Clinical Policy: Elagolix (Orilissa), Elagolix/Estradiol/Norethinedrone (Oriahnn)

Reference Number: IL.PHAR.136
Effective Date: 08.01.20
Last Review Date: 11.15.23
Line of Business: Medicaid

Revision Log

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

Description

Elagolix (Orilissa™) is a gonadotropin-releasing hormone (GnRH) receptor antagonist.

Elagolix/estradiol/norethinedrone; elagolix (Oriahnn™) is a combination of a GnRH receptor antagonist with an estrogen and progestin.

FDA Approved Indication(s)

Orilissa is indicated for the management of moderate to severe pain associated with endometriosis.

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

Limitation(s) of use: Use of Oriahnn 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 Orilissa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Endometriosis Pain (must meet all):

1. Diagnosis of pain due to endometriosis;
2. Request is for Orilissa;
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Failure of a 3-month trial within the last year of an agent from one of the following, unless contraindicated or clinically significant adverse effects are experienced (a or b):
   a. A non-steroidal anti-inflammatory drug *(see Appendix B for examples)*;
   b. An oral contraceptive agent *(see Appendix B for examples)*;

6. Member has not already received ≥ 24 cumulative months of treatment with elagolix-containing products (e.g., Orilissa, Oriahnn);
7. Dose does not exceed 400 mg per day.

Approval duration: 6 months for 200 mg twice daily; 12 months for 150 mg once daily

Total duration of therapy should not exceed 6 months for 200 mg twice daily or 24 months for 150 mg once daily.

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

1. Diagnosis of uterine leiomyomas (fibroids) confirmed by ultrasound;
2. Request is for Oriahnn;
3. Age ≥ 18 years;
4. Member has experienced heavy menstrual bleeding for at least 2 consecutive cycles;
5. Failure of a 3 month trial of a combination estrogen-progestin contraceptive agent (*see Appendix B for examples*);
6. Member has not already received ≥ 24 cumulative months of treatment with elagolix-containing products (e.g., Orilissa, Oriahnn);
7. Dose does not exceed 600 mg of elagolix per day.

Approval duration: 12 months

Total duration of therapy should not exceed 24 months.

C. Other diagnoses/indications

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.
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II. Continued Therapy

A. Endometriosis Pain (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Request is for Orilissa;
4. Member is responding positively to therapy as evidenced by improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, or size of endometrial lesions;
5. Member has not already received ≥ 24 cumulative months of treatment with elagolix-containing products (e.g., Orilissa, Oriahnn);
6. If request is for a dose increase, new dose does not exceed 400 mg per day.

Approval duration: up to 6 months for 200 mg twice daily; up to 12 months for 150 mg once daily

Total lifetime duration of therapy should not exceed 6 months for 200 mg twice daily or 24 months for 150 mg once daily. Requests for dose de-escalated continuation of therapy after 6 months of 200 mg twice daily will be denied based upon lack of clinical evidence of safety of continued dosing beyond 6 months.

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for Oriahnn;
3. Member is responding positively to therapy as evidenced by reduced menstrual blood loss;
4. Member has not already received ≥ 24 cumulative months of treatment with elagolix-containing products (e.g., Orilissa, Oriahnn);
5. If request is for a dose increase, new dose does not exceed 600 mg of elagolix 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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.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
OATP: organic anion transporting polypeptide

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
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 + (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,	1 tablet PO QD	1 tablet/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
norelgestromin, norethindrone, norgestimate, or norgestrel)		

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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 + (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):
  - Pregnancy
  - Known osteoporosis
  - Severe hepatic impairment
  - Concomitant use of strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine and gemfibrozil)
  - Orilissa only:
    - Hypersensitivity reaction to ORILISSA or any of its inactive components. Reactions have included anaphylaxis and angioedema.
  - Oriahnn only:

- With a high risk of arterial, venous thrombotic, or thromboembolic disorders. Examples include women over 35 years of age who smoke, and women who are known to have:
  - Current or history of deep vein thrombosis or pulmonary embolism
  - Vascular disease (e.g., cerebrovascular disease, coronary artery disease, peripheral vascular disease)
  - Thrombogenic valvular or thrombogenic rhythm diseases of the heart (for example, subacute bacterial endocarditis with valvular disease, or atrial fibrillation)
  - Inherited or acquired hypercoagulopathies
  - Uncontrolled hypertension
  - Headaches with focal neurological symptoms or have migraine headaches with aura if over age 35
- With current or history of breast cancer or other hormonally-sensitive malignancies, and with increased risk for hormonally-sensitive malignancies
- With undiagnosed abnormal uterine bleeding
- With known anaphylactic reaction, angioedema, or hypersensitivity to Oriahnn or any of its components

- Boxed warning(s):
  - Orilissa: None reported
  - Oriahnn: Thromboembolic disorders and vascular events

Appendix D: General Information

- Orilissa and Oriahnn cause dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment. The impact of these BMD decreases on long-term bone health and future fracture risk are unknown.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Elagolix (Orilissa)	Endometriosis pain	150 mg PO QD or 200 mg PO BID	150 mg/day x 24 months or 400 mg/day x 6 months
Elagolix/estradiol/ norethinedrone; elagolix (Oriahnn)	Heavy menstrual bleeding due to uterine fibroids	PO for up to 24 months: one capsule (elagolix 300 mg, estradiol 1 mg, norethindrone acetate 0.5 mg) in the morning and one capsule (elagolix 300 mg) in the evening	See regimen

VI. Product Availability

Drug Name	Product Availability
Elagolix (Orilissa)	Tablets: 150 mg, 200 mg

Elagolix/estradiol/ norethinedrone; elagolix (Oriahnn)	Morning (AM) capsule: elagolix 300 mg, estradiol 1 mg, norethindrone acetate 0.5 mg Evening (PM) capsule: elagolix 300 mg

VII. References

1. Orilissa Prescribing Information. North Chicago, IL: AbbVie Inc.; June 2023. Available at: http://www.orilissa.com. Accessed July 18, 2023.
2. Oriahnn Prescribing Information. North Chicago, IL: AbbVie Inc.; June 2023. Available at: http://www.oriahnn.com. Accessed July 18, 2023.
3. American College of Obstetricians and Gynecologists. Practice bulletin: clinical management guidelines for obstetrician-gynecologist: management of endometriosis. Am J Obstet Gynecol 2010;116(1):223-236.
4. 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.
5. American College of Obstetricians and Gynecologists. Practice bulletin: management of symptomatic uterine leiomyomas. Am J Obstet Gynecol. 2021;137(6):e100-e115.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.22.19	11.19
Added HIM line of business.	02.13.20	
Policy created, adapted from CP.PHAR.136 **Elagolix (Orilissa)** for migration to HFS PDL.	7.21.20	
3Q 2021 annual review: 3-month trial within the last year and oral contraceptive added ; reviewed and updated reference	7.6.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 Annual Review: Added Elagolix/estradiol/norethinedrone; elagolix (Oriahnn™); removed the requirement for confirmation that the member does not have osteoporosis; Rrevised continuation of therapy auth duration language to emphasize that the 6-month duration of 200 mg twice daily is a lifetime limit, and that dose de-escalated continuation of therapy after 6 months of 400 mg/day will not be covered; Removed CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace for other diagnosis/indication; Updated Appendix C: Contraindications/Boxed Warnings; Updated *Appendix B: Therapeutic Alternatives*; references reviewed and updated.	3.17.22	
4Q 2023 Annual Review: added requirement that member has not previously received 24 or more months of cumulative elagolix therapy, added Appendix D; updated Appendix C with "hypersensitivy reaction to any of its active ingredients" for Orilissa to align with prescribing information; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	11.15.23	

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.