Orilissa (elagolix)
Policy Number: C15417-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
1/1/2019	6/5/2019	6/5/2019
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
NA	PA	Q3 2019 20190828C15414-A

PRODUCTS AFFECTED:
Orilissa (elagolix)

DRUG CLASS:
GHRH/LHRH antagonists

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Retail Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

AVAILABLE DOSAGE FORMS:
Orilissa tablets 150mg NDC #0074-0038-28 and Orilissa tablets 200mg NDC# 0074-0039-56

FDA-APPROVED USES:
For moderate to severe pain due to endometriosis in women 18 years of age and older

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
moderate to severe pain due to endometriosis

REQUIRED MEDICAL INFORMATION:
A. FOR ALL INDICATIONS:

1. Documentation of moderate to severe pelvic pain associated with endometriosis
   AND
2. Documentation patient has tried/failed or has an absolute contraindication to ALL of the following: (i) ONE formulary NSAID (i.e. Ibuprofen, naproxen) AND (ii) ONE of the following hormonal agents: a formulary preferred oral estrogen-progestin contraceptives, medroxyprogesterone or norethindrone acetate
   AND
3. Documentation 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 child

bearing potential, liver function tests, bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis
AND
4. (a) Documentation that patient is naïve to Orilissa
OR
(b) Start date is provided and does not exceed a total duration lifetime duration of 24 months
AND
5. Prescriber attests that patient has not had a greater than the lifetime maximum of GnRH therapy

DURATION OF APPROVAL:
Initial authorization: 3 months, continuing authorization: 3 months- cannot exceed lifetime max of 24 months for 150mg once daily and 6 months for 200mg twice daily

QUANTITY:
150mg orally daily for up to 24 months (menstrual and non-menstrual pelvic pain dose)
200mg twice a day for up to 6 months (dyspareunia dose)

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified endocrinologist or gynecologist

AGE RESTRICTIONS:
18 years of age and older

GENDER:
Female

CONTINUATION OF THERAPY:
A. MENSTRUAL AND NONMENSTRUAL PELVIC PAIN:
1. Patient has experienced a clinically significant improvement in endometriosis-associated pain
AND
2. Patient has not exceeded a total lifetime duration of 150mg once daily x 24 months.
AND
3. Prescriber attests 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.

B. DYSPAREUNIA:
1. Patient has not exceeded a total lifetime duration of 200mg twice daily x 6 months
AND
2. Patient has experienced a clinically significant improvement in dyspareunia
AND
3. Prescriber attests continued monitoring as clinically appropriate: pregnancy test in a woman of child bearing potential, liver function tests, bone mineral density in a woman with risk factors for bone loss or risk factors for osteoporosis

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Pregnancy, severe (Child-Pugh class C) hepatic impairment, known osteoporosis. Orilissa is contraindicated with the use of cyclosporine and gemfibrozil. All other uses of Orilissa (elagolix) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
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 3. 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
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

APPENDIX:
None

REFERENCES:
1. Orilissa (elagolix) [prescribing information]. North Chicago, IL: AbbVie Inc; July 2018.

2. 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
3. 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
4. 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
5. 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