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Susan F. Smith Center
for Women's Cancers

Dana-Farber Breast Oncology Center

Consensus Statement Regarding the Use of Elinzanetant in Patients with a History of Breast Cancer and Vasomotor Symptoms

Consensus: Obtained at Breast Oncology Center meetings on 07/25/2025 and 03/13/2026.

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Synopsis

Consensus Statement Regarding the Use of Elinzanetant in Patients with A History of Breast Cancer and Vasomotor Symptoms

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Consensus statements regarding the use of elinzanetant in patients with previous breast cancer and vasomotor symptoms.

Clinical Question	Consensus Statement
Q1. Is current evidence (with no long-term oncologic outcomes) sufficient to support the prescription of elinzanetant to patients with early-stage hormone receptor-positive (HR+) breast cancer on adjuvant endocrine therapy (ET)?	The BOC group reached consensus supporting the use of elinzanetant 120 mg daily during adjuvant ET, despite the absence of long-term oncologic outcome data. This position reflects the hypothalamic mechanism of action, which may reduce estradiol levels, as well as the potential of elinzanetant to improve adherence to ET.
Q2. Which is the preferred systemic agent for patients with early-stage HR+ breast cancer and vasomotor symptoms (VMS) affecting quality of life (QoL) <u>during</u> adjuvant ET?	For patients with early-stage HR+ breast cancer or ductal carcinoma <i>in situ</i> (DCIS) and VMS affecting QoL during (neo)adjuvant ET, elinzanetant 120 mg daily is the preferred systemic treatment when pharmacologic therapy is indicated. In patients deriving partial benefit from a non-NKR inhibitor and without relevant drug–drug interactions, the BOC favors switching to elinzanetant rather than adding it to the existing therapy. Elinzanetant can be considered in patients receiving (neo)adjuvant ET with a CDK4/6 inhibitor. In these patients, elinzanetant should be administered: • at the 120 mg daily dose in combination with abemaciclib (any dose) • at the 60 mg daily dose in combination with ribociclib 400 mg daily
Q3. Which is the preferred systemic agent for patients with early-stage HR+ breast cancer (any HR status) and VMS affecting QoL <u>after</u> adjuvant systemic therapies?	For patients with early-stage breast cancer (any HR status) or DCIS and VMS affecting QoL after adjuvant systemic therapies, elinzanetant and fezolinetant are the preferred systemic treatments when pharmacologic therapy is indicated, with the caveat that fezolinetant has not been studied in patients with a previous malignant tumor <5 years. • In case of concomitant mood disorders and/or chronic anxiety disorders, SSRI/SNRI are the preferred option. • In case of patients who develop VMS on anti-depressant drugs, including SSRI/SNRI, there is no evidence on efficacy of elinzanetant or fezolinetant (exclusion criterion in both clinical trials).
Q4. What are the toxicity management considerations for elinzanetant?	• Perform bloodwork to evaluate for hepatic function and injury, prior to initiation and 3 months after. • Patients should be advised about the potential for somnolence and other nervous system effects. Those who experience these effects should refrain from driving or engaging in hazardous occupations or activities. • Exclude pregnancy in females of reproductive potential prior to initiating elinzanetant.

Introduction

For patients with early-stage hormone receptor-positive (HR+) breast cancer, adjuvant endocrine therapy (ET) for at least 5 years is the standard of care, with addition of ovarian function suppression (OFS) in premenopausal patients.¹ Unfortunately, ET often causes vasomotor symptoms (VMS), including hot flashes and night sweats. These symptoms arise from disruption of hypothalamic thermoregulation driven by reduced estradiol levels and affect most patients receiving ET, including up to 80% of women on tamoxifen and up to 93% of those undergoing OFS, with younger patients typically experiencing more severe manifestations.^{2,3}

In women with a history of breast cancer, VMS may emerge through multiple mechanisms, including as a direct consequence of ET, as a side effect of gonadotoxic chemotherapy, and because of natural aging. Regardless of etiology, the clinical impact of VMS is substantial. VMS significantly impair quality of life and threaten treatment adherence. More than 20% of patients discontinue oral ET or OFS due to VMS, with discontinuation rates in routine clinical practice exceeding those observed in clinical trials.^{2,3}

Despite their high prevalence and clinical significance, several gaps persist in the management of VMS. There is no standardized method for defining symptom severity in the clinical setting, though regulatory frameworks classify hot flashes as:⁴

- Mild (sensation of heat without sweating)
- Moderate (heat with sweating but continued activity)
- Severe (heat with sweating causing cessation of activity).

Evidence suggests that a comprehensive menopausal assessment intervention can lead to substantial improvements in symptom control.⁵ This underscores the importance of proactive, structured approaches to this common clinical challenge.

Both pharmacological and non-pharmacological strategies² can be considered for the management of VMS. Non-pharmacological approaches include:

- Weight control and dietary intervention
- Stellate ganglion block procedure
- Cognitive behavioral therapy
- Acupuncture
- Hypnosis
- Yoga and relaxation training

Pharmacological strategies include:²

- SSRI/SNRI: venlafaxine, duloxetine, escitalopram, paroxetine (FDA-approved), sertraline
- Gabapentin and pregabalin
- Oxybutynin
- Neurokinin Receptor Antagonists: elinzanetant, fezolinetant
- Menopause Hormone Therapy (MHT), contraindicated in breast cancer survivors

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Historically, the most effective treatment for VMS was MHT, which is contraindicated in breast cancer survivors.²

In general, studies evaluating the efficacy of these strategies among patients with a history of breast cancer have been small, have not compared treatments directly, and have yielded mixed results. Moreover, each potential strategy has limitations for individual patients, including accessibility, acceptability, and side-effect profile. In addition, many patients express understandable trepidation when considering the possibility of adverse effects from a medication prescribed to manage the long-term side effects of another medication (**Table 1**).²

***Table 1.** Adverse events related to pharmacological approaches for the management of VMS. Derived from Franconi et al. 2021²*

Neurokinin Receptor Antagonists: Mechanism of action

The hypothalamic thermoregulatory center is innervated by kisspeptin/neurokinin B/dynorphin (KNDy) neurons located in the arcuate nucleus. Under physiologic conditions, these neurons are stimulated by neurokinin B (NKB) acting at the neurokinin 3 receptor (NK3R) and inhibited by estrogen (**Figure 1**). During the menopausal transition or following ET for breast cancer, declining estradiol levels lead to hypertrophy and hyperactivation of KNDy neurons, with upregulated expression of neurotransmitters including NKB and substance P (SP). This hyperactivation disrupts thermoregulatory set points, inappropriately triggering heat dissipation effectors. Cutaneous vasodilation causes heat loss, producing hot flashes, sweating, and chills. Neurokinin receptor antagonists represent the first class of non-hormonal agents specifically designed to target this neurobiological pathway.⁶

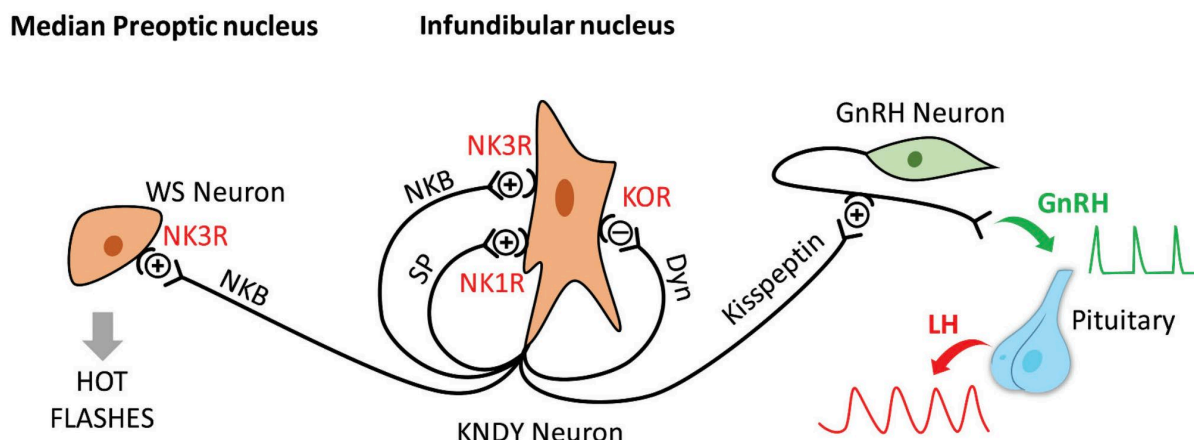


Figure 1. Diagram of the regulatory network between KNDy neurons, regulation of GnRH secretion, and vasomotor area in the hypothalamus. Reprinted from Sassarini et al. 2024⁶ under the Creative Commons Attribution-NonCommercial-NoDerivatives License.

