Elagolix/Relugolix Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date 2/1/2024

Date of Origin 4/1/2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Myfembree® (relugolix, estradiol hemihydrate, norethindrone acetate) Tablet	Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal patients Management of moderate to severe pain associated with endometriosis in premenopausal patients Limitations of Use: Use of Myfembree should be limited to 24 months due to the risk of continued bone loss which may not be reversible.		3
Oriahnn® (elagolix, estradiol, norethindrone acetate) Capsule	Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal patients Limitations of Use: Use of Oriahnn should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.		2
Orilissa® (elagolix) Tablet	Management of moderate to severe pain associated with endometriosis Limitations of Use: Limit the duration of use based on the dose and coexisting condition (refer to labeling for additional details).		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Endometriosis	Endometriosis is an estrogen-dependent, benign, inflammatory disease that affects patients during their premenarcheal, reproductive, and postmenopausal hormonal stages. While endometriosis is a common and nonmalignant process, ectopic endometrial tissue and resultant inflammation can cause dysmenorrhea, dyspareunia, chronic pain, and infertility. Symptoms can range from minimal to severely debilitating. While definitive diagnosis of endometriosis requires tissue biopsy and histologic confirmation, the combination of symptoms, signs, and imaging findings can be used to make a presumptive, nonsurgical diagnosis of endometriosis.(4,5) The first line option for the treatment of mild and moderate pain associated with endometriosis is hormonal contraceptives as combined (oral, vaginal ring or transdermal), oral progestin-only, levonorgestrel-releasing intrauterine system, or an

	etonogestrel-releasing subdermal implant as this therapy has low risk with few side effects and provides symptom relief for many patients. For those who have severe pain or continue to experience symptoms on hormonal contraceptive therapy, the use of gonadotropin-releasing hormone (GnRH) antagonists are recommended as second-line (e.g., if hormonal contraceptives or progestins have been ineffective). Patients who do not respond to medical treatment may move on to laparoscopy or hysterectomy for treatment.(5,12)
Uterine Leiomyomas	Uterine Leiomyomas, also known as myomata or fibroids, are the most common gynecologic benign tumors. Uterine leiomyomas are classified based on their location in the uterine wall and are referred to as submucous, intramural, and subserosal. Uterine leiomyomas are monoclonal tumors that arise from the muscular layer of the uterus and consist of large amounts of collagen, fibronectin, and proteoglycan. Leiomyomas can become enlarged causing significant distortion of the uterine surface or cavity.(6,7) Many patients with uterine leiomyomas are asymptomatic, but symptomatic patients may experience significant symptoms that interfere with daily living. The clinical characteristics can be broken down into three categories: • Heavy or abnormal uterine bleeding (the most common symptom) • Pelvic pressure and pain • Reproductive dysfunction (i.e., infertility, miscarriages, preterm labor) Uterine leiomyomas are generally diagnosed via pelvic examination and pelvic ultrasound. Other imagining, such as saline-infused sonogram, MRI, and hysteroscopy, are used if further evaluation of the leiomyomas is needed.(8,9) Hysterectomy is the only definitive treatment and eliminates the possibility of recurrence for patients who do not desire future childbearing or do not wish to retain their uterus. The American College of Gynecology and Obstetrics indicates the following are alternative options to hysterectomy:(9) • Hormonal contraceptives (combined hormonal contraceptive pills, progestin-only pills, levonorgestrel releasing IUDs) are widely used for control of abnormal menstruation and are often first line therapy, however, they only offer short term relief and direct data to support their effectiveness is limited • Tranexamic acid, an antifibrinolytic medication that prevents fibrin degradation, is an effective treatment for heavy menstrual bleeding, but limited data is associated with a statistically significant decrease in abnormal uterine bleeding • Gonadotropn releasing hormone antagonists, with hormonal add-back therapy, are recommended for treatment of heavy menstrual bleeding associated with uterine leiomyomas for up to two years • Gonadotropin releasing hormone agonists, with or without hormonal add-back therapy are recommended for the short-term treatment of abnormal uterine bleeding and uterine enlargement associated with leiomyomas and as a bridge to other treatment strategies • Uterine artery embolization, laparoscopic radiofrequency ablation, or myomectomy are alternatives for patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes
Efficacy	**Myfembree(3)** The efficacy and safety of Myfembree in patients with heavy menstrual bleeding associated with uterine fibroids were evaluated in two replicate, 24-week, multinational, randomized, double-blind, placebo-controlled studies in a total of 768 premenopausal patients with heavy menstrual bleeding associated with uterine fibroids in Study L1 (NCT03049735) and Study L2 (NCT03103087). For study inclusion, patients had to have uterine fibroids confirmed by ultrasound examination, and menstrual blood loss (MBL) volume of greater than or equal to 80 mL per cycle for two

