


Pr **VEOZAH**[®]
fezolinetant 45mg
tablets

**THE FIRST NON-HORMONAL
NEUROKININ B (NKB) ANTAGONIST**
INDICATED IN THE TREATMENT OF VMS
ASSOCIATED WITH MENOPAUSE^{1-3*}

**NON-HORMONAL
NKB ANTAGONIST**



**HELP FIGHT MODERATE
TO SEVERE VMS,
ALSO KNOWN AS
HOT FLASHES
and NIGHT SWEATS^{1,4}
WITH VEOZAH**

VEOZAH (fezolinetant film-coated tablets) is indicated for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.¹

VEOZAH achieved statistically significant reductions from baseline in the frequency of moderate to severe VMS vs. placebo at Week 12 ($p < 0.001$, coprimary endpoint)^{1†}.

63.5% reduction in the frequency of moderate to severe VMS per 24 hours with VEOZAH vs. 43.1% with placebo (LS mean change from baseline: -7.5 vs. -5.0, respectively).

DISCOVER AN OPTION TO TREAT MODERATE TO SEVERE VMS¹

LS: least squares.

* Comparative clinical significance unknown.

† SKYLIGHT 2 was a phase 3, randomized, double-blind, placebo-controlled, parallel-group study in which post-menopausal women were randomized to VEOZAH 45 mg (n=167) or placebo (n=167) once daily for 12 weeks. After the 12-week, double-blind treatment period, women on placebo were then re-randomized to VEOZAH for a 40-week extension to evaluate safety for up to 52 weeks of total exposure. The study included post-menopausal women who had a minimum average of 7 moderate to severe VMS per day. The coprimary efficacy endpoints were change from baseline in moderate to severe VMS frequency and severity to Weeks 4 and 12. Baseline mean frequency of moderate to severe VMS per 24 hours: 11.8 for VEOZAH, 11.6 for placebo.¹

CONSIDER VEOZAH

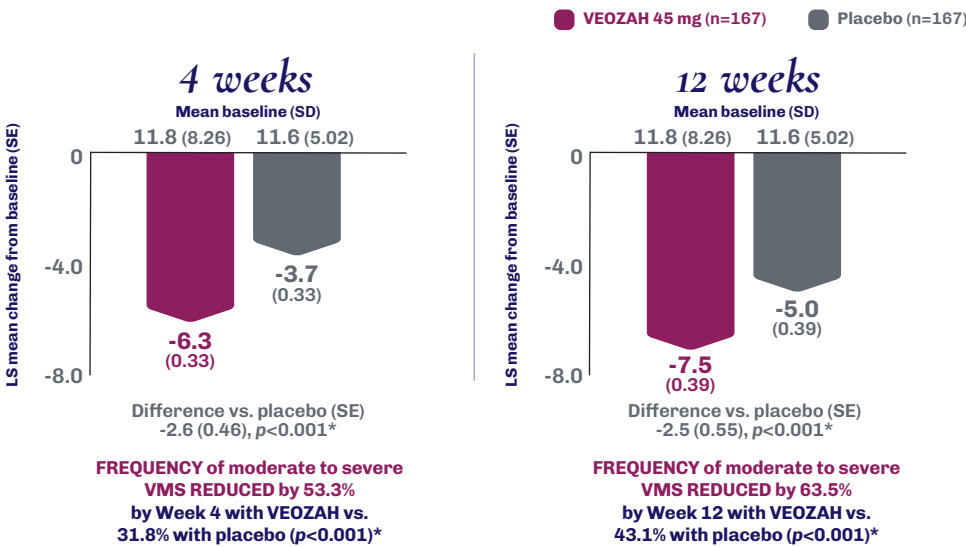
The efficacy of VEOZAH was evaluated in the first 12-week, randomized, placebo-controlled, double-blind portion of the SKYLIGHT 2 phase 3 study. After the first 12 weeks, post-menopausal women on placebo were then re-randomized to VEOZAH for a 40-week extension to evaluate safety for up to 52 weeks of total exposure. The study included post-menopausal women who had a minimum average of 7 moderate to severe VMS per day. Coprimary endpoints were mean change from baseline in moderate to severe VMS frequency and severity at Weeks 4 and 12.¹

