Oscar Clinical Guideline: Osphena (ospemifene) (PG169, Ver. 2)

Osphena (ospemifene)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Ospemifene (Osphena) is an oral selective estrogen receptor modulator (SERM) indicated for the treatment of moderate to severe dyspareunia and vaginal dryness, both of which are symptoms of vulvar and vaginal atrophy due to menopause. Unlike traditional hormone replacement therapies, ospemifene is not a hormone and offers an alternative specifically tailored for women experiencing exclusive genitourinary menopausal symptoms.

> **Important Consideration:** *Dyspareunia is categorized as a sexual pain disorder due to its implications on sexual function. From a medical perspective, it is characterized by pain during sexual intercourse that interferes with sexual activity. Therefore, the Plan considers the use of ospemifene for dyspareunia to be primarily for the treatment of sexual dysfunction rather than pain.*
>
> **NOTE:** Treatment for sexual dysfunctions is an excluded benefit for certain Plans. Coverage for medications to treat sexual dysfunction, including dyspareunia, varies depending on a member's

benefit policy. Please review the member's coverage benefits to determine if treatment for sexual dysfunctions is a covered benefit.

As a SERM, ospemifene exerts beneficial effects on vaginal tissue by acting as an estrogen agonist. It effectively stimulates lubrication and growth, as well as supports healthy bone and endometrial tissue. However, it's important to note that ospemifene also exhibits antagonist effects on breast tissue. In clinical trials, ospemifene was shown to effectively treat dyspareunia and vaginal dryness with improvement seen as early as 4-6 weeks. However, ospemifene comes with a boxed warning highlighting its potential to stimulate endometrial hyperplasia, a condition where the lining of the uterus thickens, which can be a precursor to endometrial cancer. Another notable risk associated with ospemifene is its potential to cause thrombotic and hemorrhagic strokes, as well as deep venous thrombosis, although at a lower incidence compared to estrogen-based hormone replacement therapies.

- When ospemifene is prescribed for postmenopausal women with an intact uterus, the concomitant use of progestin therapy should be considered to reduce the risk of endometrial hyperplasia and endometrial cancer. Progestin therapy is not necessary for women without an intact uterus. Clinical surveillance, including periodic evaluations and diagnostic measures such as endometrial sampling when indicated, is essential to rule out malignancy in women with persistent or recurrent abnormal genital bleeding.
- Ospemifene therapy should be used for the shortest duration consistent with treatment goals and the individual member's risk profile. Periodic reevaluation is recommended to determine if continued treatment is necessary. Clinicians should weigh the benefits of symptom relief against the potential risks of long-term therapy, including thromboembolic events and endometrial changes.
- Clinical trials evaluating ospemifene predominantly included white women (90–99%), which may limit the generalizability of efficacy and safety data to diverse populations. Clinicians should consider individual member factors, including racial and ethnic differences, when extrapolating trial data to clinical practice.

Definitions

"**Arterial Thromboembolic Disease**" refers to conditions where blood clots form in the arteries, which can lead to serious conditions like heart attacks or strokes.

"**Deep Venous Thrombosis**" is a blood clot that forms in a deep vein, usually in the legs.

"**Dyspareunia**" is a medical term that describes pain during sexual intercourse.

"**Endometrial Hyperplasia**" is a condition characterized by the excessive growth of the lining of the uterus. It can be a precursor to endometrial cancer.

"**Estrogen-Dependent Neoplasia**" refers to a type of cancer that grows in response to estrogen.

"**Low-dose Vaginal Estrogen Therapy**" refers to treatment involving the application of estrogen directly to the vaginal tissues to alleviate symptoms of vaginal atrophy. Examples include Yuvafem 10mcg Vaginal Insert and Estradiol 0.01% Vaginal Cream.

"**Noncoital Sexual Pain**" refers to pain that occurs during sexual activities other than intercourse.

"**Sexual Dysfunction**" refers to any of a group of sexual disorders characterized by inhibition either of sexual desire or of the psychophysiological changes that usually characterize sexual response. Included are female sexual arousal disorder, male erectile disorder and hypoactive sexual desire disorder.

"**Vaginismus**" is a condition where there is an involuntary spasm of the muscles surrounding the vaginal entrance, making intercourse painful or impossible.

"**Vulvar and Vaginal Atrophy**" is a condition in which the vaginal and vulvar tissues become thinner, drier, and less elastic as a result of reduced estrogen levels typically associated with menopause.