	menstrual cycles or greater than or equal to 160 mL during one cycle to be included in the studies. Patients with hemoglobin less than 8.0 g/dL were excluded from the study. Iron therapy was required for patients with hemoglobin greater than or equal to 8 g/dL and less than or equal to 10 g/dL. Patients were allowed, but not required, to take calcium and vitamin D during the study. Treatment was initiated within the first seven days after the onset of menses. The primary endpoint of both studies was the proportion of patients in the Myfembree group compared with patients in the placebo group, who achieved menstrual blood loss volume of less than 80 mL and at least a 50% reduction from baseline MBL volume over the last 35 days of treatment. Key secondary endpoints were related to amenorrhea, MBL volume, and change in hemoglobin. In both Study L1 and Study L2, a statistically higher proportion of patients treated with Myfembree achieved the primary endpoint of both an MBL volume of less than 80 mL and at least a 50% reduction from baseline in MBL volume over the last 35 days of treatment compared with placebo. In Studies L1 and L2, 50.0% and 50.4% of patients treated with Myfembree, respectively, achieved amenorrhea compared to 6.2% and 3.1% treated with placebo, respectively, over the last 35 days of treatment. The mean MBL volumes in Studies L1 and L2 at baseline were 243.8 mL and 246.7 mL in the Myfembree group and 223.2 mL and 211.8 mL in the placebo group, respectively. The mean reduction in MBL volume from baseline to Week 24 in the Myfembree group was 82.0% in Study L1 and 84.3% in Study L2, compared with placebo which was 19.1% and 15.1%, respectively. A hemoglobin response was defined as a hemoglobin increase greater than 2 g/dL from baseline to Week 24 in the subgroup of patients with anemia at baseline (hemoglobin less than or equal to 10.5 g/dL). A statistically higher proportion treated with Myfembree compared with placebo had greater than 2 g/dL improvement in hemoglobin levels. The efficacy of Myfembree in premenopausal patients with moderate to severe pain associated with endometriosis was assessed in two 24-week, multinational, randomized, double-blind, placebo-controlled studies; Study S1 (NCT03204318) and Study S2 (NCT03204331). Study S1 included at total of 424 patients and Study S2 a total of 405. For study inclusion, patients had to have endometriosis confirmed by direct visualization during surgery and/or histology in addition to pain associated with endometriosis during a placebo run-in period. Dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP) were assessed daily using an 11-point numerical rating scale (NRS) ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine"). The co-primary endpoints of studies S1 and S2 were dysmenorrhea and non-menstrual pelvic pain response. Participants in Study S1 showed a 47.6% difference from placebo in dysmenorrhea response and a 18.9% difference in non-menstrual pelvic pain response at week 24, and Study S2 showed differences of 44.6% and 23.4%, respectively. **Orilissa(1,11)** The efficacy of Orilissa 150 mg once daily and 200 mg twice daily for the management of moderate to severe pain associated with endometriosis was demonstrated in two multinational double-blind, placebo-controlled trials in 1686 premenopausal patients [Study EM-1 (NCT01620528) and Study EM-2 (NCT01931670)]. Each placebo-controlled trial assessed the reduction in moderate to severe endometriosis-associated pain over 6 months of treatment. Each element is scored from 0 (absent) to 3 (severe) for a maximum total score of 15. Subjects were required to have non-menstrual pelvic pain for at least four days in the preceding 35 days, a bone mineral density (BMD) greater then -1.5, and the diagnosis of endometriosis was surgically confirmed. Patients were excluded if they had clinically significant gynecologic conditions (e.g., persistent or complex ovarian cyst(s), cancer, pelvic inflammatory disease), a history of osteoporosis, or other metabolic bone disease. 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 pelvic pain not related to menses (also known as non-menstrual pelvic pain) responded to treatment at Month 3. A higher proportion of patients treated with

Orilissa 150 mg once daily or 200 mg twice daily were responders for dysmenorrhea and non-menstrual pelvic pain compared to placebo in a dose-dependent manner at Month 3.