Fezolinetant, a selective NK3R antagonist approved by the FDA in 2023, blocks NKB signaling at KNDy neurons to restore normal thermoregulatory sensitivity (**Table 2**). Similarly, elinzanetant, a dual NK-1 and NK-3 receptor antagonist approved by the FDA in 2025, was designed to address both VMS (via NK3R blockade) and sleep disturbances and peripheral vasodilation (via NK-1R/substance P pathway inhibition), according to the rationale that NK-1 receptors may also have a role in peripheral vasodilation and primary insomnia.⁶

Agent	Target (MoA)	Data from Clinical Trials	Regulatory Approval
Fezolinetant (45 mg once daily)	NK3 receptor antagonist	>61% reduction (vs. placebo) of hot-flash frequency in women without previous early-stage breast cancer (SKYLIGHT trial; N=2205)⁷ - No data in cancer survivors or during adjuvant endocrine therapy	- FDA and EMA: treatment of moderate to severe hot flashes (breast cancer <u>is not a contraindication</u>) - AST/ALT monitoring during the first cycles
Elinzanetant (120 mg once daily)	NK1 and NK3 receptor antagonist	- Decrease in frequency and severity of moderate-to-severe VMS in women without previous early-stage breast cancer (vs. placebo; N=796; OASIS-1 and OASIS-2 trials)⁸ - Benefit in patients with early-stage breast cancer on endocrine therapy⁹	- FDA: Review in progress - New Drug Application accepted - EMA: Under review - MHRS (UK): approved

Table 2. Mechanism of action and clinical data related to fezolinetant and elinzanetant efficacy.

The OASIS-4 trial

OASIS-4 (NCT05587296) is the first phase 3 randomized controlled trial to evaluate a neurokinin receptor antagonist specifically in women with VMS caused by ET for HR+ breast cancer.⁹

Trial Design. OASIS-4 was a 52-week, multicenter, randomized, double-blind, placebo-controlled phase 3 trial. Women aged 18–70 years who were receiving ET (tamoxifen or aromatase inhibitors, with or without ovarian function suppression) for early-stage HR+ breast cancer (or for its prevention in high-risk individuals) and experiencing ≥ 35 moderate-to-severe VMS per week were eligible. Participants were randomized 2:1 to receive elinzanetant 120 mg once daily for 52 weeks or placebo for 12 weeks followed by elinzanetant 120 mg for 40 weeks. A total of 316 participants were assigned to elinzanetant and 158 to placebo–elinzanetant. The co-primary endpoints were the change from baseline in the mean daily frequency of moderate-to-severe VMS at week 4 and week 12. Key secondary endpoints included changes in sleep disturbance (PROMIS SD SF 8b total T-score) and menopause-related quality of life (MENQOL total score) from baseline to week 12.⁹

Efficacy Results.

Baseline patient characteristics were well balanced between the two treatment groups. The mean age (SD) was 50.8 years (7.5) in the elinzanetant group versus 51.5 years (6.7) in the placebo–elinzanetant group. Most participants were white (elinzanetant: 88.0%; elinzanetant-placebo: 88.6%) and were taking ET for the treatment of breast cancer (elinzanetant: 99.7%; elinzanetant-placebo: 100%). Participants were receiving either tamoxifen (elinzanetant: 55.4%; elinzanetant-placebo: 57.0%) or an aromatase inhibitor (elinzanetant: 44.6%; elinzanetant-placebo: 43.0%). The median duration of ET prior to study entry was 20.4 months (range: 0.0 – 97.2) in the elinzanetant group versus 18.0 months (range: 1.2 – 116.4) in the elinzanetant-placebo group.⁹