SKYLIGHT 2

VEOZAH provided clinically meaningful (≥ 2 hot flashes per 24 hours) reductions in the frequency of moderate to severe VMS and provided statistically significant reductions in the severity of moderate to severe VMS symptoms vs. placebo.¹

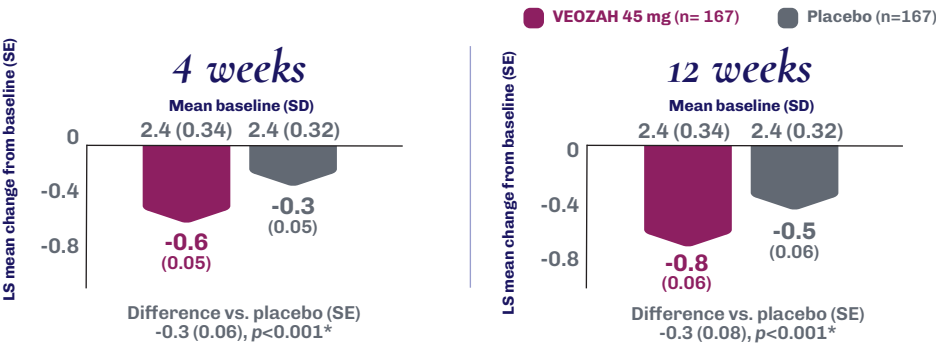
FREQUENCY

MEAN CHANGE FROM BASELINE TO WEEKS 4 AND 12
IN MODERATE TO SEVERE VMS FREQUENCY PER 24 HOURS¹



SEVERITY

MEAN CHANGE FROM BASELINE TO WEEKS 4 AND 12
IN MODERATE TO SEVERE VMS SEVERITY PER 24 HOURS¹



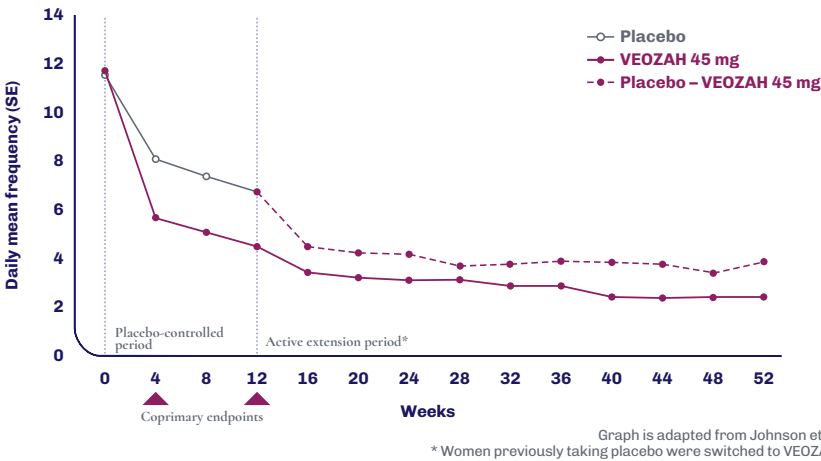
Statistically significant difference between VEOZAH vs. placebo was observed at Week 1 for VMS frequency (secondary endpoint).⁵⁻⁷

- Mean (SD) change from baseline in VMS frequency with VEOZAH: 3.91 (4.30) vs. 2.34 (3.34) with placebo
- Baseline (SD) VMS frequency in VEOZAH group 11.8 (8.26) vs. 11.6 (5.02) with placebo
- LS mean difference vs. placebo (SE): -1.71 (0.40); 95% CI: -2.51, -0.91; $p < 0.001$, without multiplicity analysis

