



### Lynkuet (fezolinetant)

#### Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

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## Summary

Vasomotor symptoms (VMS), including hot flashes and night sweats, are common symptoms of menopause that can significantly impact quality of life. They are caused by the decline in estrogen levels during the menopausal transition. Systemic menopausal hormone therapy (MHT) with estrogen, with or without progestin, is the most effective treatment for VMS. However, MHT may not be appropriate for all women, such as those with a history of breast cancer, cardiovascular disease, venous thromboembolism, a history of stroke, or active liver disease. In November, 2025, the FDA released that they would be beginning the process of removing several boxed warnings from MHT estrogen products - including references to risks of cardiovascular disease, breast cancer and probable dementia.

Nonhormonal treatment options for VMS include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and other medications like gabapentin, clonidine and oxybutynin. Lynkuet (elinzanetant) is a non-hormonal once-daily oral neurokinin-3 receptor antagonist approved for the treatment of moderate to severe VMS associated with menopause. It provides an additional nonhormonal treatment option for women who cannot or choose not to use MHT.

Lynkuet (elinzanetant) is available in 60 mg capsules, but the recommended dose is 120 mg (two 60 mg capsules) once daily. It can be taken with or without food, and unlike the Veozah (fezolinetant), it does not have a boxed warning for the risk of hepatotoxicity. However, it is still recommended that liver function tests are performed prior to initiation of Lynkuet (elinzanetant) to assess for baseline liver function and injury. Additionally, it is not recommended the Lynkuet (elinzanetant) is initiated in those with serum transaminase concentrations greater than or equal ( $\geq$ ) to 2 times the upper limit of normal (ULN) or if total bilirubin is  $\geq$  two times the ULN.

## Definitions

"Menopause" refers to the point in time 12 months after a woman's last menstrual period, marking the end of the menopausal transition.

"Perimenopause" is the menopausal transition, a span of time starting when a woman begins experiencing menstrual irregularity through 12 months after the final menstrual period.

"Postmenopause" refers to the time after menopause has occurred, starting 12 months after the final menstrual period.

"Vasomotor symptoms (VMS)" refer to hot flashes (sensations of heat, sweating, flushing) and night sweats associated with the menopausal transition.

## Clinical Indications

### Medical Necessity Criteria for Initial Clinical Review

#### Initial Indication-Specific Criteria

##### Postmenopausal Women with Vasomotor Symptoms (VMS)

The Plan considers Lynkuet (elinzanetant) medically necessary when ALL of the following criteria are met:

1. The member is a postmenopausal woman with moderate to severe vasomotor symptoms (VMS);  
*AND*
2. The member is unable to use, or has tried and failed an 8-week trial of **BOTH** of the following:
  - a. Hormonal pharmacologic treatments (i.e., estrogen, with progestin if uterus present), such as **ONE** (1) of the following (see [Appendix A](#), Table 1):
    - i. Oral estrogens - e.g., estradiol (Estrace), conjugated estrogens (Cenestin, Enjuvia, Premarin), esterified estrogens (Menest); *or*
    - ii. Transdermal estrogens - e.g., estradiol patch (Alora, Climara, Dotti, Estraderm, Lyllana, Menostar, VivelleDot, Minivelle); *or*
    - iii. Topical Products - e.g., estradiol gel (Divigel, Elestrin, EstroGel), estradiol emulsion (Estrasorb), estradiol transdermal spray (Evamist), estradiol vaginal cream (Estrace), estradiol vaginal insert (Estring, Imvezzy, Vagifem, Yuvaferm); *or*
    - iv. Oral estrogen/progestin combinations - e.g., Prempro or Premphase (conjugated estrogens/medroxyprogesterone), Activella or Mimvey (estradiol/norethindrone), Angeliq (estradiol/drospirenone), Bijuva (estradiol/progesterone); *or*
    - v. Transdermal estrogen/progestin combinations - e.g., CombiPatch (estradiol/norethindrone), Climara Pro (estradiol/levonorgestrel); *or*
    - vi. Duavee (conjugated estrogens, bazedoxifene); *or*
    - vii. Oral estrogens/methyltestosterone combinations - e.g., Esterified estrogens/methyltestosterone (Covaryx, EEMT HS, Estratest); *or*
    - viii. Progesterone only oral therapy - e.g., Prometrium (progesterone), Provera (medroxyprogesterone); *or*
    - ix. Intrauterine systems - e.g., Femring (estradiol) or progesterone only intrauterine devices (e.g., levonorgestrel [Kyleena, Liletta, Mirena, Skyla]; *and*
  - b. Nonhormonal pharmacologic treatments, such as **ONE** (1) of the following:
    - i. SSRIs (selective serotonin reuptake inhibitors) - e.g., paroxetine (Paxil, Brisdelle), citalopram (Celexa), escitalopram (Lexapro); *or*
    - ii. SNRIs (serotonin norepinephrine reuptake inhibitors) - e.g., venlafaxine (Effexor), desvenlafaxine (Pristiq); *or*
    - iii. Gabapentinoid (e.g., gGabapentin or pregabalin); *or*
    - iv. Oxybutynin;
    - v. Clonidine; *AND*
3. The requested medication is being used within the Plan's Quantity Limit of 2 capsules daily.