Patients in these studies also provided a daily self-assessment of their endometriosis pain using a numeric rating scale (NRS) that asked subjects to rate their endometriosis pain at its worst over the last 24 hours on a scale from 0 (no pain) to 10 (worst pain ever). In Study EM-1, baseline NRS scores were 5.7 for Orilissa 150 mg once daily, 5.5 for Orilissa 200 mg twice daily and 5.6 for placebo. In Study EM-2, baseline NRS scores were 5.7 for Orilissa 150 mg once daily, 5.3 for Orilissa 200 mg twice daily and 5.6 for placebo. Patients taking Orilissa 150 mg once daily and 200 mg twice daily reported a statistically ($p<0.001$) significant reduction from baseline in NRS scores compared to placebo at Month 3 in both Studies EM-1 and EM-2 (Study EM-1: 0.7 points for Orilissa 150 mg once daily and 1.3 points for Orilissa 200 mg twice daily; Study EM-2: 0.6 points for Orilissa 150 mg once daily and 1.2 points for Orilissa 200 mg twice daily). In addition, both Orilissa treatment groups showed statistically significantly greater mean decreases from baseline compared to placebo in dysmenorrhea and non-menstrual pelvic pain scores at Month 6.

Oriahnn(2,10)

The efficacy of Oriahnn in the management of heavy menstrual bleeding (HMB) associated with uterine fibroids was demonstrated in two randomized, double-blind, placebo-controlled studies [Study UF-1 (NCT02654054) and Study UF-2 (NCT02691494)] in which 790 premenopausal patients with heavy menstrual bleeding received Oriahnn (elagolix 300 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg in the morning and elagolix 300 mg in the evening) or placebo for 6 months. Patients were eligible if they were premenopausal females, had ultrasound confirmed diagnosis of uterine fibroids with heavy bleeding. Heavy menstrual bleeding at baseline was defined as having at least two menstrual cycles with greater than 80 mL of menstrual blood loss (MBL) as assessed by alkaline hematin (AH) method (an objective, validated measure to quantify MBL volume on sanitary products). Eligible patients were required to complete a washout period if previously treated with hormonal/antihormonal therapies. Patients were excluded if they had persistent or complex ovarian cyst(s), cancer, pelvic inflammatory disease, history of osteoporosis, or a bone mineral density (BMD) T score of -1.5 or less.

The primary endpoint in both studies was the proportion of responders, defined as patients who achieved both 1) MBL volume less than 80 mL at the Final Month and 2) 50% or greater reduction in MBL volume from baseline. A higher proportion of Oriahnn-treated patients were responders compared to placebo-treated patients.

	Study UF-1		Study UF-2	
	Oriahnn N=206	Placebo N=102	Oriahnn N=189	Placebo N=94
Patients with MBL volume less than 80 mL and greater than or equal to 50% reduction in MBL volume from Baseline to the Final Month	68.5%	8.7%	76.5%	10.5%
Difference from	59.8% (51.1, 68.5)		66.0% (57.1, 75.0)	

placebo % 95% CI P-value	less than 0.001		less than 0.001		

In Study UF-1, mean baseline MBL was 238 mL for Oriahnn and 255 mL for placebo. In Study UF-2, mean baseline MBL was 228 mL for Oriahnn and 254 mL for placebo. Patients taking Oriahnn had a mean reduction of MBL volume from Baseline to Final Month in both Studies UF-1 and UF-2 compared to patients taking placebo (Study UF-1: -177 mL for Oriahnn and 1 mL for placebo; Study UF-2: -169 mL for Oriahnn and -4 mL for placebo). In Studies UF-1 and UF-2, a greater proportion (57% and 61%, respectively) of patients receiving Oriahnn experienced suppression of bleeding, defined as no bleeding (but spotting allowed), at Final Month, compared to 4% and 5%, respectively, of patients receiving placebo. In Studies UF-1 and UF-2, a greater proportion of Oriahnn-treated patients who were anemic with baseline Hgb less than or equal to 0.5 g/dL achieved an increase greater than 2 g/dL in Hgb from Baseline to Month 6 compared to placebo-treated patients. Over 90% of patients with baseline Hgb less than or equal to 10.5 g/dL took supplemental iron.

Safety

Myfembree has the following boxed warnings:(3)

- Estrogen and progestin combinations, including Myfembree, increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism (PE), deep vein thrombosis (DVT), stroke and myocardial infarction (MI), especially in patients at increased risk for these events.
- Myfembree is contraindicated in patients with current or a history of thrombotic or thromboembolic disorders and in patients at increased risk for these events, including patients over 35 years of age who smoke or patients with uncontrolled hypertension.

