New Drug Overview

Lynkuet (elinzanetant)

PDL Category: Endocrine Metabolic Agents

Introduction

Disease Background:

- Perimenopause is considered the menopausal transition that happens following the reproductive years but before menopause. It is generally described as irregular menstrual cycles, endocrine changes, and symptoms such as hot flashes (*Casper 2025*).
  - This transition generally begins in the mid-to-late 40s and can last on average between 4-10 years (*Hickey et al 2026*).
- Menopause is a part of life denoted by the end of menses and lack of fertility; this happens in response to loss of ovarian follicle and thus a decrease in estrogen and progesterone secretion (*Hickey et al 2026*).
  - It is generally assessed retrospectively when amenorrhea has occurred for 12 months with no other clear reason for occurrence (pathologic or physiologic cause) (*Casper 2025*).
  - While physiologic changes can lead to naturally occurring menopause, it can also happen when induced by surgery (oophorectomy), chemotherapy or radiation (*Hickey et al 2026*).
- The trademark symptom of the menopausal transition/perimenopause, as well as early post-menopausal years, is vasomotor symptoms, which may be referred to as hot flushes, hot flashes, or night sweats. Other symptoms may include sleep disturbances and new-onset depression. The association of other symptoms, such as joint pain and memory loss, is not as clear (*Casper 2025, Hickey et al 2026*).
  - Hot flashes are reported to happen in close to 80% of women. Nevertheless, it is estimated that about 20-30% obtain medical attention for treatment (*Casper 2025*).
- Lynkuet was FDA approved in 2025.

Pharmacology/Usage

- 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 the thermoregulation associated with hot flashes.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Lynkuet (elinzanetant)
• For the treatment of moderate to severe vasomotor symptoms (VMS) due to menopause.	✔

(Prescribing information: Lynkuet 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Lynkuet (elinzanetant)	Capsules	Oral	Once daily at bedtime at about the same time each day. Take with or without food; take with water and swallow whole.	• Exclude pregnancy in females of reproductive potential. • Perform baseline hepatic laboratory tests to assess for hepatic function and injury before starting treatment. Do not start treatment if ALT or AST is ≥2 times upper limit of normal (ULN) or if the total bilirubin is ≥2 times ULN. • Dosage adjustments are not required with mild to severe renal impairment, but the effects of end-stage renal disease on the pharmacokinetics of Lynkuet has not been studied. • Lynkuet is not recommended in patients with moderate or severe hepatic impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Lynkuet was demonstrated in the first 12 weeks of two randomized, double-blind, placebo-controlled, multicenter clinical trials.
  - In OASIS 1 and OASIS 2, menopausal women (N=796) were randomized to receive Lynkuet 120mg or placebo once daily at bedtime for 12 weeks.
    - In both trials, after the first 12 weeks, women on placebo were switched over to Lynkuet and all women were then treated with Lynkuet for a 14-week extension for up to 26 weeks total exposure.
  - Women who had at least 50 moderate to severe hot flashes (HFs), including night-time HFs, per week, were enrolled in OASIS 1 and OASIS 2.
  - In these trials, postmenopausal status was defined as at least 12 months of spontaneous amenorrhea, or at least 6 months of spontaneous amenorrhea with serum follicle stimulating hormone levels >40mIU/ml and a serum estradiol concentration of <30 pg/ml, or at least 6 months after hysterectomy with serum follicle-stimulating hormone >40mIU/ml and serum estradiol <30 pg/ml, or at least 6 weeks post-surgical bilateral oophorectomy with or without hysterectomy.

- In OASIS 1 and OASIS 2, the mean age of women was 54.6 years (range 40-65), while 80.4% were White. The study population included women with prior hysterectomy (38.8%), prior uni-/bilateral oophorectomy (20.6%), or prior menopausal hormone therapy (MHT) use (31.4%).
- The primary efficacy endpoints in both trials were the mean change in frequency and severity of moderate to severe vasomotor symptoms from baseline to weeks 4 and 12, including day and night HFs measured using the Hot Flash Daily Diary (HFDD).
  - In both trials, Lynkuet treatment groups demonstrated statistically significant and clinically meaningful reduction (≥2 hot flashes over 24 hours) in the frequency of moderate to severe HFs from baseline to weeks 4 and 12 compared to placebo.
  - In both trials, Lynkuet treatment groups demonstrated a statistically significant reduction in severity of moderate to severe vasomotor symptoms from baseline to weeks 4 and 12 compared to placebo.
  - Results of the co-primary endpoints for change from baseline to weeks 4 and 12 in mean frequency and severity of moderate to severe vasomotor symptoms over 24 hours from OASIS 1 and OASIS 2 are presented in the tables below, which were adapted from the prescribing information.

