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Policy Number: C30293-A

Lynkuet (elinzanetant)

PRODUCTS AFFECTED

Lynkuet (elinzanetant)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Vasomotor symptoms due to menopause

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. VASOMOTOR SYMPTOMS DUE TO MENOPAUSE:
1. Documented diagnosis of severe vasomotor symptoms due to menopause
AND
2. Documentation of a trial and failure (after a 3-month period), serious side effect, or labeled contraindication to BOTH of the following classes of therapies:
   a) Formulary/PDL preferred menopause hormone therapy (i.e., estrogen products)
   AND
   b) Formulary/PDL preferred generic non-hormone therapy recommended by the North American Menopause Society (NAMS) [i.e. SSRI, SNRI, or gabapentin – all level 1]
AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Lynkuet (elinzanetant) include: pregnancy. Avoid concomitant use of strong CYP3A4 inhibitors, strong CYP3A4 inducers, and moderate CYP3A4 inducers with Lynkuet. Do not start Lynkuet if ALT or AST is ≥ 2 x ULN or if the total bilirubin is ≥ 2 x ULN for the evaluating laboratory.]

CONTINUATION OF THERAPY:

A. VASOMOTOR SYMPTOMS DUE TO MENOPAUSE:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by a decrease in severity and/or frequency of vasomotor symptoms
AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Lynkuet (elinzanetant) include: pregnancy. Avoid concomitant use of strong CYP3A4 inhibitors, strong CYP3A4 inducers, and moderate CYP3A4 inducers with Lynkuet.]

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
None

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
120 mg once daily

Maximum Quantity Limits –
Concomitant use with moderate CYP3A4 inhibitors: reduce dosage of Lynkuet (elinzanetant) to 60

mg once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Neurokinin 1 & 3 (NK1/NK3) Receptor Antagonists

FDA-APPROVED USES:
Indicated for the treatment of moderate to severe vasomotor symptoms due to menopause

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Vasomotor symptoms (VMS) or "hot flashes" occur in approximately 75% to 80% of menopausal women in the United States. VMS most often begin in the perimenopausal period, although, in some women, they do not begin until after menopause. VMS are almost always due to menopause. Other causes, including carcinoid syndrome, are uncommon.

VMS are the most common complaint during the menopausal transition, occurring in up to 80% of women, although the frequency appears to vary by culture and ethnicity. Many to most women describe their symptoms as severe, but only approximately 20% to 30% of women seek medical attention for treatment. Some women first develop VMS that cluster around menses during their late reproductive years, but symptoms are typically mild and do not require treatment. Symptoms become far more common during the menopausal transition, with a frequency of approximately 40% in the early transition and increasing to 60% to 80% in the late menopausal transition and early postmenopausal stage.

VMS typically begin as a sudden sensation of heat centered on the upper chest and face, which spreads throughout the body and often lasts 2 to 4 minutes. VMS are often accompanied by profuse sweating and are sometimes followed by chills, shivers, and anxiety. When symptoms occur at night, they can disrupt sleep. The frequency of VMS episodes can range from one per day to one per hour.

The intensity of VMS can be classified as mild (sensation of heat without sweating), moderate (sensation of heat with sweating), or severe (sensation of heat with sweating, causing cessation of activity). VMS can vary in duration, with a median total duration of approximately 7.4 years. However, the intensity and duration of VMS can differ by ethnicity and race, with African American women experiencing longer and more intense symptoms. VMS can have a significant impact on quality of life, including sleep, mood, and productivity. In addition, there is evidence to suggest that severe and prolonged VMS may be associated with worse long-term health outcomes, such as increased risk for cardiovascular disease (CVD), and increased risk of low bone density and fractures.

Management of VMS currently includes menopausal hormone therapy (MHT), nonhormonal therapies, and/or nonpharmacologic interventions.

The North American Menopause Society (NAMS) ranked nonhormone options for the treatment of VMS in a 2023 position statement. Cognitive-behavioral therapy, clinical hypnosis, selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors, gabapentin, fezolinetant (Level I); oxybutynin (Levels I-II); weight loss, stellate ganglion block (Levels II-III).