At baseline, the mean daily frequency of moderate-to-severe vasomotor symptoms was 11.4 episodes (95% CI: 10.7 to 12.2) in the elinzanetant group versus 11.5 episodes (95% CI: 10.5 to 12.5) in the placebo–elinzanetant group. At week 4, the mean change from baseline in the daily frequency of moderate-to-severe VMS was -6.5 episodes (95% CI: -7.2 to -5.8) in the elinzanetant group versus -3.0 episodes (95% CI: -3.9 to -2.2) in placebo–elinzanetant group, representing a least mean squares difference between groups of -3.5 episodes (95% CI: -4.4 to -2.6; $p < 0.001$).⁹

At week 12, the mean change from baseline in the daily frequency of moderate-to-severe VMS was -7.8 episodes (95% CI: -8.5 to -7.1) in the elinzanetant group versus -4.2 episodes (95% CI: -5.2 to -3.2) in the placebo–elinzanetant group, representing a least mean squares difference between groups of -3.4 episodes (95% CI: -4.2 to -2.5; $p < 0.001$).⁹

In an exploratory analysis, 74.3% (95% CI: 69.3% to 79.3%) of elinzanetant-treated participants achieved a $\geq 50\%$ reduction in the frequency of moderate-to-severe VMS at week 12, compared with 35.8% (95% CI: 28.1% to 43.5%) on placebo–elinzanetant.⁹

Elinzanetant significantly improved sleep disturbance (PROMIS SD SF 8b LS mean difference -6.1 ; $P < 0.0001$) and menopause-related quality of life (MENQOL LS mean difference -0.7 ; $P < 0.0001$) at week 12, with benefits sustained through 52 weeks.

A 2026 ASCO subgroup analysis confirmed these improvements were consistent across all ET types (tamoxifen, aromatase inhibitors, with and without OFS).⁹

Safety. During weeks 1–12, adverse events occurred in 69.8% of elinzanetant recipients versus 62.0% on placebo, with the most common being headache, fatigue, and somnolence. Serious adverse events were infrequent (2.5% vs. 0.6%).⁹ Critically, the liver safety monitoring board found no substantive hepatotoxicity signal with elinzanetant over 52 weeks, a differentiator from fezolinetant, which carries an FDA boxed warning for hepatotoxicity and has postmarketing reports of drug-induced liver injury occurring within 40 days of initiation. In addition, no endometrial hyperplasia or meaningful bone density changes were observed.⁹

Limitations and Clinical Significance. The OASIS-4 trial population was predominantly White and European, limiting generalizability. Only one participant was taking ET for breast cancer prevention, precluding conclusions in that subgroup. Breast cancer recurrence and survival were not prespecified outcomes. Finally, none of the participants received an adjuvant CDK4/6 inhibitor.⁹ Nonetheless, the high retention rate and the observation that 91.6% of participants completing 52 weeks of elinzanetant elected to continue into a 2-year extension suggest high treatment satisfaction.⁹

Development of the Consensus Statements

The Dana-Farber Cancer Institute's Breast Oncology Center (BOC) held multidisciplinary meetings on 07/25/2025 and 03/13/2026 to discuss recommendations for the use of elinzanetant in patients with a history of breast cancer and vasomotor symptoms. Data were reviewed from the OASIS-4 trial. Additional relevant data were reviewed to address the questions in this document as noted below. The gathered evidence was presented for discussion to a multidisciplinary group, which included Dana-Farber physicians, nurses, clinical investigators, lab investigators, translational researchers, administrators, and patient advocates. The discussion and suggestions for improvements continued via email exchanges following the meeting. The final consensus statements were consolidated in August of 2026.

The consensus statements can be subject to future variations and periodic updates, based on emerging evidence and new reports from ongoing clinical studies. Therefore, the information provided in this document should not be considered as being complete or inclusive of all proper assessments, treatments or methods of care or as a statement of the standard of care. This information does not mandate any particular course of medical care and is not intended to be a substitute for the independent professional judgment of a health care provider. The document is based on the opinion of a multidisciplinary team at Dana-Farber but does not represent the official institutional position and overall must be considered as a consensus based on the positions and ideas of the Dana-Farber providers.

