

DRUG DETERMINATION POLICY

Title: DDP-44 Gonadotropin-Releasing Hormone Receptor Antagonists

Effective Date: 2/22/23



Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Orilissa is an agent used to treat moderate to severe pain associated with endometriosis and Oriahnn and Myfembree are agents used to treat heavy menstrual bleeding. These criteria were developed and implemented to ensure appropriate use of preferred medications prior to these agents.

3.0 Clinical Determination Guidelines:

- A. Age: at least 18 years.
- B. Diagnosis and severity [must meet both listed below]:
 1. Pre-menopausal.
 2. Diagnosis.
 - a. Orilissa (elagolix): moderate to severe pain associated with endometriosis.
 - b. Oriahnn (elagolix, estradiol, norethindrone), Myfembree (relugolix, estradiol, norethindrone): heavy menstrual bleeding associated with uterine leiomyomas (fibroids).
- C. Other therapies: contraindication, inadequate response or significant adverse effects to two analgesics for one month each and one hormone therapy for four months [must meet both listed below]:
 1. Analgesics: ibuprofen, meloxicam, naproxen.
 2. Hormones: hormonal contraceptives, progesterones (e.g., norethindrone).

D. Dosage regimen:

1. Orilissa (elagolix):
 - a. Endometriosis: 150mg daily for a maximum treatment duration of two years.
 - b. Endometriosis with dyspareunia: 200mg two times daily for maximum treatment duration of six months.
2. Oriahnn (elagolix, estradiol, norethindrone): elagolix 300mg/estradiol 1mg/norethindrone 0.5mg every morning and elagolix 300mg every evening for maximum treatment duration of two years.
3. Myfembree (relugolix, estradiol, norethindrone): one tablet daily for a maximum treatment duration of two years.

E. Approval:

1. Initial: six months.
2. Reapproval:
 - a. Endometriosis or heavy menstrual bleeding: one year up total duration of two years.
 - b. Endometriosis with dyspareunia: not indicated (total duration six months).

F. Exclusions [any listed below]:

1. Osteoporosis.
2. Severe hepatic impairment (Child-Pugh Class C).
3. Pregnancy.
4. Use of strong organic anion transporting polypeptide (OATP)-1B1 inhibitor (e.g., cyclosporine, gemfibrozil).
5. High risk of arterial, venous thromboembolic disorders.
6. Hyper coagulopathies.
7. Uncontrolled hypertension.
6. Current history of breast cancer or other hormone-sensitive malignancies.

4.0 Coding:

None.

5.0 References, Citations, Resources & Associated Documents:

1. Lexi comp Online® Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Orilissa, Oriahnn and Myfembree accessed December 2022.
2. UpToDate: Endometriosis - Treatment of Pelvic pain accessed February 2022, https://www.uptodate.com/contents/endometriosis-treatment-of-pelvic-pain?search=endometriosis%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
3. Long-Term Outcomes of Elagolix in Women With Endometriosis: Results From Two Extension Studies. Obstet Gynecol 2018; 132:147.

6.0 Appendices:

See page 4.

7.0 Revision History:

Original Effective Date: 06/03/2020

Next Review Date: 01/27/2022

Revision Date	Reason for Revision
12/20	Annual review, added drug Oriahnn diagnosis, dosage and monitoring/patient safety, simplified criteria instructions, approved by P&T 2/24/21
7/21	Off cycle review, added drug Myfembree, clarified criteria instructions, added exclusions
12/21	Annual Review
12/22	Annual Review, no change

Appendix I - Monitoring and patient safety

Drug	Adverse Reactions	Monitoring & Contraindications	REMS
Orilissa elagolix	<ul style="list-style-type: none"> • Central Nervous System: headache (17-20%) • Dermatological: night sweats (46%) • Endocrine and metabolic: amenorrhea (4-57%), hot flash (46%) • Gastrointestinal: nausea (16%) • Neuromuscular and Skeletal: decrease bone mineral density (21%) 	<ul style="list-style-type: none"> • Pregnancy • Labs: liver function tests, bone mineral density (after 12 months) • Mental status • Contraindications listed in exclusions 	<ul style="list-style-type: none"> • None
Oria elagolix, estradiol, norethindrone Myfembree (relugolix, estradiol, norethindrone)	<ul style="list-style-type: none"> • Endocrine and metabolic: hot flash (22%) 	<ul style="list-style-type: none"> • Pregnancy • Labs: liver function tests, bone mineral density (after 12 months), hgb, lipid profile • Mental status • Cardiovascular: signs and symptoms of thromboembolic disorders • Contraindications listed in exclusions 	<ul style="list-style-type: none"> • Medication Guide