NAMS concluded that MHT remains the most effective treatment for VMS and should be considered in menopausal women within 10 years of their final menstrual periods. For women who are not good candidates for MHT because of contraindications (eg, estrogen-dependent cancers or cardiovascular disease) or personal preference, it is important for healthcare professionals to be well informed about nonhormone treatment options for reducing VMS that are supported by the evidence.

On November 10, 2025, the FDA announced that it will remove the Boxed Warning from all estrogen-containing MHT products, including vaginal estrogens. This decision was based on updated evidence, including the results of the WHI and recommendations from a July 17, 2025, FDA expert panel meeting. The FDA is collaborating with manufacturers to update product labeling to remove references to risks of CVD, breast cancer, and probable dementia from all combined estrogen-progestogen, estrogen-only, progestogen-only, and estrogen-containing products. The Boxed Warning for endometrial cancer will remain for systemic estrogen-only products. Treatment with MHT should remain individualized, taking into account factors such as age, symptom severity, risk profile, comorbidities, and patient preferences.

On October 24, 2025, the FDA approved Lynkuet (elinzanetant), an NK1 and NK3 receptor antagonist, indicated for the treatment of moderate to severe VMS due to menopause. Lynkuet will be an additional nonhormonal option for women who cannot or will not take MHT.

Lynkuet will compete directly with Veozah (fezolinetant), an NK3 receptor antagonist. Lynkuet is a dual NK1/NK3 receptor antagonist. While NK3 receptor antagonism appears to reduce the frequency and severity of VMS, blocking NK1 receptors may play a role in sleep disturbances. There are no head-to-head Phase 3 trials comparing Lynkuet and Veozah, and cross-trial

comparisons are limited by differences in patient populations. The two products appear comparable in reducing the frequency and severity of VMS; however, Lynkuet appears to improve sleep disturbances to a greater degree than Veozah.

Unlike Veozah, Lynkuet does not have a Boxed Warning for hepatotoxicity and has the advantage of only requiring liver function tests at baseline and at 3 months after initiation. Veozah carries a Boxed Warning for liver toxicity and requires monitoring at baseline, and every month for the first 3 months, and at 6 and 9 months after initiation. Less frequent monitoring could be a significant advantage for Lynkuet for both patients and physicians, particularly in high-volume primary care settings. It should be noted, however, that Veozah's Boxed Warning for liver toxicity was added after FDA approval and broader patient use and not during its clinical development program.

The efficacy of Lynkuet for the treatment of moderate to severe VMS due to menopause was evaluated in two Phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trials: OASIS-1 (NCT05042362) and OASIS-2 (NCT05099159). A third randomized, double-blind, placebo-controlled, multicenter trial, OASIS-3 (NCT05030584), was conducted to evaluate the long-term safety of Lynkuet up to 52 weeks.

In both trials, Lynkuet treatment groups showed statistically significant and clinically meaningful reductions (≥ two hot flashes over 24 hours) in the frequency and severity of moderate to severe hot flashes from baseline to Weeks 4 and 12 compared to placebo. Reductions in the frequency and severity of VMS, as well as improvement in sleep disturbances and quality of life, were maintained throughout the 26-week treatment period.

By Week 12, more than 70% of women on Lynkuet achieved at least a 50% reduction in VMS frequency (based on published literature, a 50% reduction in frequency from baseline is considered clinically significant). Lynkuet also showed statistically significant improvement in sleep disturbances and menopause-related quality of life at Week 12.

In OASIS-3, adverse reactions leading to treatment discontinuation (≥1% in the Lynkuet group and greater than the placebo group) were abdominal pain (1.6%), fatigue (1.6%), depression (1.6%), and headache (1.3%).

Endometrial Safety

In all three OASIS trials, endometrial biopsies were performed to evaluate endometrial safety. A total of 477 patients who received Lynkuet 120 mg underwent end-of-treatment endometrial biopsies. Among these, 140 received Lynkuet for up to 52 weeks, 162 received Lynkuet for up to 26 weeks, and 175 received Lynkuet for up to 14 weeks. In addition, 132 women in the placebo group in OASIS-3 also had end-of-treatment endometrial biopsies. No endometrial malignancies were identified. The rate of endometrial abnormalities was 0.8% (four in 477) in patients who received Lynkuet, in line with the expected background rate.

