BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES		**ORIGINAL EFFECTIVE DATE:**	**11/17/2016**
SECTION:	**DRUGS**	**LAST REVIEW DATE:**	**11/18/2021**
		LAST CRITERIA REVISION DATE:	**11/18/2021**
		ARCHIVE DATE:	

OSPHENA® (ospemifene) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Osphena (ospemifene) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older

  2. A confirmed diagnosis of moderate to severe dyspareunia or vaginal dryness (symptoms of vulvar and vaginal atrophy) due to menopause

  3. Individual has failure, contraindication per FDA label or intolerance to **THREE** of the following products (Note: a woman with an intact uterus should use estrogen product with a progestin; a progestin is not needed if the woman has had a hysterectomy):
     a. Oral estrogen tabs:
        i. Conjugated estrogen (such as Premarin)
        ii. Esterified estrogen (such as Menest)
        iii. Estradiol (such as Estrace)
        iv. Estropipate
     b. Transdermal estrogen:
        i. Estradiol transdermal (such as Alora, Climara, Vivelle-Dot)
     c. Vaginal estrogen:
        i. Conjugated estrogen Cream (such as Premarin)
        ii. Estradiol acetate cream (such as Estrace)
        iii. Estradiol ring (such as Femring)
        iv. Estradiol tablet (such as Vagifem)
     d. Esterified Estrogen-Progestin, oral tabs (such as Prempro, Premphase, Mimvey)
     e. Estrogen-Progestin, transdermal (such as CombiPatch)
     f. Progestins, if needed:
        i. Medroxyprogesterone
        ii. Micronized progesterone

  4. 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

  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 rifampin

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

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9. 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) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition responded while on therapy
    a. Response is defined as:
        i. Achieved and maintains at least a 50% reduction in dyspareunia
        ii. Achieved and maintains at least a 50% reduction in vaginal dryness

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    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

4. There are no significant interacting drugs

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 a Non-cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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 of the signs and symptoms these signs and symptoms are not better accounted for by another diagnosis.

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, and paroxetine and venlafaxine, a selective serotonin norepinephrine reuptake inhibitor.

Definitions:

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:
Is characterized by dryness, inflammation, and thinning of the epithelial lining of the vagina and lower urinary tract due to loss of estrogen.

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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 Shionogi Inc 01-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 13, 2021.

Bachmann G, Santen RJ. 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. Accessed September 13, 2021.

Martin KA, Barbieri RL. Treatment of menopausal symptoms with hormone therapy. In: UpToDate, Crowley WF, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 13, 2021.