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

Reference Number: CP.PHAR.529
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Commercial, HIM, 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 the 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.

It is the policy of health plans affiliated with Centene Corporation® that Orgovyx and Myfembree are **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: 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 ≥ 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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: 12 months

B. Heavy Menstrual Bleeding Associated with Uterine Fibroids (must meet all):
1. Currently receiving medication via Centene benefit 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. 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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 for all relevant lines of business 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, meclofenamate, 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 +	1 tablet PO QD	1 tablet/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone		
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 orally on the first day of treatment followed by 120 mg PO QD. Avoid use with combined P-gp and strong CYP3A inducers (e.g., rifampin). If unavoidable, increase	First dose: 360 mg/day Maintenance dose: 240 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Orgovyx dose to 240 mg PO daily.	
Relugolix/estradiol/ norethinedrone (Myfembree)	Heavy menstrual bleeding due to uterine fibroids	Up to 24 months: 1 tablet PO QD	1 tablet/day

VI. Product Availability

Drug Name	Product Availability
Relugolix (Orgovyx)	Tablets: 120 mg
Relugolix/estradiol/ Norethinedrone (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 https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214846s000lbl.pdf. Accessed June 23, 2021.
2. Orgovyx Prescribing Information. Brisbane, CA: Myovant Sciences, Inc.; December 2020. Available at https://www.myovant.com/wp-content/uploads/2020/12/NDA-214621-Final-USPIandPI.pdf. Accessed January 14, 2021.
3. National Comprehensive Cancer Network. Prostate Cancer Version 3.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed January 12, 2021.
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.

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	

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. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.