Orilissa™ (elagolix)

Policy # 00659
Original Effective Date: 02/20/2019
Current Effective Date: 07/13/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Orilissa™‡ (elagolix) for the treatment of endometriosis to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Orilissa (elagolix) will be considered when the following criteria are met:

- Patient has a diagnosis of endometriosis; AND
- Patient is a pre-menopausal female; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient is not pregnant; AND
- Patient is 18 years of age or older; AND
- Patient meets ONE of the following criteria:
  - Patient has tried and failed (e.g. intolerance or inadequate response) a contraceptive (e.g., combination oral contraceptives, levonorgestrel-releasing intrauterine systems [e.g., Mirena®‡, Liletta®‡]) or a progesterone product (e.g., norethindrone tablets, depo-medroxyprogesterone injection) unless there is clinical evidence or patient history that suggests the use of the required treatments will be ineffective or cause an adverse reaction to the patient; OR
  - Patient has previously used a gonadotropin-releasing hormone [GnRH] agonist (e.g., Lupron Depot®‡); AND

  *(Note: These specific patient selection criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met).*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Orilissa (elagolix) for patients who are not premenopausal females OR when the patient has not tried and failed a contraceptive or progesterone product OR when the patient is not experiencing moderate to severe pain despite treatment with other agents to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Orilissa (elagolix) for conditions other than endometriosis OR for patients who are younger than 18 years of age OR patients who are pregnant to be **investigational.***

Based on review of available data, the Company considers the use of Orilissa (elagolix) 150 mg tablets taken once daily for longer than 24 months of duration OR 200 mg tablets taken twice daily for longer than 6 months of duration to be **investigational.***

Background/Overview

Orilissa is an oral gonadotropin-releasing hormone (GnRH) antagonist that is indicated for the management of moderate to severe pain associated with endometriosis. It inhibits endogenous GnRH signaling by binding to GnRH receptors in the pituitary gland. This results in suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) which decreases the blood concentrations of estradiol and progesterone. Orilissa is available as 150 mg and 200 mg tablets and has two approved dosing options. Patients can take 150 mg once daily for up to 24 months or 200 mg twice daily for up to 6 months. If patients have dyspareunia, the dose of 200 mg twice daily for up to 6 months is preferred. Therapy should not be continued longer than the recommended duration due to the increased risk of bone loss in patients taking Orilissa. In addition, Orilissa can reduce the efficacy of estrogen-containing contraceptives and reduce the ability to recognize pregnancy due to change in menstrual bleeding pattern. Because Orilissa is contraindicated in pregnancy and may increase the risk of early pregnancy loss, all patients should be advised to use non-hormonal

contraceptives during treatment with Orilissa and for one week after discontinuing Orilissa. Orilissa should be discontinued if pregnancy occurs during treatment.

Endometriosis is a condition where the tissues similar to the lining of the uterus (or endometrium) migrate outside of the womb to other body sites. The migrated tissues are generally found in the pelvic cavity (e.g., peritoneum, uterosacral ligaments, rectal-vaginal septum, or any spaces between the bladder, uterus, vagina, and rectum) and can attach to any of the female reproductive organs. The migrated tissue is less commonly found outside the pelvic cavity or on the intestines, colon, appendix, or rectum. Endometriosis impacts up to 10% of patients of reproductive age in the United States. Many women are not diagnosed and, therefore, not treated. The most common symptom of endometriosis is pelvic pain, which often correlates to the menstrual cycle. Symptoms can range from minimal to severely debilitating. Many women with endometriosis also experience dyspareunia and infertility. The definitive diagnosis of endometriosis can only be made by histology of lesions removed at surgery (laparoscopy), although empiric therapy is commonly used in the course of evaluating the condition. There is no cure for the condition, but many treatments are available to help relieve symptoms associated with endometriosis. Non-FDA approved therapies which are commonly used include: non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids, and some contraceptives. FDA-approved products for the management of endometriosis include GnRH agonists (Lupron Depot [leuprolide acetate], Zoladex®‡ [goserelin acetate], Synarel®‡ [nafarelin acetate]), progesterone therapies (depo-subQ Provera®‡ [medroxyprogesterone], norethindrone tablets), and synthetic androgen therapy (danazol capsules). Additionally, surgery can be performed to reduce endometriosis-associated pain by removing all visible endometriosis and any associated adhesions. There is a significant rate of pain recurrence with medical management and conservative surgical treatment.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Orilissa was approved in 2018 for the management of moderate to severe pain associated with endometriosis.

Rationale/Source

The efficacy of Orilissa was evaluated in two multinational double-blind, placebo-controlled trials in 1686 premenopausal women (Study EM-1 and EM-2). In both studies, patients were randomized

to receive Orilissa 150 mg once daily, 200 mg twice daily, or placebo for 6 months. Moderate to severe pain associated with endometriosis was required for entry into the trials and was assessed during screening using the composite pelvic signs and symptoms score (CPSSS) and other baseline criteria. Subjects were also required to have non-menstrual pelvic pain for at least 4 days in the preceding month, defined as 35 days. The co-primary efficacy endpoints were (1) the proportion of subjects whose dysmenorrhea responded to treatment at month 3 and (2) the proportion of subjects whose non-menstrual pelvic pain responded to treatment at month 3. Dysmenorrhea and non-menstrual pelvic pain were evaluated daily using the Endometriosis Daily Pain Impact Scale that asked subjects to rate their pain severity and its impact on daily activities during the prior 24 hours as non, mild, moderate, or severe. Scores at baseline and at each month were averaged over a 35-day interval.

In the EM-1 study, a statistically significantly higher proportion of patients in both treatment groups achieved a response to treatment at month 3 in dysmenorrhea (46% in Orilissa 150 mg group, 76% in Orilissa 200 mg group, and 20% in placebo group) and non-menstrual pelvic pain (50% in Orilissa 150 mg group, 55% in Orilissa 200 mg group, and 36% in placebo). In the EM-2 study, a statistically significantly higher proportion of patients in both treatment groups achieved a response to treatment at month 3 in dysmenorrhea (43% in Orilissa 150 mg group, 72% in Orilissa 200 mg group, and 23% in placebo group), and non-menstrual pelvic pain (50% in Orilissa 150 mg, 58% in Orilissa 200 mg group, and 37% in placebo group). In addition, both Orilissa treatment groups showed statistically significantly greater mean decreases from baseline compared to placebo in dysmenorrhea and non-menstrual pelvic pain at month 6.

References

1. Orilissa [package insert]. AbbVie, Inc. North Chicago, IL. July 2018
2. Orilissa Drug Evaluation. Express Scripts. August 2018.
3. Gonadotropin-Releasing Hormone (GnRH) Antagonists- Orilissa (elagolix) Prior Authorization Policy. Express Scripts. September 2018.

Policy History

Original Effective Date: 02/20/2019
Current Effective Date: 07/13/2020
02/07/2019 Medical Policy Committee review

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02/20/2019	Medical Policy Implementation Committee approval. New policy.
06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. Updated medical necessity information to clarify that treatment of patients who are not pre-menopausal females is considered not medically necessary**.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Clarified that 150 mg tablets taken once daily for longer than 24 months of duration OR 200 mg tablets taken twice daily for longer than 6 months of duration is considered investigational.

Next Scheduled Review Date: 06/2021

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

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A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.