If the above prior authorization criteria are met, the requested product will be authorized for up to 6-months.

#### *Continued Care*

#### Medical Necessity Criteria for Subsequent Clinical Review

##### Subsequent Indication-Specific Criteria

#### Postmenopausal Women with Vasomotor Symptoms (VMS)

Reauthorization for continued coverage of Lynkuet (elinzanetant) for up to an additional 12 months may be granted if the member has recent (within the last 3 months) clinical chart documentation indicating ALL of the following criteria:

1. The member continues to meet the above applicable **Medical Necessity Criteria**; **AND**
2. Clinically significant reduction in the frequency and/or severity of VMS from baseline, such as:
  - a. Reduction in the frequency of moderate to severe hot flashes; *or*
  - b. Reduction in the symptomatic severity of hot flashes; *or*
  - c. Improvement in VMS-related quality of life, sleep, or other member-reported outcomes;**AND**

#### Experimental or Investigational / Not Medically Necessary

Lynkuet (elinzanetant) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Use in perimenopausal women (before menopause has been reached), as efficacy and safety have not been established in this population.
- Use for treatment of mild VMS, as pivotal trials only included women with moderate to severe VMS defined as  $\geq 7$  moderate to severe hot flashes per day or  $\geq 50$  per week.

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## Appendix

**Table 1: Generally Recognized Absolute and Relative Contraindications to Estrogen-based Menopausal Hormone Therapy (MHT)**

Absolute contraindications (Generally recommended to Avoid Estrogen Therapy)		Relative contraindications (Caution Should be Exercised)	
I.	Acute cardiovascular disease	XI.	Active gallbladder disease
II.	Acute or decompensated liver disease	XII.	Increased risk of cardiovascular disease*
III.	History of breast cancer	XIII.	Migraine with aura

IV. History of cardiovascular disease (coronary artery disease or stroke) V. History of estrogen-dependent neoplasia including endometrial cancer VI. History of venous thromboembolism Hypertriglyceridemia VII. Pregnancy VIII. Protein C, protein S, or antithrombin deficiency or other known thrombophilic IX. Prolonged immobilization X. Unexplained vaginal bleeding	XIV. Hypertriglyceridemia
<p><i>There are no agreed upon guideline-defining absolute and relative contraindications. The above are based on the Endocrine Society Clinical Guideline on the Treatment of Symptoms of Menopause (2015). Provider discretion should guide therapeutic appropriateness for the individual being treated.</i></p> <p><i>*As of November 2025, the FDA has recommended removal of the boxed warning in reference to the increased risk of cardiovascular disease, breast cancer, and probable dementia from package labeling of hormone replacement therapy; however package inserts have not yet all been updated to reflect this change.</i></p>	

#### Clinical Guideline Revision / History Information

Original Date: 03/02/2026  
Reviewed/Revised: