BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

LYNKUET® (elinzanetant) oral
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/or 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.

Medical Necessity Requirements for LYNKUET (elinzanetant) and VEOZAH (fezolinetant)

Criteria for Initial Therapy:

Indication
- Female with moderate to severe vasomotor symptoms due to menopause

Age Requirement
- 18 years of age or older

ORIGINAL EFFECTIVE DATE: 08/17/2023 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 02/19/2026

PHARMACY COVERAGE GUIDELINE

LYNKUET® (elinzanetant) oral
VEOZAH™ (fezolinetant) oral
Generic Equivalent (if available)

Baseline Clinical Evaluation

- Serum transaminase concentrations less than two times the upper limit of normal
- Serum bilirubin (total and direct) less than two times the upper limit of normal
- A minimum average of 7 moderate to severe vasomotor symptoms per day
- **For Lynkuet:** There is a negative pregnancy test in a woman of childbearing potential

Alternative Therapies

- Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for **BOTH** of the following:
  - Low dose of either paroxetine or citalopram
  - Low dose estrogen plus progestin therapy (or estrogen alone if no uterus)

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- **For Veozah:** there is **NONE** of the following:
  - Known cirrhosis
  - Severe renal impairment or end stage renal disease (eGFR less than 30 mL/min/1.73m²)
  - Concomitant use with CYP1A2 inhibitors (e.g., ciprofloxacin, cimetidine, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton)
  - Does not have Child Pugh Class C hepatic impairment
- **For Lynkuet:** There is **NONE** of the following:
  - Concomitant use with CYP3A4 inhibitors and grapefruit juice
  - Concomitant use with strong and moderate CYP3A4 inducers
  - Currently pregnant
  - End stage renal disease (estimated glomerular filtration rate of less than 15 mL per minute) with or without hemodialysis
  - Moderate or severe hepatic impairment (Child Pugh Class B or C)

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (serum transaminase and bilirubin values)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

ORIGINAL EFFECTIVE DATE: 08/17/2023 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 02/19/2026

PHARMACY COVERAGE GUIDELINE

LYNKUET® (elinzanetant) oral
VEOZAH™ (fezolinetant) oral
Generic Equivalent (if available)

Clinical Response
- Positive clinical response documented as:
  - Improvement in severity of vasomotor symptoms from baseline
  - Improvement in frequency of vasomotor symptoms from baseline

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- **For Veozah:** There is **NONE** of the following:
  - Known cirrhosis
  - Severe renal impairment or end stage renal disease (eGFR less than 30 mL/min/1.73m²)
  - Concomitant use with CYP1A2 inhibitors (e.g., ciprofloxacin, cimetidine, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton)
  - Does not have Child Pugh Class C hepatic impairment
  - Liver toxicity indicated by **ONE** of the following:
    1. Signs or symptoms suggesting liver injury (e.g., fatigue, jaundice, dark urine)
    2. Serum transaminase concentrations greater than five times the upper limit of normal
    3. Serum transaminase concentrations greater than three times the upper limit of normal and total bilirubin greater than two times the upper limit of normal
- **For Lynkuet:** There is **NONE** of the following:
  - Concomitant use with CYP3A4 inhibitors and grapefruit juice
  - Concomitant use with strong and moderate CYP3A4 inducers
  - Currently pregnant
  - End stage renal disease (estimated glomerular filtration rate of less than 15 mL per minute) with or without hemodialysis
  - Moderate or severe hepatic impairment (Child Pugh Class B or C)

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Criteria for Off Label Use Requests:

PHARMACY COVERAGE GUIDELINE

LYNKUET® (elinzanetant) oral
VEOZAH™ (fezolinetant) oral
Generic Equivalent (if available)

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.

Lynkuet (elinzanetant) is indicated for the treatment of moderate to severe vasomotor symptoms due to menopause. Lynkuet (elinzanetant) is a neurokinin 1 (NK1) and neurokinin 3 (NK3) receptor antagonist. Inhibition of Substance P and Neurokinin B through antagonism of NK1 and NK3 receptor signaling on kisspeptin/neurokinin B/dynorphin (KNDy) neurons can modulate neuronal activity in thermoregulation associated with hot flashes.

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

PHARMACY COVERAGE GUIDELINE

LYNKUET® (elinzanetant) oral
VEOZAH™ (fezolinetant) oral
Generic Equivalent (if available)

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. 12 2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2025.

Lynkuet (elinzanetant) product information, revised by Bayer HealthCare Pharmaceuticals, Inc. 10 2025. Available at U.S. Food and Drug administration. Accessed October 29, 2025.

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. Re evaluated July 02, 2025.

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 2025. Topic last updated November 20, 2023. Accessed July 02, 2025.

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 2025. Topic last updated April 21, 2025. Accessed July 02, 2025.

Casper RF. Menopausal hot flashes. In: UpToDate, Barbieri RL, Martin KA. Editor(s) (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2025. Topic last updated December 17, 2024. Accessed July 02, 2025.