Clinical Questions

This document summarizes the discussions and consensus among the Dana-Farber BOC group regarding the following clinical questions:

- **Q1. Is current evidence (with no long-term oncologic outcomes) sufficient to support the prescription of elinzanetant to patients with early-stage hormone receptor-positive (HR+) breast cancer on adjuvant endocrine therapy (ET)?**
- **Q2. Which is the preferred systemic agent for patients with early-stage HR+ breast cancer and vasomotor symptoms (VMS) affecting quality of life (QoL) during adjuvant ET?**
- **Q3. Which is the preferred systemic agent for patients with early-stage breast cancer (any HR status) and VMS affecting QoL after adjuvant systemic therapies?**
- **Q4. What are the toxicity management considerations for elinzanetant?**

1. Is current evidence (with no long-term oncologic outcomes) sufficient to support the prescription of elinzanetant to patients with early-stage hormone receptor-positive (HR+) breast cancer on adjuvant endocrine therapy (ET)?

In terms of safety and breast cancer outcomes, no signal of detriment nor difference in breast cancer recurrences were reported in the OASIS-4 study, including only 4 invasive breast cancer-free survival (IBCFs) events during the 13- to 32-week window.⁹

Furthermore, estradiol levels seem to decrease in patients receiving elinzanetant: both a study in healthy premenopausal women¹⁰ and the estradiol subanalysis of the OASIS-4 trial¹¹ suggested this trend.

Consensus Statement

The BOC group reached consensus supporting the use of elinzanetant 120 mg daily during adjuvant ET, despite the absence of long-term oncologic outcome data. This position reflects the hypothalamic mechanism of action, which may even reduce estradiol levels, as well as its potential to improve adherence to ET.

2. Which is the preferred systemic agent for patients with early-stage HR breast cancer and VMS affecting quality of life (QoL) during adjuvant ET?

In terms of efficacy of NK inhibitors, a recent Bayesian network meta-analysis compared the efficacy of fezolinetant 45 mg, MHT, and other pharmacological strategies in postmenopausal women without a previous diagnosis of breast cancer (25 publications). This study showed that changes in VMS frequency did not differ significantly between fezolinetant and any of the 27 MHT regimens studied, and that fezolinetant reduced the frequency of moderate to severe VMS events per day significantly more than all other

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approached evaluated (paroxetine, venlafaxine and gabapentin), and significantly more than placebo.¹²

Furthermore, based on the data of the OASIS-4 trial, the NCCN Survivorship Guidelines now list elinzanetant as a preferred NK receptor antagonist, specifically noting that its pivotal trial was the only one conducted in the breast cancer population.¹³

Patients receiving adjuvant ribociclib or abemaciclib were not included in the OASIS-4 trial.⁹ Since elinzanetant is a sensitive substrate and weak inhibitor of CYP3A4, potential interactions with ribociclib have been hypothesized.¹⁴ Therefore, elinzanetant should not be used in breast cancer patients receiving ribociclib 600 mg (the dose used in the metastatic setting). For patients with early-stage HR+ breast cancer receiving adjuvant ribociclib at 400 mg, a dose reduction of elinzanetant from 120 mg daily to 60 mg daily should be considered.¹⁴

Consensus Statement

For patients with early-stage HR-positive breast cancer or ductal carcinoma *in situ* (DCIS) and VMS affecting QoL during (neo)adjuvant ET, elinzanetant 120 mg daily is the preferred systemic treatment when pharmacologic therapy is indicated. In patients deriving partial benefit from a non-NKR inhibitor and without relevant drug–drug interactions, the BOC favors switching to elinzanetant rather than adding it to the existing therapy.

Elinzanetant can be considered in patients receiving (neo)adjuvant ET with a CDK4/6 inhibitor. In these patients, elinzanetant should be administered:

- at the 120 mg daily dose in combination with abemaciclib (any dose)
- at the 60 mg daily dose in combination with ribociclib 400 mg daily.

3. Which is the preferred systemic agent for patients with early-stage breast cancer (any HR status) and VMS affecting QoL after adjuvant systemic therapies?

