Clinical Policy: Ospemifene (Osphena)

Reference Number: CP.PMN.168
Effective Date: 08.28.18
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ospemifene (Osphena®) is a selective estrogen receptor modulator (SERM).

FDA Approved Indication(s)

Osphena is indicated for the treatment of moderate to severe dyspareunia and vaginal dryness, symptoms of vulvar and vaginal atrophy, due to menopause.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Osphena is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Dyspareunia or Vaginal Dryness (must meet all)**:**

1. Diagnosis of dyspareunia or vaginal dryness due to menopause;
2. Age ≥ 18 years;
3. Failure of two vaginal lubricants or vaginal moisturizers (*see Appendix B for examples*), unless clinically significant adverse effects are experienced or all are contraindicated;
4. Failure of ≥ 4 weeks of one vaginal estrogen (e.g., estradiol vaginal cream, Premarin® vaginal cream) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Dose does not exceed 60 mg (1 tablet) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Dyspareunia or Vaginal Dryness (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy (e.g., dyspareunia symptom reduction);
3. If request is for a dose increase, new dose does not exceed 60 mg (1 tablet) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
SERM: selective estrogen receptor modulator

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
estradiol vaginal cream (Estrace®)	Initial: 2 to 4 gm vaginally QD for 1 to 2 weeks, gradually reduce to 50% of initial dose for 1 to 2 weeks Maintenance: 1 gm 1 to 3 times a week	Varies
Premarin® (conjugated estrogens) vaginal cream	0.5 gm intravaginally twice per week continuously	Varies
estradiol vaginal tablet (Vagifem®)	1 tablet intravaginally QD for 2 weeks, followed by 1 tablet twice weekly	1 tablet/day
Estring® (estradiol vaginal ring)	2 mg intravaginally for 90 days	2 mg every 90 days
Vaginal lubricants: *Water-based* Astroglide®, FemGlide®, Just Like Me®, K-Y Jelly®, Pre-Seed®, Slippery Stuff®, Summer's Eve® *Silicone-based* ID Millennium®, Pink®, Pjur®, Pure Pleasure®	Apply intravaginally before sex	Varies
Vaginal moisturizers: Fresh Start®, K-Y Silk-E®, Moist Again®, Replens®, K-Y Liquibeads®	Apply intravaginally before sex	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): undiagnosed abnormal genital bleeding; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism, or a history of these conditions; active thromboembolic disease (for example, stroke and myocardial infarction) or a history of these conditions; hypersensitivity (for example,

angioedema, urticaria, rash, pruritis) to Osphena or any ingredients; known or suspected pregnancy
- Box warning(s): endometrial cancer and cardiovascular disorders (stroke and deep vein thrombosis).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Moderate to severe dyspareunia or vaginal dryness due to menopause	60 mg PO QD	60 mg/day

VI. Product Availability

Tablet: 60 mg

VII. References

1. Osphena Prescribing Information. Florham Park, NJ: Shionogi Inc.; February 2024. Available at: http://www.osphena.com/. Accessed July 17, 2024.
2. American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Gynecology. ACOG Practice Bulletin No. 213: Female sexual dysfunction. Obstet Gynecol. 2019 Jul;134(1):203-205
3. Pinkerton JV, Aguirre FS, Blake J, et al. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 2017;24(7):728-753. doi:10.1097/GME.0000000000000921.
4. Faubion S, Sood R, Kapoor E. Genitourinary Syndrome of Menopause: Management Strategies for the Clinician. Mayo Clin Proc. 2017 Dec;92(12):1842-1849. doi: 10.1016/j.mayocp.2017.08.019.
5. Stuenkel C, Davis S, Gompel A, et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 11, 1 November 2015, Pages 3975–4011, https://doi.org/10.1210/jc.2015-2236
6. Vaginal and Vulvar Comfort: Effective Treatments for Sexual Problems. The North American Menopause Society. Available at: https://www.menopause.org/for-women/sexual-health-menopause-online/effective-treatments-for-sexual-problems. Accessed July 31, 2024.
7. Shifren JL and Gass MLS. The North American Menopause Society recommendations for clinical care of medlife women. Menopause 2014;21(10):1-25.
8. Vaginal Dryness. The North American Menopause Society. Available at: https://www.menopause.org/docs/default-source/for-women/mn-vaginal-dryness.pdf. Accessed July 31, 2024.
9. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 31, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.13.20	11.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	06.22.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less.	04.27.22	08.22
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.16.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.06.23	11.23
4Q 2024 annual review: no significant changes; removed "at up to maximally indicated doses" for vaginal lubricant/moisturizer trial requirement since there are no maximum doses for these products; added an example of positive response to therapy to align with Intrarosa criteria; references reviewed and updated.	07.31.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.