Original Effective Date: 01/01/2019
Current Effective Date: 08/23/2023
Last P&T Approval/Version: 07/26/2023
Next Review Due By: 07/2024
Policy Number: C15417-A

Orilissa (elagolix), Oriahnn (elagolix, estradiol, and norethindrone acetate capsules)

PRODUCTS AFFECTED

Orilissa (elagolix), Oriahnn (elagolix, estradiol, and norethindrone acetate capsules)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Moderate to severe pain due to endometriosis; heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. FOR ALL INDICATIONS:
1. (a) FOR ORILISSA:
(i) Documentation of moderate to severe pelvic pain associated with endometriosis with or without dyspareunia
AND

(ii) Documentation member has tried/failed or has an absolute contraindication to ALL of the following:
1) ONE formulary NSAID (i.e., Ibuprofen, naproxen)
AND
2) ONE of the following hormonal agents: a formulary preferred oral estrogen-progestin contraceptives, medroxyprogesterone or norethindrone acetate

OR

(b) FOR ORIAHNN: Documentation of a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
AND

2. Prescriber attestation of the following baseline tests completed prior to initiation of treatment and plan for continued monitoring as clinically appropriate: pregnancy test in a woman of childbearing potential, liver function tests, blood pressure (Oriahnn ONLY), bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis
AND
3. (a) Documentation that member is naïve to Orilissa or Oriahnn
OR
(b) Start date is provided and does not exceed a total duration lifetime duration of 24 months
AND
4. Prescriber attests that member has not had a greater than the lifetime maximum of GnRH therapy
AND
5. Prescriber attests member is premenopausal
AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Oriahnn (elagolix, estradiol, and norethindrone) include: High risk of arterial, venous thrombotic or thromboembolic disorder, Pregnancy, Known osteoporosis, Current or history of breast cancer or other hormone-sensitive malignancies, Known liver impairment or disease, Undiagnosed abnormal uterine bleeding, Known hypersensitivity to ingredients of ORIAHNN, women with uncontrolled hypertension; Contraindications to Orilissa (elagolix) include: Pregnancy, known osteoporosis, severe hepatic impairment, organic anion transporting polypeptide (OATP) 1B1 inhibitors that significantly increase elagolix plasma concentrations, hypersensitivity reactions]

CONTINUATION OF THERAPY:

A. MENSTRUAL AND NONMENSTRUAL PELVIC PAIN [ORILISSA ONLY]:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Documentation member has experienced a clinically significant improvement in endometriosis associated pain
AND
3. Documentation member has not exceeded a total lifetime duration of 24 months of 150mg once daily
AND
4. Prescriber attests to continued monitoring as clinically appropriate: pregnancy test in a woman child-bearing potential, liver function tests, bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis.
AND
5. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

B. DYSPAREUNIA [ORILISSA ONLY]:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documentation member has not exceeded a total lifetime duration of 6 months of 200mg twice daily
   AND
3. Documentation member has experienced a clinically significant improvement in dyspareunia
   AND
4. Prescriber attests to continued monitoring as clinically appropriate: pregnancy test in a woman of childbearing potential, liver function tests, bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis
   AND
5. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

C. HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE LEIOMYOMAS [ORIAHNN ONLY]

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documentation member has experienced a clinically significant improvement with less menstrual blood loss
   AND
3. Documentation member has not exceeded a total lifetime duration of 24 months of GnRH therapy
   AND
4. Prescriber attests to continued monitoring as clinically appropriate: pregnancy test in a woman child-bearing potential, liver function tests, blood pressure, bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis.
   AND
5. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 3 months, Continuation of Therapy: 3 months
Cannot exceed lifetime max of 24 months for Orilissa 150mg once daily or Oriahnn; Cannot exceed lifetime max of 6 months for Orilissa 200mg twice daily

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified endocrinologist or gynecologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Orilissa:
Pain associated with endometriosis: 150mg orally daily for up to 24 months
Coexisting dyspareunia: 200mg twice a day for up to 6 months

Oriahnn:
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 for up to 24 months

Maximum Quantity Limits – Orilissa: 56 tabs/28 days, Oriahnn: 56 capsules/28 days

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Estrogen-Progestin-GnRH Antagonist, GnRH/LHRH Antagonists

FDA-APPROVED USES:
ORILISSA (elagolix) is indicated

- for the management of moderate to severe pain associated with endometriosis
  Limitations of Use: Limit the duration of use based on the dose and coexisting condition

ORIAHNN (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated

- for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.
  Limitation of Use: Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Orilissa Efficacy:
There have been 5 clinical studies, three Phase II studies and two Phase III randomized controlled studies. The 2 Phase III studies were the EM-1 (NCT01620528) and EM-2 (NCT01931670). There were 4 studies that had a placebo arm and 2 studies with comparators, depot medroxyprogesterone acetate (DMPA) and leuprorelin acetate. Not all studies had the same endpoints, and in addition, not all studies had comparable patient populations. The co-primary efficacy endpoints were the proportion of subjects whose dysmenorrhea responded to treatment at Month 3 and the proportion of subjects whose pelvic pain not related to menses (non-menstrual pelvic pain) responded to treatment at Month 4. In two Phase III trials comparing two different doses of the oral GnRH antagonist elagolix (150 mg once daily or 200 mg twice daily) with placebo on endometriosis-related dysmenorrhea and non- cyclic pelvic pain, women in both elagolix groups reported significantly reduced symptoms at three months of treatment. In both trials, at three months, meaningful reductions in dysmenorrhea pain were reported by about 44 percent of the low-dose elagolix group,74 percent of the high-dose elagolix group, and 21 percent of the placebo group. Nonmenstrual pelvic pain was decreased in 50, 56, and 36 percent of women in the low-dose, high-dose, and placebo groups, respectively. The improvement in dysmenorrhea in the low-dose elagolix group is modest compared with the approved GnRH agonist, depot-leuprolide acetate