In this setting, we can extrapolate data from trials assessing NK3 inhibitors mainly in patients without a previous diagnosis of breast cancer. The efficacy and safety of both elinzanetant and fezolinetant were initially established in postmenopausal women without breast cancer.

Fezolinetant was evaluated in the SKYLIGHT program, comprising three phase 3 trials (SKYLIGHT 1, 2, and 4) enrolling more than 3,000 postmenopausal women aged 40–65 years with ≥ 7 moderate-to-severe VMS per day.^{7,15,16} Both fezolinetant 30 mg and 45 mg once daily significantly reduced VMS frequency and severity versus placebo at weeks 4 and 12, with improvements observed as early as week 1 and sustained over 52 weeks.

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Interestingly, the DAYLIGHT trial (phase 3b) further demonstrated efficacy of fezolinetant over placebo in 452 women specifically considered unsuitable for hormone therapy (contraindicated, caution, stoppers, or averse), including due to a history breast cancer >5 years from randomization, although the proportion of this subgroup is unknown.^{17,18}

Fezolinetant has not been studied in patients with a previous malignant tumor within 5 years, and its role in breast cancer survivors remains under investigation in the ongoing HIGHLIGHT 1 trial (NCT06440967), which is currently recruiting women with stage 0–3 HR-positive breast cancer receiving adjuvant ET.¹⁹

Elinzanetant was evaluated in the OASIS program. The pivotal OASIS 1 and 2 trials enrolled postmenopausal women aged 40–65 years with ≥ 50 moderate-to-severe VMS per week. Elinzanetant 120 mg once daily significantly reduced VMS frequency and severity at weeks 4 and 12, with additional significant improvements in sleep disturbance and menopause-related quality of life.⁸ The 52-week OASIS 3 trial confirmed sustained efficacy and safety, with no liver toxicity signal.²⁰ As with the fezolinetant trials, OASIS 1, 2, and 3 excluded patients with a current or recent history of malignancy within the last 5 years.

A critical limitation shared by all pivotal trials of both elinzanetant and fezolinetant is the **systematic exclusion of patients taking SSRI/SNRI or other antidepressant medications**. In the OASIS 1–4 program, participants underwent a prescreening washout period of prohibited concomitant medications, which explicitly included antidepressant therapies that may influence VMS or the pharmacokinetics of elinzanetant. Similarly, the SKYLIGHT and DAYLIGHT fezolinetant trials required washout of medications that could affect VMS assessment, including antidepressants. This exclusion criterion was applied consistently across both the general menopausal population trials and the breast cancer-specific OASIS-4 trial.^{7-9,15-20}

Accordingly, there is currently no evidence on the efficacy of elinzanetant or fezolinetant in patients who develop VMS while already receiving SSRI/SNRI therapy. This represents a significant evidence gap, particularly relevant in clinical practice where SSRI/SNRI are commonly prescribed for mood disorders, anxiety, and as first-line non-hormonal VMS management in breast cancer patients.^{21,22}

For patients with concomitant mood disorders and/or chronic anxiety disorders, SSRI/SNRI remain the preferred pharmacologic option, as these agents address both the psychiatric condition and VMS simultaneously.

Consensus Statement

For patients with early-stage breast cancer (any HR status) or DCIS and VMS affecting QoL after adjuvant systemic therapies, elinzanetant and fezolinetant are the preferred systemic treatments when pharmacologic therapy is indicated, with the caveat that fezolinetant has not been studied in patients with a previous malignant tumor <5 years.

- In case of concomitant mood disorders and/or chronic anxiety disorders, SSRI/SNRI are the preferred option.
- In case of patients who develop VMS on anti-depressant drugs, including SSRI/SNRI, there is no evidence on efficacy of elinzanetant or fezolinetant (exclusion criterion in both clinical trials).

