Effective Date.....**11/15/2023**
Next Review Date.....**11/15/2024**
Coverage Policy Number **IP0216**

Vaginal Estrogen Products and Ospemifine

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following vaginal estrogen products and ospemifine:

- **Estrace**® (estradiol) vaginal cream
- **Femring**® (estradiol acetate) vaginal ring
- **Imvexxy**™ (estradiol) vaginal insert
- **Osphena**® (ospemifene) oral tablet
- **Vagifem**® (estradiol) vaginal insert

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

The products in the table below are considered medically necessary when the following are met:

Employer Group Non-Covered Products and the Preferred Covered Alternatives:

Non-Covered Product	Criteria
Estrace (estradiol) vaginal cream	The individual has tried **estradiol vaginal cream** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Femring (estradiol acetate) vaginal ring	The individual has had an inadequate response, contraindication, or is intolerant to **TWO** of the following: A. estradiol vaginal cream B. estradiol vaginal tablet (generic Vagifem) C. Estring (estradiol) vaginal ring D. Premarin (conjugated estrogens) vaginal cream
Imvexxy (estradiol) vaginal insert	There is documentation of **ONE** of the following (A or B): A. The individual has had an inadequate response, contraindication, or is intolerant to **TWO** of the following: i. estradiol vaginal cream ii. estradiol vaginal tablet (generic Vagifem) iii. Estring (estradiol) vaginal ring iv. Premarin (conjugated estrogens) vaginal cream B. The individual requires a low-dose vaginal product and has had an inadequate response, contraindication, or is intolerant to Estring (estradiol) vaginal ring
Osphena (ospemifene) oral tablet	The individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: A. estradiol vaginal cream (generic for Estrace) B. estradiol vaginal tablet (generic Vagifem) C. Estring (estradiol) vaginal ring D. Premarin (conjugated estrogens) vaginal cream
Vagifem (estradiol) vaginal insert	The individual has tried **estradiol vaginal tablet** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Vaginal estrogen products are considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

Background

OVERVIEW

All of the vaginal estrogen products and estrogen modifiers are indicated for the treatment of **vulvar and vaginal atrophy symptoms associated with menopause**; however, there are some differences in the wording of this indication among the products, which are noted in the prescribing information.[1-9] Femring delivers a systemic dose of estrogen and thus it is also indicated for the treatment of **moderate to severe vasomotor symptoms of menopause**.[3] Intrarosa is the only medication in this class that does not carry a warning or caution for estrogen dependent neoplasm, deep vein thrombosis, or stroke.[1-9]

Guidelines

According to the North American Menopause Society guidelines on the genitourinary syndrome of menopause (GSM) [2020], GSM describes the signs and symptoms resulting from the effect of estrogen deficiency on the female genitourinary tract, including the labia, vagina, urethra, and bladder.[10] The syndrome includes genital symptoms of dryness, burning, and irritation; urinary symptoms and conditions of dysuria, urgency, and recurrent urinary tract infections; and sexual symptoms of pain and dryness. Vulvar and vaginal atrophy is a component of GSM. The guidelines note that low-dose vaginal estrogen, vaginal dehydroepiandrosterone, and ospemifene are effective treatment for moderate to severe GSM. Also noted is that low-dose vaginal estrogen formulations, including the estradiol (vaginal) tablet, insert, and ring (Estring), result in serum estradiol within the postmenopausal range and similar to that of placebo.

References

1. Estrace Cream [prescribing information]. Madison, NJ: Allergan; December 2022.
2. Estring vaginal ring [prescribing information]. New York, NY: Pfizer; December 2021.
3. Femring vaginal ring [prescribing information]. East Hanover, NJ: Millicent; January 2019.
4. Premarin vaginal cream [prescribing information]. Philadelphia, PA: Pfizer; September 2018.
5. Vagifem vaginal tablets [prescribing information]. Plainsboro, NJ: Novo Nordisk; September 2022.
6. Yuvafem™ vaginal tablets [prescribing information]. Bridgewater, NJ: Amneal; February 2021.
7. Imvexxy vaginal tablets [prescribing information]. Boca Raton, FL: TherapeuticsMD; November 2021.
8. Intrarosa vaginal inserts [prescribing information]. East Hanover, NJ: Millicent; November 2020.
9. Osphena tablets for oral use [prescribing information]. Florham Park, NJ: Shionogi; April 2023.
10. North American Menopause Society (NAMS). NAMS Position Statement. The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Available at: http://www.menopause.org/publications/professional-publications/position-statements-other-reports. Accessed on June 20, 2023.