Orilissa Side Effects:

Bone Density Loss In Studies EM-1 and EM-2, there was a dose-dependent decrease in BMD in Orilissa treated subjects compared to an increase in placebo-treated subjects. In Study EM-1, compared to placebo, the mean change from baseline in lumbar spine BMD at 6 months was -0.9% with Orilissa 150 mg once daily and -3.1% with Orilissa 200 mg twice daily. The percentage of subjects with greater than 8% BMD decrease in
lumbar spine, total hip or femoral neck at any time point during the placebo-controlled treatment period was 2% with Orilissa 150 mg once daily, 7% with Orilissa 200 mg twice daily and < 1% with placebo. In the blinded extension Study EM-3, continued bone loss was observed with 12 months of continuous treatment with
Orilissa. The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the extension treatment period was 8% with continuous Orilissa 150 mg once daily and 21% with continuous Orilissa 200 mg twice daily. In Study EM-2, compared to placebo, the mean change from baseline in lumbar spine BMD at 6 months was -1.3%with Orilissa 150 mg once daily and -3.0% with Orilissa 200 mg twice daily. The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the placebo-controlled treatment period was < 1% with Orilissa 150 mg once daily, 6% with Orilissa 200 mg twice daily and 0% with placebo. In the blinded extension Study EM-4, continued bone loss was observed with 12 months of continuous treatment with Orilissa. The percentage of subjects with greater than 8% BMD decrease in lumbar spine, total hip or femoral neck at any time point during the extension treatment period was 2% with continuous Orilissa 150 mg once daily and 21% with continuous Orilissa 200 mg twice daily

Oriahnn Efficacy:

Oriahnn was studied in two randomized, double-blind placebo-controlled trials: Study UF-1 (NCT02654054) and Study UF-2 (NCT02691494). Women (n=790) with heavy menstrual bleeding (defined as at least two menstrual cycles with greater than 80 mL of menstrual blood loss) were assigned to treatment with Oriahnn or placebo for 6 months. The primary endpoint was a 50% of greater reduction in menstrual blood loss volume from baseline to the final months. In the Study UF-1 the difference from placebo was 59.8% (95% CI 51.1,68.5; p-value <0.001) for the treatment arm. In the Study UF-2 the difference from placebo was 66.0% (95% CI 57.1,75.0; p-value <0.001) for the treatment arm.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Orilissa (elagolix) & Oriahnn (elagolix, estradiol, and norethindrone acetate capsules) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Oriahnn (elagolix, estradiol, and norethindrone) include: High risk of arterial, venous thrombotic or thromboembolic disorder, Pregnancy, Known osteoporosis, Current or history of breast cancer or other hormone-sensitive malignancies, Known liver impairment or disease, Undiagnosed abnormal uterine bleeding, Known hypersensitivity to ingredients of ORIAHNN, women with uncontrolled hypertension; Contraindications to Orilissa (elagolix) include: Pregnancy, known osteoporosis, severe hepatic impairment, organic anion transporting polypeptide (OATP) 1B1 inhibitors that significantly increase elagolix plasma concentrations, hypersensitivity reactions.

OTHER SPECIAL CONSIDERATIONS:

Orihann (elagolix, estradiol, and norethindrone) has a Black Box Warning for thromboembolic disorders and vascular events.

Oriahnn and Orilissa changes menstrual bleeding patterns and reduces the ability to recognize pregnancy. Women should be advised to use non-hormonal contraception during treatment with and one week following discontinuation of Oriahnn and Orilissa. Oriahnn and Orilissa may delay the ability to recognize the occurrence of pregnancy because it alters menstrual bleeding. Additionally, Oriahnn contains FD&C Yellow No 5 (tartrazine), which may cause allergic-reactions in certain susceptible persons.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Orilissa tablets 150mg and Orilissa tablets 200mg
Oriahnn CPPK 300-1-0.5 & 300MG

REFERENCES

1. Orilissa (elagolix) [prescribing information]. North Chicago, IL: AbbVie Inc; February 2021.
2. Oriahnn (elagolix, estradiol, and norethindrone) [prescribing information]. North Chicago, IL: Abbvie Inc; August 2021.
3. Institute for Clinical and Economic Review Final Report Highlights Limitations in Evidence on Long-term Safety and Effectiveness of Elagolix for Endometriosis, Discusses Options for Insurance Coverage Criteria. August 3, 2018
4. A Clinical Study to Evaluate the Safety and Efficacy of Elagolix in Subjects with Moderate to Severe Endometriosis-Associated Pain - Full Text View - ClinicalTrials.gov. (2018). Retrieved from https://clinicaltrials.gov/ct2/show/NCT01620528
5. Hirsch, M., Begum, M., Paniz, É., Barker, C., Davis, C., & Duffy, J. (2017). Diagnosis and management of endometriosis: a systematic review of international and national guidelines. BJOG: An International Journal Of Obstetrics & Gynaecology, 125(5), 556-564. doi: 10.1111/1471- 0528.14838
6. Taylor, H., Giudice, L., Lessey, B., Abrao, M., Kotarski, J., & Archer, D. et al. (2017). Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. New England Journal of Medicine, 377(1), 28-40. doi: 10.1056/nejmoa1700089

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Quantity Contraindications/Exclusions/Discontinuation Other Special Considerations	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file