BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VEOZAH™ (fezolinetant) oral
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:** Veozah (fezolinetant) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is a female
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of moderate to severe vasomotor symptoms due to menopause
4. Individual has a minimum average of 7 moderate to severe vasomotor symptoms per day

ORIGINAL EFFECTIVE DATE: 08/17/2023 | ARCHIVE DATE: | LAST REVIEW DATE: 08/15/2024 | LAST CRITERIA REVISION DATE: 08/15/2024

5. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Serum transaminase concentrations are less than two times the upper limit of normal (ULN)
    b. Serum bilirubin (total and direct) are less than two times the upper limit of normal (ULN)

6. **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)

7. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **BOTH** of the following:
    a. Low dose of either paroxetine or citalopram
    b. Low-dose estrogen plus progestin therapy (or estrogen alone if the individual does not have a uterus)

8. There are **NO** FDA-label contraindications such as:
    a. Known cirrhosis
    b. Severe renal impairment or end-stage renal disease (eGFR less than 30 mL/min/1.73m^2)
    c. Concomitant use with CYP1A2 inhibitors (such as, (e.g., ciprofloxacin, cimetidine, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton, others)

9. Individual does not have Child-Pugh Class C hepatic impairment

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Veozah (fezolinetant) 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's condition has responded while on therapy with response defined as the following:
    a. Improvement in severity of vasomotor symptoms from baseline
    b. Improvement in frequency of vasomotor symptoms from baseline

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 such as:
    a. Known cirrhosis
    b. Severe renal impairment or end-stage renal disease
    c. Concomitant use with CYP1A2 inhibitors (such as, (e.g., ciprofloxacin, cimetidine, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton, others)

d. Serum transaminase concentrations greater than three times the upper limit of normal (ULN)

5. Individual does not have Child-Pugh Class C hepatic impairment

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:

Veozah (fezolinetant) is a small molecule neurokinin 3 (NK3) receptor antagonist indicated for the treatment of moderate to severe vasomotor symptoms due to menopause. It blocks neurokinin B (NKB) binding on the kisspeptin/neurokinin B/dynorphin (KNDy) neuron to modulate neuronal activity in the thermoregulatory center. Fezolinetant has high affinity for the NK3 receptor which is more than 450-fold higher than binding affinity to NK1 or NK2 receptors.

The physiologic mechanism whereby a hot flash occurs is thought to be an elevation in body temperature leading to cutaneous vasodilation, which results in flushing and sweating in association with a subsequent decrease in temperature and chills. A recent hypothesis suggests that KNDy (kisspeptin, neurokinin B, and dynorphin) neurons mediate the LH and thermoregulatory changes.

The thermoregulatory center in the hypothalamus is innervated by kisspeptin/neurokinin B/dynorphin (KNDy) neurons that are stimulated by neurokinin B (NKB) and inhibited by estrogen. After menopause, estrogen levels fall and NKB signaling is increased. It has been proposed that this results in unregulated KNDy neuron activation and vasomotor symptoms. Antagonism of NKB signaling at its receptor (neurokinin 3 receptor [NK3R]) has been studied as an alternative to hormonal therapy for management of hot flashes.

Classic 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. Numerous studies have shown the efficacy of hormonal replacement therapy in controlling menopausal symptoms. Estrogen plus progestin therapy (or estrogen alone if the individual does not have a uterus) 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, itching, and burning) associated with menopause. Hormonal therapy may also alleviate sleep disturbances and joint symptoms of menopause.

For women who cannot use estrogen for control of severe vasomotor symptoms, non-estrogen containing medications have been used. Agents that have been shown to be effective in the management of menopausal symptoms include other Selective Serotonin Re-uptake Inhibitors (SSRIs) such as citalopram, escitalopram, and paroxetine. Low dose paroxetine is FDA approved for the vasomotor symptoms of menopause. Venlafaxine, a

Serotonin Norepinephrine Reuptake Inhibitor (SNRIs), the antihypertensive clonidine, and the anticonvulsant gabapentin have also shown efficacy in the management of vasomotor symptoms.

Based on the American Association of Clinical Endocrinologists/American College of Endocrinology position statement on menopause, the Endocrine Society guideline on the treatment of menopause symptoms, and the North American Menopause Society position statement on nonhormonal management of menopause-associated vasomotor symptoms, SSRIs (including citalopram) are effective and recommended alternatives for the management of vasomotor symptoms associated with menopause in patients with contraindications to hormonal therapy or who prefer not to use hormonal therapy. Based on the American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline, SSRIs may be used to help mitigate vasomotor symptoms of premature menopause in patients previously treated for breast cancer.

Definitions:

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

Resources:

Veozah (fezolinetant) product information, revised by Astellas Pharma US, Inc. 05-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 07, 2024.

Paroxetine capsule product information, revised by Padagis US, LLC. 09-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 19, 2024.

Khan SJ, Kapoor E, Faubion SS, Kling JM. Vasomotor Symptoms During Menopause: A Practical Guide on Current Treatments and Future Perspectives. International Journal of Women's Health 2023:15 273–287. Accessed July 20, 2024.

Martin KA, Barbieri RL. Treatment of menopausal symptoms with hormonal therapy. In: UpToDate, Snyder PJ, Mulder JE (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated November 20, 2023. Accessed July 19, 2024.

Bachmann G, Pinkerton JV. Genitourinary syndrome of menopause (vulvovaginal atrophy): Treatment. In: UpToDate, Barbieri RL, Burnstein HJ, Chakrabarti A (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated July 15, 2024. Accessed July 19, 2024.

Casper RF. Menopausal hot flashes. In: UpToDate, Barbieri RL, Crowley WF, Martin KA. Editor(s) (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated August 31, 2023. Accessed July 19, 2024.