Myfembree is contraindicated in patients:(3)

- With a high risk of arterial, venous thrombotic, or thromboembolic disorders. Examples include patients over 35 years of age who smoke, and patients 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 migraine headaches with aura if over 35 years of age
- Who are pregnant. Exposure to Myfembree early in pregnancy may increase the risk of early pregnancy loss
- With known osteoporosis, because of the risk of further bone loss
- With current or history of breast cancer or other hormone-sensitive malignancies, and with increased risk for hormone-sensitive malignancies
- With known hepatic impairment or disease
- With undiagnosed abnormal uterine bleeding
- With known anaphylactic reaction, angioedema, or hypersensitivity to Myfembree or any of its components. Anaphylactoid reactions have been reported.

Orilissa has no boxed warnings.(1)

Orilissa has the following contraindications:(1)

- Pregnancy

	• Known osteoporosis • Severe hepatic impairment • Organic anion transporting polypeptide (OATP) 1B1 that significantly increase elagolix plasma concentrations • Hypersensitivity reactions Oriahnn has the following boxed warnings:(2) • Estrogen and progestin combinations, including Oriahnn, increase the risk of thrombotic or thromboembolic disorders including pulmonary embolism, deep vein thrombosis, stroke and myocardial infarction, especially in patients at increased risk for these events. • Oriahnn is contraindicated in patients with current or a history of thrombotic or thromboembolic disorders and in patients at increased risk for these events, including patients over 35 years of age who smoke and patients with uncontrolled hypertension. Oriahnn is contraindicated in patients:(2) • With a high risk of arterial, venous thrombotic, or thromboembolic disorders. Examples include patients over 35 years of age who smoke, and patients 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 • Who are pregnant. Exposure to Oriahnn early in pregnancy may increase the risk of early pregnancy loss • With known osteoporosis because of the risk of further bone loss • With current or history of breast cancer or other hormonally-sensitive malignancies, and with increased risk for hormonally-sensitive malignancies • With known hepatic impairment or disease • With undiagnosed abnormal uterine bleeding • With known anaphylactic reaction, angioedema, or hypersensitivity to Oriahnn or any of its components • Taking inhibitors of organic anion transporting polypeptide (OATP)1B1 (a hepatic uptake transporter) that are known or expected to significantly increase elagolix plasma concentrations Elagolix causes a dose-dependent decrease in bone mineral density (BMD). BMD 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. Consider assessment of BMD in patients with a history of a low-trauma fracture or other risk factors for osteoporosis or bone loss, and do not use in patients with known osteoporosis.(1)

REFERENCES

Number	Reference
1	Orilissa prescribing information. AbbVie Inc. June 2023.
2	Oriahnn prescribing information. AbbVie Inc. June 2023.
3	Myfembree prescribing information. Myovant Sciences, Inc. February 2023.