VEOZAH WEEK 52 DATA^{5,6}

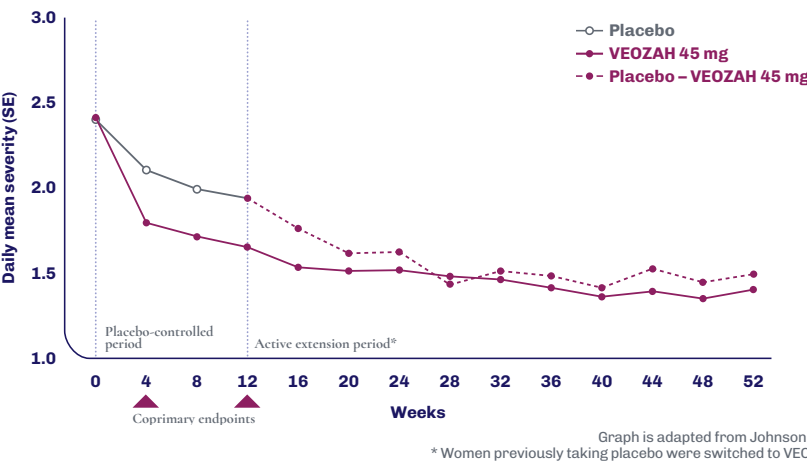
FREQUENCY

CHANGE IN MODERATE TO SEVERE VMS UP TO WEEK 52⁵



SEVERITY

CHANGE IN MODERATE TO SEVERE VMS UP TO WEEK 52⁵



The duration of this study is longer than that of the efficacy data included in the VEOZAH Product Monograph. Mean change in the frequency and severity of moderate to severe VMS from baseline to each visit in the extension period was an exploratory endpoint. Assessments after the 12-week placebo-controlled period were descriptive only.

CI: confidence interval; SD: standard deviation; SE: standard error.

LS: least squares; VMS: vasomotor symptoms.

* Statistically significantly superior compared to placebo at the 0.05 level with multiplicity adjustment.¹

FREQUENCY: Measured as a daily mean and analyzed as weekly average (calculated as the average frequency over nonmissing days from 7 days).⁵

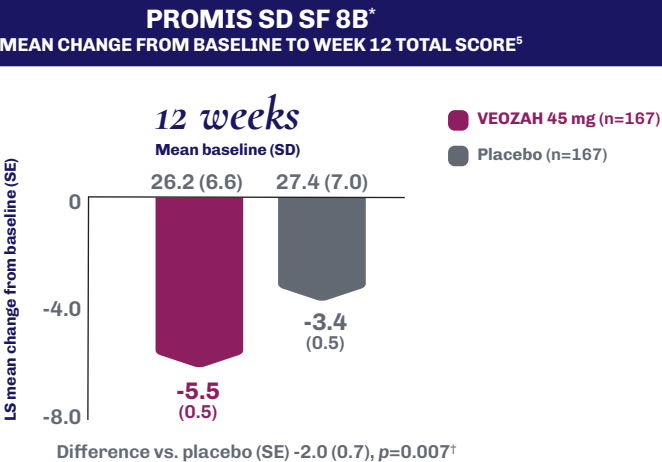
SEVERITY: Measured as a daily mean and analyzed as weekly average (calculated as the average severity over nonmissing days from 7 days).⁵

LS mean: least squares mean estimated from a mixed model for repeated measures analysis of covariance.¹



VEOZAH demonstrated powerful reductions in self-reported sleep disturbances related to VMS, as measured by the PROMIS SD SF 8B (key secondary endpoint)⁵

In the management of VMS, VEOZAH improved sleep disturbances vs. placebo at Week 12 (*p*=0.007)⁵



DATA FROM SKYLIGHT 2 TRIAL⁵



The content that follows is a prespecified exploratory endpoint of SKYLIGHT 2 trial and was not statistically powered to make inferences. Results from this analysis should be interpreted with caution.

Exploratory endpoint

Mean change from baseline in MENQOL[‡] total score at Week 12

- Placebo (n=167): LS mean change from baseline was -0.95 (SE 0.10)
- VEOZAH (n=167): LS mean change from baseline was -1.43 (SE 0.10)
- LS mean difference vs. placebo was -0.47 (SE 0.15); *p*=0.001

Key study limitations:

The trial was not powered for this endpoint, and statistical analyses were not adjusted for multiplicity. *P*-values should therefore be interpreted with caution.

