BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OSPHENA® (ospemifene) oral tablet
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Osphena (ospemifene) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is 18 years of age or older

2. Individual has a confirmed diagnosis of moderate to severe vaginal dryness (a symptom of vulvar and vaginal atrophy) due to menopause (see Definitions section)

3. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **TWO** trials of an estrogen product (see Definitions section for some examples)

(**Note**: A postmenopausal woman with an intact uterus should use estrogen product with a progestin; a progestin is not needed if the woman has had a hysterectomy)

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. There are **NO** FDA-label contraindications such as:
    a. Undiagnosed abnormal genital bleeding
    b. Known or suspected estrogen-dependent neoplasia
    c. Active DVT, pulmonary embolism (PE), or a history of these conditions
    d. Active arterial thromboembolic disease (for example, stroke and myocardial infarction [MI]), or a history of these conditions)
    e. Known or suspected pregnancy

6. Will not be used simultaneously with other estrogens, or estrogen agonist/antagonists

7. Will not be used simultaneously with fluconazole

8. Will not be used simultaneously with strong inducers of 3A4 or moderate inducers of 2C9 and 2C19 (such as rifampin, carbamazepine, dabrafenib, enzalutamide, letermovir, phenobarbital, phenytoin, etc.)

9. Will not be used in an individual with severe hepatic impairment (Child-Pugh Class C)

10. Will not be used in an individual with known or suspected breast cancer or a history of breast cancer

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Osphena (ospemifene) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual has documentation of positive clinical response to therapy defined as achieved and maintains at least a 50% reduction in vaginal dryness

2. Individual has been adherent with the medication

3. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy
    b. Significant adverse effect such as:
        i. Thromboembolic or hemorrhagic stroke
        ii. Venous thromboembolism

iii. Endometrial cancer
iv. Breast cancer
v. Severe hepatic impairment

5. Will not be used simultaneously with other estrogens, or estrogen agonist/antagonists

6. Will not be used simultaneously with fluconazole

7. Will not be used simultaneously with strong inducers of 3A4 or moderate inducers of 2C9 and 2C19 (such as rifampin, carbamazepine, dabrafenib, enzalutamide, letermovir, phenobarbital, phenytoin, etc.)

8. Will not be used in an individual with severe hepatic impairment (Child-Pugh Class C)

9. Will not be used in an individual with known or suspected breast cancer or a history of breast cancer

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Osphena (ospemifene) is an estrogen agonist-antagonist with tissue selective effects is indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause and for the treatment of moderate to severe vaginal dryness, a symptom of vulvar and vaginal atrophy, due to menopause. Osphena (ospemifene) has agonistic effects on the endometrium, when a product with estrogenic agonistic effects on the endometrium is used, a progestin should be considered to reduce the risk of endometrial cancer. A woman without a uterus does not need a progestin. The use of Osphena (ospemifene) with a progestin was not evaluated in clinical trials.

Menopausal symptoms include hot flushes and night sweats but may also include other symptoms such as sleep disturbance, joint aches, irritability, mood changes, and genitourinary problems.

The term genitourinary syndrome of menopause (GSM) encompasses all of the atrophic symptoms women may have in the vulvovaginal and bladder-urethral areas from loss of estrogen that occurs with menopause. GSM replaced the term vaginal atrophy (other terms include vulvovaginal atrophy, urogenital atrophy, or atrophic vaginitis). involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra, and bladder. The syndrome may include but is not limited to genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, discomfort or pain, and impaired function; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all the signs and symptoms these signs and symptoms are not better accounted for by another diagnosis.

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For symptoms of vaginal dryness, discomfort, or dyspareunia associated with vaginal atrophy, first-line treatments are non-hormonal vaginal moisturizers and lubricants. If these do not provide adequate symptom relief, estrogen therapy or other hormonal medications are prescribed if there are no contraindications.

Numerous studies have been conducted that show the efficacy of hormonal replacement therapy in controlling menopausal symptoms. Treatment options for dyspareunia or vaginal dryness include vaginal moisturizers and lubricants, vaginal estrogen replacement (e.g., ring, vaginal tablet, cream), and oral estrogen replacement.

Estrogen-containing products are the most effective FDA-approved therapies for treatment of moderate to severe vasomotor symptoms (such as hot flashes and night sweats) associated with menopause and for treatment of moderate to severe symptoms of vulvar and vaginal atrophy (such as dryness, dyspareunia, itching, and burning) associated with menopause. Estrogen alone may be prescribed for women who have undergone a hysterectomy. In women with an intact uterus, a progestational agent should be added to the estrogen to protect the endometrium from the risk of unopposed estrogen causing development of hyperplasia and endometrial cancer.

For women who cannot use estrogen for control of severe vasomotor symptoms, non-estrogen containing medications have been used. Other agents that have been shown to be effective in the management of menopausal symptoms include other selective serotonin receptor inhibitors such as citalopram, escitalopram, fluoxetine, paroxetine and venlafaxine, a selective serotonin norepinephrine reuptake inhibitor.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Moderate to severe dyspareunia is classified as a form of sexual dysfunction which could be a benefit exclusion.

Estrogens: (not an all inclusive list)

- Oral estrogen tabs:
  - Conjugated estrogen (such as Premarin)
  - Esterified estrogen (such as Menest)
  - Estradiol (such as Estrace)
  - Estropipate
- Transdermal estrogen:
  - Estradiol transdermal (such as Alora, Climara, Vivelle-Dot)
- Vaginal estrogen:
  - Conjugated estrogen Cream (such as Premarin)
  - Estradiol acetate cream (such as Estrace)
  - Estradiol ring (such as Femring)
  - Estradiol tablet (such as Vagifem)
- Esterified Estrogen-Progestin, oral tabs (such as Prempro, Premphase, Mimvey)
- Estrogen-Progestin, transdermal (such as CombiPatch)

Progestins, if needed:

- Medroxyprogesterone

- Micronized progesterone

Genitourinary syndrome of menopause (GSM):
A collection of symptoms and signs associated with a decrease in estrogen and other sex steroids involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra and bladder.

Vaginal atrophy: also known as atrophic vaginitis, vulvovaginal atrophy, or urogenital atrophy:
It is characterized by dryness, inflammation, and thinning of the epithelial lining of the vagina and lower urinary tract due to loss of estrogen.

Dyspareunia:
Painful sexual intercourse which can be moderate to severe, is a symptom of vulvar & vaginal atrophy from menopause.

Resources:

Osphena (ospemifene) product information, revised by Duchesnay USA, Inc. 02-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Casper RF. Menopausal hot flashes. In: UpToDate, Barbieri RL, Martin KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2025. Topic last updated December 17, 2024. Accessed September 23, 2025.

Martin KA, Barbieri RL. Treatment of menopausal symptoms with hormone therapy. In: UpToDate, Snyder PJ, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2025. Topic last updated November 20, 2023. Accessed September 23, 2025.

Bachmann G, Pinkerton JV. Genitourinary syndrome of menopause (vulvovaginal atrophy): Treatment. In: UpToDate, Barbieri RL, Burstein HJ, Chakrabarti A (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2025. Topic last updated April 21, 2025. Accessed September 23, 2025.