Number	Reference
4	Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. *Nat Rev Endocrinol* 2014; 10:261.
5	American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 114: management of endometriosis. *Obstet Gynecol* 2010; 116:223. Reaffirmed 2018.
6	Sabry, M., & Al-Hendy, A. (2012). Medical treatment of uterine leiomyoma. *Reproductive sciences (Thousand Oaks, Calif.)*, *19*(4), 339–353. https://doi.org/10.1177/1933719111432867.
7	Munro MG, Critchley HO, Fraser IS, FIGO Menstrual Disorders Working Group. The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. *Fertil Steril* 2011; 95:2204.
8	American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol*. 2012;120(1):197-206. Reaffirmed 2016. doi:10.1097/AOG.0b013e318262e320.
9	American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Gynecology. Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228. *Obstet Gynecol*. 2021;137(6):e100-e115.
10	Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for Heavy Menstrual Bleeding in Women with Uterine Fibroids. *N Engl J Med* 2020; 382:328-340.
11	Taylor HS, Giudice LC, Lessey BA, et al. Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. *N Engl J Med* 2017; 377:28.
12	Becker CM, Bokor A, et al. ESHRE Endometriosis Guideline Group. ESHRE guideline: endometriosis. *Hum Reprod Open.* 2022 Feb 26;2022(2):hoac009. doi: 10.1093/hropen/hoac009.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Orilissa	elagolix sodium tab	150 MG ; 200 MG	M ; N ; O ; Y	N		
Oriahnn	elagolix-estrad-noreth	300-1-0.5 & 300 MG	M ; N ; O ; Y	N		
Myfembree	relugolix-estradiol-norethindrone acetate tab	40-1-0.5 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Myfembree	Relugolix-Estradiol-Norethindrone Acetate Tab	40-1-0.5 MG	30	Tablets	30	DAYS			
Oriahnn	Elagolix-Estrad-Noreth 300-1-0.5MG & Elagolix 300MG Cap Pack	300-1-0.5 & 300 MG	56	Capsules	28	DAYS			
Orilissa	Elagolix Sodium Tab 150 MG (Base Equiv)	150 MG	30	Tablets	30	DAYS			
Orilissa	Elagolix Sodium Tab 200 MG (Base Equiv)	200 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Myfembree	relugolix-estradiol-norethindrone acetate tab	40-1-0.5 MG	Medicaid
Oriahnn	elagolix-estrad-noreth	300-1-0.5 & 300 MG	Medicaid
Orilissa	elagolix sodium tab	150 MG ; 200 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Myfembree	Relugolix-Estradiol-Norethindrone Acetate Tab	40-1-0.5 MG	Medicaid
Oriahnn	Elagolix-Estrad-Noreth 300-1-0.5MG & Elagolix 300MG Cap Pack	300-1-0.5 & 300 MG	Medicaid
Orilissa	Elagolix Sodium Tab 150 MG (Base Equiv)	150 MG	Medicaid
Orilissa	Elagolix Sodium Tab 200 MG (Base Equiv)	200 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Myfembree	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) and BOTH of the following: 1. The patient's diagnosis of uterine fibroids was confirmed via imaging (e.g., ultrasound) **AND** 2. The patient has NOT had a hysterectomy **OR** B. The patient has a diagnosis of moderate to severe pain associated with endometriosis **AND** 2. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 3. The prescriber has confirmed the patient's bone health allows for initiating therapy with the requested agent **AND** 4. ONE of the following: A. The patient's medication history includes at least ONE hormonal contraceptive used in the treatment of the requested indication AND ONE of the following: 1. The patient has had an inadequate response to at least ONE hormonal contraceptive used in the treatment of the requested indication **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over hormonal contraceptives used in the treatment of the requested indication **OR** B. The patient has an intolerance or hypersensitivity to at least ONE hormonal contraceptive used in the treatment of the requested indication **OR** C. The patient has an FDA labeled contraindication to ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**

Module	Clinical Criteria for Approval
	E. The prescriber has provided documentation that ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 5. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. ONE of the following: A. The patient is initiating therapy with the requested agent **OR** B. The patient is not initiating therapy with the requested agent and BOTH of the following: 1. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** 2. The total duration of treatment with the requested agent has NOT exceeded 24 months per lifetime **Length of Approval:** Up to 6 months, with a lifetime maximum of 24 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The prescriber has assessed the patient's bone health AND confirmed the patient's bone health allows for continued therapy with the requested agent **AND** 5. The patient has NOT had a fragility fracture since starting therapy with the requested agent **AND** 6. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 8. BOTH of the following: A. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** B. The total duration of treatment with the requested agent has NOT exceeded 24 months per lifetime **Length of Approval:** Up to 6 months, with a lifetime maximum of 24 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.
Oriahnn	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) **AND** 2. The patient's diagnosis of uterine fibroids was confirmed via imaging (e.g., ultrasound) **AND**

Module	Clinical Criteria for Approval
	3. The patient has NOT had a hysterectomy **AND** 4. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 5. The prescriber has confirmed the patient's bone health allows for initiating therapy with the requested agent **AND** 6. ONE of the following: A. The patient's medication history includes at least ONE hormonal contraceptive used in the treatment of the requested indication AND ONE of the following: 1. The patient has had an inadequate response to at least ONE hormonal contraceptive used in the treatment of the requested indication **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over hormonal contraceptives used in the treatment of the requested indication **OR** B. The patient has an intolerance or hypersensitivity to at least ONE hormonal contraceptive used in the treatment of the requested indication **OR** C. The patient has an FDA labeled contraindication to ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 7. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 8. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 9. ONE of the following: A. The patient is initiating therapy with the requested agent **OR** B. The patient is not initiating therapy with the requested agent and BOTH of the following: 1. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** 2. The total duration of treatment with the requested agent has NOT exceeded 24 months per lifetime **Length of Approval:** Up to 6 months, with a lifetime maximum of 24 months **Renewal Evaluation** **Target Agent** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The prescriber has assessed the patient's bone health AND confirmed the patient's bone health allows for continued therapy with the requested agent **AND**