Coverage Criteria

The Plan will provide coverage for **Osphena (ospemifene)** when **BOTH** the following criteria are met:

1. **IF** the information reviewed indicates the medication is being used for treatment of sexual dysfunction (i.e., dyspareunia), the member must meet **ONE** of the following:
    a. The Plan does not explicitly exclude coverage for treatments for sexual dysfunctions; ***or***
    NOTE: *Treatment for sexual dysfunctions is an excluded benefit for certain Plans. Coverage for medications to treat sexual dysfunction, including dyspareunia, varies depending on a member's benefit policy. Please review the member's coverage benefits to determine if treatment for sexual dysfunctions is a covered benefit.*
    b. Clinical documentation indicates symptoms (e.g., irritation, itching, vaginal dryness, pain) extend beyond sexual activities (i.e., also manifest in association with other non-

sexual activities, such as pain during routine activities, e.g., inserting a tampon, during gynecological examinations, or wearing tight-fitting clothes); ***AND***

2. The member meets the **Medical Necessity Criteria** listed below:

Medical Necessity Criteria for Initial Authorization

The Plan considers **Osphena (ospemifene)** medically necessary when **ALL** of the following criteria are met:

1. The member is 18 years of age or older; ***AND***
2. The member has **ONE** of the following diagnoses:
    a. moderate to severe dyspareunia associated with menopause; ***and/or***
    b. moderate to severe vaginal dryness associated with menopause; ***AND***
3. The member is unable to use, or has tried and failed **BOTH** of the following:
    a. Over-the-counter (OTC) non-hormonal vaginal moisturizers and/or lubricants (Replens, K-Y, and others); ***and***
    b. Low-dose vaginal estrogen therapy (e.g., Yuvafem 10mcg Vaginal Insert, Estradiol 0.01% Vaginal Cream, and others); ***AND***
4. The member does **NOT** have **ANY** of the following:
    a. Active arterial thromboembolic disease (e.g., stroke and myocardial infarction), or a history of these conditions; ***and/or***
    b. Active deep vein thrombosis, pulmonary embolism, or a history of these conditions; ***and/or***
    c. Is currently pregnant; ***and/or***
    d. Known or suspected estrogen-dependent neoplasia; ***and/or***
    e. Undiagnosed abnormal genital bleeding.

If the above prior authorization criteria are met, Osphena (ospemifene) will be approved for 12-weeks.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if the member has recent (within the last 3 months) clinical chart documentation indicating that the member has experienced a documented improvement in dyspareunia or vaginal dryness symptoms.

Experimental or Investigational / Not Medically Necessary

Osphena (ospemifene) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

References

1. DeBonaventura M, Luo X, Moffatt M, et al. The association between vulvovaginal atrophy symptoms and quality of life among postmenopausal women in the United States and Western Europe. J Womens Health (Larchmt). 2015;24(9):713-722.
2. Faubion SS, Sood R, Kapoor E. Genitourinary syndrome of menopause: management strategies for the clinician. Mayo Clin Proc. 2017;92(12):1842-1849.
3. Kingsberg SA, Wysocki S, Magnus, L, Krychman ML. Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey. J Sex Med. 2013;10(7):1790-1799.
4. NAMS Position Statement. The 2023 nonhormone therapy postion statement of The North American Menopause Society. Menopause 2023; 30:573. doi:10.1097/gme.0000000000002200
5. Osphena (ospemifene) [prescribing information]. Princeton, NJ: Duchesnay USA Inc; February 2024.
6. Osphena (ospemifene) [prescribing information]. Florham Park, NJ: Shionogi Inc; January 2019.
7. Pinkerton JV, Sánchez Aguirre F, Blake J, et al. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 2017;24(7):728-753.
8. Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society. Menopause. 2014;21(10):1063-1068.
9. Stuenkel CA, Davis SR, Gompel A, et al. Treatment of symptoms of the menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(11):3975-4011. doi: 10.1210/jc.2015-2236.
10. "The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-794. doi: 10.1097/GME.0000000000002028. PMID: 35797481.
11. The NAMS 2020 GSM Position Statement Editorial Panel. The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Menopause. 2020 Sep;27(9):976-992. doi: 10.1097/GME.0000000000001609. PMID: 32852449.

Clinical Guideline Revision / History Information

Original Date: 9/21/2023
Reviewed/Revised: 12/19/2024