Hepatic Enzyme Elevations

Elevations in serum transaminase (alanine aminotransferase and/or aspartate aminotransferase) concentrations equal to or greater than three times the upper limit of normal occurred in 0.6% of patients receiving Lynkuet and 0.4% of patients receiving placebo up to 12 weeks in three clinical trials. In OASIS-3, Lynkuet was not associated with hepatotoxic effects.

Central Nervous System (CNS) Effects

In the three OASIS trials, CNS effects (including somnolence, fatigue, vertigo, dizziness, and presyncope) occurred in 11.9% of patients on Lynkuet compared to 3.5% on placebo. Lynkuet labeling advises patients who experience these effects to refrain from driving or engaging in hazardous occupations or activities until the effects have resolved. Based on a post hoc analysis, the highest reported daily relative frequency of fatigue (up to 5%) was observed during the first weeks, which then decreased to less than 3% after Week 13.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Lynkuet (elinzanetant) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Lynkuet (elinzanetant) include: pregnancy. Avoid concomitant use of Lynkuet (elinzanetant) with strong CYP3A4 inhibitors and grapefruit (juice). Avoid concomitant use of Lynkuet (elinzanetant) with strong and/or moderate CYP3A4 inducers.

Exclusions/Discontinuation:

Lynkuet (elinzanetant) may cause pregnancy loss or stillbirth when administered during pregnancy. Exclude pregnancy in females of reproductive potential prior to initiating Lynkuet (elinzanetant). Discontinue if pregnancy is confirmed.

Lynkuet (elinzanetant) is not recommended in patients with moderate or severe hepatic impairment. Do not start Lynkuet (elinzanetant) if ALT or AST is ≥ 2 times upper limit of normal (ULN) or if the total bilirubin is ≥ 2 times ULN.

OTHER SPECIAL CONSIDERATIONS:

CNS Depressant Effect and Daytime Impairment: Advise patients about the potential for somnolence and other nervous system effects. Advise patients who experience these effects to refrain from driving or engaging in hazardous occupations or activities until the effects have resolved.

Hepatic Transaminase Elevations: Perform bloodwork prior to initiation of Lynkuet (elinzanetant) to evaluate for hepatic function and injury. Perform follow-up evaluations of hepatic transaminase concentration 3 months after initiation. Do not start therapy if serum transaminase concentration is equal to or exceeds two times the upper limit of normal (ULN) or if the total bilirubin is equal to or exceeds two times the ULN.

Risk of Seizures: Use Lynkuet (elinzanetant) with caution in patients with a history of seizures or with conditions that potentially lower the seizure threshold.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not*

be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Lynkuet CAPS 60MG

REFERENCES

1. Lynkuet (Elinzanetant) capsules, for oral use [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; October 2025.
2. The 2023 nonhormone therapy position statement of The North American Menopause Society. Menopause. 2023;30(6):573-590. doi:10.1097/GME.0000000000002200
3. Simon JA, Anderson RA, Ballantyne E, et al. Efficacy and safety of elinzanetant, a selective neurokinin-1,3 receptor antagonist for vasomotor symptoms: a dose-finding clinical trial (SWITCH-1). Menopause 2023; 30:239.
4. Makary M, et al. Updated labeling for menopausal hormone therapy. JAMA. doi:10.1001/jama.2025.22259
5. Nappi RE, et al. Global cross-sectional survey of women with vasomotor symptoms associated with menopause: prevalence and quality of life burden [published correction appears in Menopause. 2022 Jun 01;29(6):759]. Menopause. 2021;28(8):875–882. doi:10.1097/GME.0000000000001793
6. Panay N, et al. Elinzanetant for the treatment of vasomotor symptoms associated with menopause: a phase 3 randomized clinical trial. JAMA Intern Med. 2025;185(11):13191327. doi:10.1001/jamainternmed.2025.4421
7. Pinkerton JV, et al. Elinzanetant for the treatment of vasomotor symptoms associated with menopause: OASIS 1 and 2 randomized clinical trials. JAMA. 2024;332(16):1343–1354. doi:10.1001/jama.2024.14618

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2026