4. What are the toxicity management considerations for elinzanetant?

Hepatic Transaminase Monitoring. The FDA-approved prescribing information for elinzanetant (Lynkuet) requires baseline bloodwork (including ALT, AST, alkaline phosphatase, and total and direct bilirubin) prior to initiation, with follow-up hepatic transaminase evaluation at 3 months after initiation.²³

Therapy should not be started if serum transaminase concentrations are $\geq 2\times$ the upper limit of normal (ULN) or if total bilirubin is $\geq 2\times$ ULN. Elinzanetant should be discontinued if transaminase elevations exceed $5\times$ ULN, or if transaminase elevations exceed $3\times$ ULN with total bilirubin exceeding $2\times$ ULN.²³

This monitoring requirement reflects a class-level concern with NK-3 receptor antagonists. Elevated liver enzymes were previously observed with other NK-3 receptor antagonists, including pavinetant and fezolinetant. However, the hepatic safety profile of elinzanetant appears more favorable than that of fezolinetant. In the pooled OASIS phase 3 program (phases 1–3, including 1,697 elinzanetant-treated participants), ALT or AST elevations $\geq 3\times$ ULN occurred in 1.2% of elinzanetant-treated participants versus 1.0% on placebo during weeks 1–52.²⁴

CNS Depressant Effects and Daytime Impairment. The FDA label for elinzanetant includes a warning for CNS depressant effects and daytime impairment.²³ Across the three OASIS trials, nervous system effects (including somnolence, fatigue, vertigo, dizziness, and presyncope) occurred in 11.9% of patients on elinzanetant compared with 3.5% on placebo. Most events were mild or moderate in intensity, and none were severe. Notably, fatigue showed the highest daily relative frequency (up to 5%) during the first weeks of treatment, declining to less than 3% after week 13; headache peaked around weeks 7–8 and declined to less than 2% toward the end of the treatment period.

Given these CNS effects, the FDA label recommends that elinzanetant be taken at bedtime and that patients who experience somnolence or other nervous system effects refrain from

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driving or engaging in hazardous occupations or activities until the effects have resolved.²³ The bedtime dosing strategy was specifically designed to mitigate daytime impairment while potentially leveraging the somnolence effect to improve sleep quality, a key secondary endpoint in the OASIS program.

Pregnancy Risk. Elinzanetant is contraindicated in pregnancy. Animal studies demonstrated that elinzanetant can cause pregnancy loss or stillbirth. The FDA label requires exclusion of pregnancy in females of reproductive potential prior to initiation and advises the use of effective contraception during treatment and for 2 weeks after discontinuation.²³

Seizure Risk. An additional safety consideration not included in the above recommendations is the risk of seizures. One patient with a history of seizures experienced a seizure during the elinzanetant clinical trials, and convulsions were observed in preclinical rat studies. The FDA label advises caution in patients with a history of seizures or conditions that potentially lower the seizure threshold.²³

Consensus Statement

- Perform bloodwork to evaluate for hepatic function and injury, prior to initiation and 3 months after.
- Patients should be advised about the potential for somnolence and other nervous system effects. Those who experience these effects should refrain from driving or engaging in hazardous occupations or activities.
- Exclude pregnancy in females of reproductive potential prior to initiating elinzanetant.

References

1. Pistilli, B., Lohrisch, C., Sheade, J. & Fleming, G.F. Personalizing Adjuvant Endocrine Therapy for Early-Stage Hormone Receptor-Positive Breast Cancer. *Am Soc Clin Oncol Educ Book* **42**, 1-13 (2022).
2. Franzoi, M.A., *et al.* Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. *Lancet Oncol* **22**, e303-e313 (2021).
3. Zhu, L., Hsieh, T.T., Iyer, T.K., Morgans, A.K. & Hamnvik, O.R. Management of vasomotor symptoms in cancer patients. *Oncologist* **30**(2025).
4. Scanlon, M., *et al.* Patient Satisfaction with Physician Discussions of Treatment Impact on Fertility, Menopause and Sexual Health among Pre-menopausal Women with Cancer. *J Cancer* **3**, 217-225 (2012).
5. Ganz, P.A., *et al.* Managing Menopausal Symptoms in Breast Cancer Survivors: Results of a Randomized Controlled Trial. *JNCI: Journal of the National Cancer Institute* **92**, 1054-1064 (2000).

