medication for at least 30 days;
2. Request is for Orgovyx;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):*
 - a. New dose does not exceed 120 mg (1 tablet) per day;
 - b. New dose does not exceed 240 mg (2 tablets) per day if combined with rifampin and combination use is unavoidable;
 - c. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:

Commercial – Length of Benefit

Medicaid – 12 months

B. Heavy Menstrual Bleeding Associated with Uterine Fibroids (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Myfembree;
3. Member is responding positively to therapy as evidenced by reduced menstrual blood loss;
4. Member has not received \geq 24 months of Myfembree therapy;
5. If request is for a dose increase, new dose does not exceed 40 mg of relugolix (1 tablet) per day.

Approval duration: up to 12 months

Total duration of therapy should not exceed 24 months.

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

GnRH: gonadotropin-releasing hormone

NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria.

The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Heavy Menstrual Bleeding associated with Uterine Fibroids		
NSAIDs: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclufenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam	Varies – refer to specific prescribing information	Varies – refer to specific prescribing information
Progestin-containing oral contraceptives: norethindrone*, ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone	1 tablet PO QD	1 tablet/day
Depot injection progestin contraceptives: medroxyprogesterone acetate (Depo-Provera®, Depo-SubQ Provera 104®)	IM: 150 mg every 13 weeks SC: 104 mg every 12 to 14 weeks	IM: 150 mg/3 months SC: 104 mg/3 months
Combination estrogen-progestin contraceptive agent: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel)	1 tablet PO QD	1 tablet/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

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

- Boxed warning(s):
 - Orgovyx: None reported
 - Myfembree: Thromboembolic disorders and vascular events

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Relugolix (Orgovyx)	Prostate cancer	A loading dose of 360 mg PO on the first day of treatment followed by 120 mg orally once daily. Avoid use with combined P-gp and strong CYP3A inducers (e.g., rifampin). If unavoidable, increase Orgovyx dose to 240 mg orally daily.	First dose: 360 mg/day Maintenance dose: 240 mg/day (if co-administration with combined P-gp and strong CYP3A inducers)
Relugolix/estradiol/norethindrone (Myfembree)	Heavy menstrual bleeding due to uterine fibroids	1 tablet PO QD for up to 24 months	1 tablet/day

VI. Product Availability

Drug Name	Product Availability
Relugolix (Orgovyx)	Tablet: 120 mg
Relugolix/estradiol/norethindrone (Myfembree)	Tablet: fixed-dose combination containing relugolix 40 mg, estradiol 1 mg, norethindrone acetate 0.5 mg

VII. References

1. Myfembree Prescribing Information. Brisbane, CA: Myovant Sciences, Inc.; May 2021. Available at www.myfembreehcp.com. Accessed February 15, 2022.
2. Orgovyx Prescribing Information. Brisbane, CA: Myovant Sciences, Inc.; December 2020. Available at www.orgovyx.com. Accessed February 15, 2022.
3. National Comprehensive Cancer Network. Prostate Cancer Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed February 15, 2022.
4. 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. American College of Obstetricians and Gynecologists. Practice bulletin: clinical management guidelines for obstetrician-gynecologist: alternatives to hysterectomy in the management of leiomyomas. Am J Obstet Gynecol. 2008; 112(2):387-400.
6. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	01.25.21	05.21
RT4: Criteria added following prior clinical guidance for new FDA-approved combination product and its indication: Myfembree for management of heavy menstrual bleeding due to uterine fibroids.	06.23.21	
2Q 2022 annual review: for heavy menstrual bleeding continuation of therapy added requirement that member has not received ≥ 24 months of Myfembree therapy to reemphasize existing notations for approval duration; references reviewed and updated.	02.15.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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