End of exploratory endpoint

LS: least squares; PROMIS SD SF 8b: Patient-Reported Outcomes Measurement Information System Sleep Disturbance – Short Form 8b; SD: standard deviation; SE: standard error.

* PROMIS SD SF 8b assesses self-reported sleep disturbance during the prior 7 days and includes perceptions of restless sleep; satisfaction with sleep; refreshing sleep; difficulties sleeping, getting to sleep, or staying asleep; amount of sleep; and sleep quality. Responses to the 8 items range from 1 to 5, and the range of possible summed raw scores is 8 to 40. Higher scores on PROMIS SD SF 8b indicate more disturbed sleep.

† Two-sided unadjusted *p*-value.⁵

‡ The MENQOL questionnaire is a validated, 29-item, self-administered scale that assesses the impact of menopausal symptoms over the prior week. It is comprised of four domains: vasomotor, psychosocial, physical, and sexual. Symptoms are rated on a scale from 0 (not bothersome) to 6 (extremely bothersome). A negative change in MENQOL score indicates an improvement from baseline.⁵

VEOZAH: DEMONSTRATED SAFETY *and* TOLERABILITY PROFILE UP TO 1 YEAR¹

12-WEEK SAFETY PROFILE

Adverse events that occurred in at least 2% in the VEOZAH 45-mg arm and greater than placebo in two trials*

Combined SKYLIGHT 1 and 2		
	VEOZAH N=340 n (%)	Placebo N=342 n (%)
Gastrointestinal disorders		
Abdominal pain [†]	7 (2.1%)	7 (2.0%)
Investigations		
Liver test elevation [‡]	11 (3.2%)	9 (2.6%)

Adapted from the VEOZAH Product Monograph.

52-WEEK SAFETY PROFILE

Adverse events that occurred in at least 2% in the VEOZAH 45-mg arm and greater than placebo over 52 weeks[§]

SKYLIGHT 4		
	VEOZAH N=609 n (%)	Placebo N=610 n (%)
Gastrointestinal disorders		
Abdominal pain [†]	27 (4.4%)	13 (2.1%)
Diarrhea	24 (3.9%)	16 (2.6%)
Nausea	19 (3.1%)	15 (2.5%)
General disorders		
Fatigue	17 (2.8%)	16 (2.6%)
Investigations		
Liver test elevation [¶]	32 (5.3%)	29 (4.8%)
Nervous system disorders		
Headache, cluster headache, sinus headache, and tension headache	59 (9.7%)	58 (9.5%)
Psychiatric disorders		
Insomnia, middle insomnia	24 (3.9%)	11 (1.8%)
Vascular disorders		
Hot flush, flushing	15 (2.5%)	10 (1.6%)

Adapted from the VEOZAH Product Monograph.

A numerical imbalance was observed in the incidence of other malignancies between VEOZAH and placebo groups in the long-term safety trial SKYLIGHT 4. A causal relationship between VEOZAH and increased risk of malignancies has not been established.¹ Please see the VEOZAH Product Monograph for complete adverse events information.

ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase.

* SKYLIGHT 1 and 2 were identically designed phase 3 efficacy and safety studies that were randomized, placebo-controlled, double-blind for 12 weeks, followed by re-randomization of women previously receiving placebo to VEOZAH (women on VEOZAH remained on VEOZAH) for an additional 40 weeks of active treatment.¹

† Abdominal pain includes abdominal lower pain, abdominal upper pain, and abdominal tenderness.¹

‡ Liver test elevation includes ALT abnormal/increased, AST abnormal/increased, blood ALP abnormal/increased, blood bilirubin increased, gamma-glutamyltransferase increased, hepatic enzyme abnormal/increased, transaminases increased, and liver function test abnormal/increased.¹

§ SKYLIGHT 4 was a phase 3, 52-week, randomized, placebo-controlled, double-blind, long-term safety study.¹