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6. Sassarini, J. & Anderson, R.A. Elinzanetant: a phase III therapy for postmenopausal patients with vasomotor symptoms. *Expert Opin Investig Drugs* **33**, 19-26 (2024).
7. Lederman, S., *et al.* Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (SKYLIGHT 1): a phase 3 randomised controlled study. *Lancet* **401**, 1091-1102 (2023).
8. Pinkerton, J.V., *et al.* Elinzanetant for the Treatment of Vasomotor Symptoms Associated With Menopause: OASIS 1 and 2 Randomized Clinical Trials. *JAMA* **332**, 1343-1354 (2024).
9. Cardoso, F., *et al.* Elinzanetant for Vasomotor Symptoms from Endocrine Therapy for Breast Cancer. *N Engl J Med* **393**, 753-763 (2025).
10. Pawsey, S., *et al.* Elinzanetant (NT-814), a Neurokinin 1,3 Receptor Antagonist, Reduces Estradiol and Progesterone in Healthy Women. *The Journal of clinical endocrinology and metabolism* **106**, e3221-e3234 (2021).
11. Cardoso, F., *et al.* 604P Pharmacokinetics, compliance and estradiol levels in women with breast cancer receiving elinzanetant for the treatment of endocrine therapy-associated vasomotor symptoms. *ESMO Open* **11**, 107623 (2026).
12. Morga, A., *et al.* Systematic review and network meta-analysis comparing the efficacy of fezolinetant with hormone and nonhormone therapies for treatment of vasomotor symptoms due to menopause. *Menopause* **31**, 68-76 (2024).
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Survivorship. Version 2.2026.
https://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf.
14. Brennan, D.J., *et al.* 234P Elinzanetant in breast cancer care: potential drug–drug interaction profile with targeted systemic therapies. *ESMO Open* **11**, 107188 (2026).
15. Johnson, K.A., *et al.* Efficacy and Safety of Fezolinetant in Moderate to Severe Vasomotor Symptoms Associated With Menopause: A Phase 3 RCT. *The Journal of clinical endocrinology and metabolism* **108**, 1981-1997 (2023).
16. Neal-Perry, G., *et al.* Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial. *Obstet Gynecol* **141**, 737-747 (2023).
17. Schaudig, K., *et al.* Efficacy and safety of fezolinetant for moderate-severe vasomotor symptoms associated with menopause in individuals unsuitable for hormone therapy: phase 3b randomised controlled trial. *BMJ* **387**, e079525 (2024).
18. Shapiro, C.M.M., *et al.* Effect of fezolinetant on patient-reported quality-of-life outcomes: Data from a phase 3b study (DAYLIGHT) of the treatment of moderate to severe vasomotor symptoms associated with menopause in women considered unsuitable for hormone therapy. *Maturitas* **193**, 108159 (2025).
19. Bouchard, C., *et al.* HIGHLIGHT 1: A randomized, placebo-controlled, double-blind, phase 3 clinical study to investigate the efficacy and safety of fezolinetant for treatment of moderate to severe vasomotor symptoms (hot flashes) in women with stage 0 to 3 hormone receptor–positive breast cancer who are receiving adjuvant endocrine therapy. *Journal of Clinical Oncology* **44**, TPS642-TPS642 (2026).

20. Panay, N., *et al.* Elinzanetant for the Treatment of Vasomotor Symptoms Associated With Menopause: A Phase 3 Randomized Clinical Trial. *JAMA Intern Med* **185**, 1319-1327 (2025).
21. Wojciechowski, P., *et al.* Comparative Efficacy of Elinzanetant Versus Other Non-Hormonal Pharmaceutical Therapies for the Treatment of Moderate-to-Severe Vasomotor Symptoms Associated With Menopause: A Network Meta-Analysis. *BJOG* (2026).
22. Kingsberg, S., *et al.* Treatment utilization and non-drug interventions for vasomotor symptoms in breast cancer survivors taking endocrine therapy: Real-world findings from the United States and Europe. *Maturitas* **188**, 108071 (2024).
23. LYNKUET. Highlights of prescribing information. U.S. Food and Drug Administration (FDA). Revised October 2025. Accessed July 17, 2026.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219469s000lbl.pdf.
24. Lewis, J.H., *et al.* Liver Safety of the Dual Neurokinin-1/-3 Receptor Antagonist Elinzanetant. *Drug Saf* **49**, 985-1002 (2026).