Table 3. Efficacy results

	OASIS 1		OASIS 2	
Change in Frequency	**Lynkuet 120mg (N=199)**	**Placebo (N=197)**	**Lynkuet 120mg (N=200)**	**Placebo (N=200)**
Baseline				
Mean	13.38	14.26	14.66	16.16
Change from baseline to week 4				
LS-means	-7.60	-4.31	-8.58	-5.54
Difference vs placebo	-3.29		-3.04	
p-value	<0.0001		<0.0001	
Change from baseline to week 12				
LS-means	-8.66	-5.44	-9.72	-6.48
Difference vs placebo	-3.22		-3.24	
p-value	<0.0001		<0.0001	

Table 4. Efficacy results

	OASIS 1		OASIS 2	
Change in Severity	**Lynkuet 120mg (N=199)**	**Placebo (N=197)**	**Lynkuet 120mg (N=200)**	**Placebo (N=200)**
Baseline				
Mean	2.56	2.53	2.53	2.54
Change from baseline to week 4				

LS-means	-0.73	-0.40	-0.75	-0.53
Difference vs placebo	-0.33		-0.22	
p-value	<0.0001		0.0003	
Change from baseline to week 12				
LS-means	-0.92	-0.52	-0.91	-0.62
Difference vs placebo	-0.40		-0.29	
p-value	<0.0001		<0.0001	

- The results in reduction of frequency and severity of moderate to severe vasomotor symptoms were consistent across various patient subgroups such as race, ethnicity, BMI, and smoking status.
- In all three OASIS trials, endometrial biopsies were performed to assess endometrial safety.
  - A total of 477 patients who received elinzanetant 120mg underwent end-of-treatment endometrial biopsies.
  - Of these, 140 received elinzanetant for up to 52 weeks, 162 received elinzanetant for up to 26 weeks, and 175 received elinzanetant for up to 14 weeks. In addition, 132 women in the placebo arm in OASIS 3 also had end-of-treatment endometrial biopsies.
  - No endometrial malignancies were identified. One case of endometrial hyperplasia was atypia was identified in OASIS 1 and two cases of endometrial hyperplasia without atypia were seen in OASIS 3. Also, one case of endometrial glandular hyperplastic polyp was identified in OASIS 2. The rate of endometrial abnormalities was 0.8% (4 in 477) in patients who received elinzanetant, in line with the expected background rate.
- Driving performance was assessed at 9 hours after bedtime administration of Lynkuet 120mg and 240mg (two times the recommended dose) in a randomized, double-blind, placebo-and active-controlled, four-period crossover study in healthy women (N=64; mean age 52.1 years) using a computer-based driving simulation.
  - The primary outcome measure was the difference from placebo in the Standard Deviation of Lateral Position (SDLP).
    - Driving performance was assessed using a validated threshold established in a population with blood alcohol concentration of 0.05%.
    - Although the mean SDLP did not reach the threshold for driving impairment after administration of Lynkuet 120 or 240mg, compared to placebo, driving ability was impaired in some subjects taking Lynkuet 120mg or 240mg after the initial dose.
    - For a smaller percentage of subjects driving ability was impaired after 5 days of consecutive dosing.

Clinical guidelines

- Note that guidelines do not include Lynkuet as they were published prior to this product being FDA approved.
- **The North American Menopause Society (NAMS) Position Statement: The 2023 nonhormone therapy position statement of the North American Menopause Society** (*NAMS 2023*)
  - Key points for prescription treatments include the following:
    - Mild to moderate improvements in vasomotor symptoms (VMS) are associated with SSRIs and SNRIs.
    - Gabapentin is associated with improvements in the frequency as well as the severity of VMS, while pregabalin is not recommended for VMS.
    - It has been shown that oxybutynin reduces moderate to severe VMS; however, long-term use may be associated with a decline in cognition in older adults.
    - Clonidine and suvorexant use are not recommended.
    - Fezolinetant, a first-in-class neurokinin B antagonist, is FDA approved for vasomotor symptoms management.

Safety summary

- **Contraindications:**
  - In pregnancy.

- **Box Warning:** None.