¶ Liver test elevation includes ALT abnormal/increased, AST abnormal/increased, blood ALP increased, blood bilirubin increased, gamma-glutamyltransferase increased, hepatic function abnormal, hepatic enzyme increased, transaminases increased, and liver function test abnormal/increased.¹



VEOZAH: ONE DOSE, ONE TABLET, ONCE A DAY

FLEXIBLE ADMINISTRATION WITH 45 MG
TAKEN ORALLY ONCE DAILY, WITH OR WITHOUT FOOD

Recommended dosing & administration



Same time, every day

Take VEOZAH with liquids at about the same time every day, and swallow whole. Do not cut, crush, or chew tablets.¹



Missed dose guidance

If a dose is missed or not taken at the usual time, patients should take the missed dose as soon as possible, unless there is less than 12 hours before the next scheduled dose. Return to the regular schedule the following day.¹



Special populations¹

Hepatic impairment

- VEOZAH is contraindicated in individuals with cirrhosis.
- VEOZAH is not recommended for use in individuals with Child-Pugh Class B (moderate) chronic hepatic impairment.
- VEOZAH has not been studied in individuals with Child-Pugh Class C (severe) chronic hepatic impairment and is not recommended in this population.
- No dose modification is recommended for individuals with Child-Pugh Class A (mild) chronic hepatic impairment.

Renal impairment

- VEOZAH is contraindicated in individuals with severe* renal impairment.
- VEOZAH has not been studied in individuals with end-stage renal disease† and is contraindicated in this population.
- No dose modification is recommended for individuals with mild‡ or moderate§ renal impairment.

* eGFR less than 30 mL/min/1.73 m².
† eGFR less than 15 mL/min/1.73 m².
‡ eGFR 60 to less than 90 mL/min/1.73 m².
§ eGFR 30 to less than 60 mL/min/1.73 m².

Dosing considerations¹

- Perform baseline bloodwork to evaluate hepatic function and assess for injury including serum ALT, serum AST, serum ALP, and serum bilirubin (total and direct) before initiating treatment with VEOZAH.
 - Do not start VEOZAH if ALT or AST is $\geq 2 \times$ ULN or if the total bilirubin is elevated ($\geq 2 \times$ ULN).
 - Proceed with caution if ALT or AST is between $>1.5 \times$ ULN and $<2 \times$ ULN.
- While using VEOZAH, perform follow-up evaluations of hepatic transaminase concentration monthly during the first 3 months, at 6 months, and 9 months after the initiation of therapy.
- Advise patients to discontinue VEOZAH immediately and seek medical attention including hepatic laboratory tests if they experience signs or symptoms that may suggest liver injury.
 - Signs or symptoms that may suggest liver injury include new onset fatigue, decreased appetite, nausea, vomiting, pruritus, jaundice, pale feces, dark urine, or abdominal pain.
- Discontinue VEOZAH if transaminase elevations are $\geq 5 \times$ ULN and/or transaminase elevations are $\geq 3 \times$ ULN and the total bilirubin level is $\geq 2 \times$ ULN.
 - If transaminase elevations $\geq 3 \times$ ULN occur, perform more frequent follow-up hepatic laboratory tests until resolution.
 - Exclude alternative causes of hepatic laboratory test elevations.

Please see the VEOZAH Product Monograph for complete dosing and administration information.

CONSIDER ONCE-DAILY VEOZAH FOR YOUR PATIENTS

ALP: alkaline phosphatase; ALT: alanine aminotransferase;
AST: aspartate aminotransferase; eGFR: estimated glomerular filtration rate;
ULN: upper limit of normal.