Module	Clinical Criteria for Approval
	5. The patient has NOT had a fragility fracture since starting therapy with the requested agent **AND** 6. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 8. BOTH of the following: A. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** B. The total duration of treatment with the requested agent has NOT exceeded 24 months per lifetime **Length of Approval:** Up to 6 months, with a lifetime maximum of 24 months
Orilissa	**Initial Evaluation** **Target Agent** will be approved when ALL of the following are met: 1. The patient has a diagnosis of moderate to severe pain associated with endometriosis **AND** 2. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 3. ONE of the following: A. The patient's medication history includes ONE hormonal contraceptive therapy used in the treatment of the requested indication AND ONE of the following: 1. The patient has had an inadequate response to ONE hormonal contraceptive therapy used in the treatment of the requested indication **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over hormonal contraceptive therapy used in the treatment of the requested indication **OR** B. The patient has an intolerance or hypersensitivity to ONE hormonal contraceptive used in the treatment of the requested indication **OR** C. The patient has an FDA labeled contraindication to ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL hormonal contraceptive therapy (i.e., oral, topical patches, implants, injections, IUD) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. The prescriber has confirmed the patient's bone health allows for initiating therapy with the requested agent **AND** 5. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient does NOT have coexisting moderate hepatic impairment (Child-Pugh [CP]/ Child-Turcotte-Pugh [CTP] Class B) AND ONE of the following: 1. The patient is initiating therapy with the requested agent and strength **OR** 2. The patient is not initiating therapy with the requested agent and strength and BOTH of the following: A. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** B. ONE of the following: 1. The requested strength is 150 mg AND the total duration of treatment with the requested strength has NOT exceeded 24 months per lifetime **OR** 2. The requested strength is 200 mg AND the total duration of treatment with the requested strength has NOT exceeded 6 months per lifetime **OR** B. The patient does have coexisting moderate hepatic impairment (Child-Pugh [CP]/ Child-Turcotte-Pugh [CTP] Class B) AND BOTH of the following: 1. The requested strength is 150 mg **AND** 2. ONE of the following: A. The patient is initiating therapy with the requested agent and strength **OR** B. The patient is not initiating therapy with the requested agent and strength and BOTH of the following: 1. The prescriber has provided information indicating the number of months the patient has been on therapy **AND** 2. The total duration of treatment with the requested strength has NOT exceeded 6 months per lifetime **Length of Approval:** Up to 6 months with a lifetime maximum of 24 months with the 150 mg without coexisting moderate hepatic impairment, a lifetime maximum of 6 months with the 150 mg with coexisting moderate hepatic impairment, and a lifetime maximum of 6 months with the 200 mg **Renewal Evaluation** **Target Agent** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (*please note requests for 200 mg strength should always be reviewed under initial criteria) **AND** 2. The patient is premenopausal (e.g., less than 12 months since last menstrual period) **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The prescriber has assessed the patient's bone health AND confirmed the patient's bone health allows for continued therapy with the requested agent **AND** 5. The patient has NOT had a fragility fracture since starting therapy with the requested agent **AND** 6. The patient will NOT be using the requested agent in combination with another GnRH antagonist agent targeted in this program (e.g., elagolix, relugolix) for the requested indication **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 8. BOTH of the following: A. The prescriber has provided information indicating the number of months the patient has been on therapy with the requested agent and strength **AND** B. ONE of the following:

Module	Clinical Criteria for Approval
	1. The patient does NOT have coexisting moderate hepatic impairment (Child-Pugh [CP]/ Child-Turcotte-Pugh [CTP] Class B) AND the total duration of treatment with the requested strength has NOT exceeded 24 months per lifetime **OR** 2. The patient does have coexisting moderate hepatic impairment (Child-Pugh [CP]/ Child-Turcotte-Pugh [CTP] Class B) AND the total duration of treatment with the requested strength has NOT exceeded 6 months per lifetime **Length of Approval:** Up to 6 months with a lifetime maximum of 24 months with the 150 mg without coexisting moderate hepatic impairment OR a lifetime maximum of 6 months with the 150 mg with coexisting moderate hepatic impairment

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **Length of Approval:** Myfembree and Oriahnn: Up to 6 months with a lifetime maximum of 24 months. Orilissa: Up to 6 months with a lifetime maximum of 24 months with the 150 mg without coexisting moderate hepatic impairment, a lifetime maximum of 6 months with the 150 mg with coexisting moderate hepatic impairment, and a lifetime maximum of 6 months with the 200 mg