- **Warnings and precautions:**
  - In the three phase 3 studies, nervous system effects (including somnolence, fatigue, vertigo, dizziness, and presyncope) occurred more in patients taking Lynkuet as compared to placebo (11.9% vs 3.5%).
    - 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.
  - Elevations in serum transaminase (ALT and/or AST) concentrations ≥3 times the ULN occurred in 0.6% of patients receiving Lynkuet and 0.4% of patients receiving placebo up to 12 weeks in three clinical trials.
    - Perform baseline bloodwork prior to the start of treatment to assess for hepatic function and injury (including ALT, AST, alkaline phosphatase, and total and direct bilirubin). Perform follow-up evaluations of hepatic transaminase concentration 3 months after initiation of therapy.
  - Seizure was reported in one patient with a history of seizures in the clinical trials of Lynkuet. In addition, convulsions were observed in studies conducted in rats. Use Lynkuet with caution in patients with a history of seizures or with conditions that potentially lower the seizure threshold.

- **Common adverse drug reactions:**
  - Listed % incidence for adverse drug reactions = reported % incidence for drug (Lynkuet) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    The most frequently reported adverse events included headache (2.6%), fatigue (4.4%), dizziness (4.2%), somnolence (3.8%), abdominal pain (2%), rash (2.6%), diarrhea (2.8%), and muscle spasms (2.6%).

- **Drug interactions:**
  - Elinzanetant is primarily metabolized via CYP3A4 enzyme.
    - Avoid concomitant use of Lynkuet with strong CYP3A4 inhibitors and grapefruit (juice).
    - Reduce the dosage of Lynkuet if use concomitantly with moderate CYP3A4 inhibitors.
    - Avoid the concomitant use of Lynkuet with strong and moderate CYP3A4 inducers.
  - Elinzanetant is a weak inhibitor of CYP3A4.
    - Avoid concomitant use of Lynkuet with CYP3A4 substrates unless otherwise recommended in the prescribing information for CYP3A4 substrates where minimal concentration changes may lead to serious adverse reactions.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that Lynkuet is contraindicated in pregnancy. If pregnancy occurs during Lynkuet use, discontinue treatment. Based on findings from animal reproduction studies, Lynkuet may cause pregnancy loss or stillbirth but not fetal malformations when administered during pregnancy.
    - Exclude pregnancy before starting Lynkuet treatment.
    - Pregnancy should be prevented in women of reproductive potential by using effective contraception during and for 2 weeks after stopping treatment.
  - The safety and efficacy of use have not been established in the pediatric population.

Conclusion

- Menopause is a part of life denoted by the end of menses and lack of fertility; this happens in response to loss of ovarian follicle and thus a decrease in estrogen and progesterone secretion (*Hickey et al 2026*).
- Lynkuet is a NK1 and NK3 receptor antagonist indicated for the treatment of moderate to severe vasomotor symptoms due to menopause.
- Lynkuet is contraindicated in pregnancy and it is recommended to exclude pregnancy in females of reproductive potential before starting treatment.
- Perform baseline hepatic laboratory tests to assess for hepatic function and injury before starting treatment, and do not start Lynkuet if ALT or AST is ≥2 times ULN or if the total bilirubin is ≥2 times ULN.
- The efficacy of Lynkuet was demonstrated in the first 12 weeks of two randomized, double-blind, placebo-controlled, multicenter clinical trials. Women who had at least 50 moderate to severe hot flashes, including night-time hot flashes, per week, were enrolled in the studies.
    - The primary efficacy endpoints in both trials were the mean change in frequency and severity of moderate to severe vasomotor symptoms from baseline to weeks 4 and 12, including day and night hot flashes measured using the Hot Flash Daily Diary.
        - In both trials, Lynkuet treatment groups demonstrated statistically significant and clinically meaningful reduction (≥2 hot flashes over 24 hours) in the frequency of moderate to severe hot flashes from baseline to weeks 4 and 12 compared to placebo.
        - In both trials, Lynkuet treatment groups demonstrated a statistically significant reduction in severity of moderate to severe vasomotor symptoms from baseline to weeks 4 and 12 compared to placebo.
- Lynkuet provides a non-hormonal once daily treatment option that is FDA approved for vasomotor symptoms associated with menopause, reducing the severity and frequency of hot flashes.
- Comparator treatments may include Veozah (fezolinetant).

- There is evidence to suggest that Lynkuet is more effective than placebo. It is recommend that Lynkuet be preferred, given the safety profile.

- **PDL Placement:**
    - ☒ Preferred
    - ☐ Non-Preferred

References

- Casper RF. Menopause: Clinical features and diagnosis. UpToDate Web site. Updated September 04, 2025. Accessed January 27, 2026. www.uptodate.com
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- NAMS. The 2023 nonhormone therapy position statement of The North American Menopause Society. *Menopause.* 2023; 30(6): 573-590.

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