IMPORTANT SAFETY INFORMATION

Clinical use:

- Pediatrics (<18 years of age): not indicated
- Geriatrics (≥ 65 years of age): no data available; therefore, an indication has not been recommended

Contraindications:

- Known cirrhosis
- Severe renal impairment or end-stage renal disease
- Patients using concomitant moderate or strong CYP1A2 inhibitors
- Known or suspected pregnancy

Relevant warnings and precautions:

- A numerical imbalance was observed in the incidence of other malignancies between VEOZAH and placebo groups reported in the long-term safety study. A causal relationship between VEOZAH and increased risk of malignancies has not been established.
- Across the three phase 3 studies, one case of endometrial hyperplasia and one case of endometrial malignancy, were identified in the VEOZAH group. The rate of these events was $\leq 1\%$, and within the upper bound of the one-sided 95% confidence limit of $\leq 4\%$. There was no case of endometrial hyperplasia or carcinoma in the placebo group.
- Benefit-risk consideration to treat women with previous or known breast cancer or other estrogen-dependent malignancies
- Not recommended in Child-Pugh Class B (moderate) chronic hepatic impairment; not studied in Child-Pugh Class C (severe) chronic hepatic impairment and is not recommended in this population
- Risk of hepatic transaminase elevation and hepatotoxicity
- Perform baseline bloodwork to evaluate hepatic function and assess for injury (including serum ALT, serum AST, serum ALP, and serum bilirubin [total and direct]) prior to initiating VEOZAH. Perform hepatic laboratory tests monthly for the first 3 months, at 6 months, and 9 months after initiation of therapy
- Not recommended in breast-feeding women

For more information:

Consult the Product Monograph at www.veozahmonograph.ca for important information relating to adverse reactions, drug interactions and dosing information. The Product Monograph is also available by calling **1-888-338-1824**.

ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase.
REFERENCES: **1.** VEOZAH Product Monograph. Markham, ON: Astellas Pharma Canada, Inc. **2.** The North American Menopause Society (NAMS). *Menopause*. 2023;30(6):573-590. **3.** Data on file. First and only claim. **4.** Yuksel N, Evaniuk D, Huang L, et al. Guideline No. 422a: Menopause: vasomotor symptoms, prescription therapeutic agents, complementary and alternative medicine, nutrition, and lifestyle. *J Obstet Gynaecol Can*. 2021;43(10):1188-1204.e1. **5.** Johnson KA, Martin N, Nappi RE, et al. Efficacy and safety of fezolinetant in moderate to severe vasomotor symptoms associated with menopause: a phase 3 RCT. *J Clin Endocrinol Metab*. (Epub) 02-03-2023. **6.** Data on file. SKYLIGHT 2 study protocol. **7.** Data on file. Clinical efficacy summary.



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CONSIDER VEOZAH FOR THE TREATMENT OF MODERATE TO SEVERE VMS, ALSO KNOWN AS HOT FLASHES *and* NIGHT SWEATS^{1,4}



DEMONSTRATED EFFICACY PROFILE

- Patients taking VEOZAH experienced statistically significant reductions in the frequency and severity of moderate to severe VMS from baseline to Weeks 4 and 12 vs. placebo.¹
- Patients also experienced a significant reduction in sleep disturbances related to VMS while taking VEOZAH at Week 12 vs. placebo.⁵



DEMONSTRATED SAFETY PROFILE OVER 52 WEEKS

- Across the two 12-week studies, the most common adverse drug reaction ($\geq 3\%$ in patients receiving VEOZAH 45 mg and greater than placebo) was liver test elevation (3.2%).¹
- During the 52-week study, the most frequent adverse drug reactions ($\geq 3\%$ in patients receiving VEOZAH 45 mg and greater than placebo) were headache (9.7%), liver test elevation (5.3%), abdominal pain (4.4%), diarrhea (3.9%), insomnia (3.9%), and nausea (3.1%).¹
 - A numerical imbalance was observed in the incidence of other malignancies between VEOZAH and placebo groups in SKYLIGHT 4. A causal relationship between VEOZAH and increased risk of malignancies has not been established.¹

DISCOVER AN OPTION TO TREAT MODERATE TO SEVERE VMS¹



ONE DOSE, ONE TABLET, ONCE A DAY

Flexible administration with 45 mg taken orally once daily, with or without food.¹



Actual size shown.
Tablet is 7 mm in diameter

For complete dosing and administration information, please refer to the Product Monograph.

* Comparative clinical significance unknown.

To find more information and resources, scan the QR code or visit [Veozaahcp.ca](https://veozahhcp.ca)

