Treat moderate to severe Vasomotor Symptoms (VMS) due to menopause, commonly referred to as hot flashes and night sweats^{1,2}

FIGHT the FIRE

VEOZAH[™] (fezolinetant) is a first-in-class selective neurokinin 3 receptor (NK3R) antagonist that works differently to directly block neurokinin B (NKB), a known trigger of VMS, from binding on the KNDy neuron.^{1,3,4}

HOW VMS STARTS IN THE HYPOTHALAMUS

Thermoregulatory homeostasis

KNDy neurons in the hypothalamus are inhibited by estrogen and stimulated by the neuropeptide NKB. This balance contributes to **body temperature regulation**.³

Impact of NKB

REDUCTION

OF ESTROGEN

Estrogen decline during the menopause transition disrupts this balance with NKB. **Unopposed**, **NKB signaling** causes heightened KNDy neuronal activity. This **triggers heat dissipation mechanisms**, including vasodilation and sweating—VMS.³

HOW VEOZAH DISRUPTS HOT FLASHES

VEOZAH inhibits binding of NKB to NK3R

KNDy NEURON

NK3 RECEPTOR

VEOZAH is a nonhormonal selective NK3R antagonist that blocks NKB binding on the KNDy neuron to modulate neuronal activity in the thermoregulatory center. This action helps to reduce the number and intensity of hot flashes and night sweats. VEOZAH directly targets NK3R with a high affinity, more than 450-fold higher than NK1 or NK2 receptors.^{1.5}

KNDy=kisspeptin/neurokinin B/dynorphin.

KNDy NEURON

NHIBITED

BY ESTROGEN

Watch the mechanism of action of VEOZAH at <u>VEOZAHhcp.com/MOAvideo</u>

UNOPPOSED NKB

STIMULATION

ΝКΒ

INDICATIONS AND USAGE

VEOZAH™ (fezolinetant) is a neurokinin 3 (NK3) receptor antagonist indicated for the treatment of moderate to severe vasomotor symptoms due to menopause.

KNDy NEURON

ESTROGEN

ALPHA RECEPTOR

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

VEOZAH is contraindicated in women with any of the following:

TIMULATED

BY NKB

ESTROGEN

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- Known cirrhosis Severe renal impairment or end-stage renal disease
- Concomitant use with CYP1A2 inhibitors

Please see additional Important Safety Information on next page.

Please click here for full Prescribing Information for VEOZAH™ (fezolinetant).



A NONHORMONAL OPTION FOR PATIENTS WITH MODERATE TO SEVERE VASOMOTOR SYMPTOMS (VMS) DUE TO MENOPAUSE^{1,5}

REDEFINE <u>how</u> YOU TARGET VMS

VEOZAH directly targets a source of VMS kisspeptin/neurokinin B/dynorphin (KNDy) neurons in the hypothalamus. Give your patients another way to treat the heat day and night.¹



<u>Reduce</u> KNDy NEURONAL ACTIVITY

Block

THE BINDING OF NKB

<u>Balance</u> THERMOREGULATORY ACTIVITY

Explore the mechanism of action of VEOZAH at VEOZAHhcp.com/MOAvideo

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Hepatic Transaminase Elevation

Elevations in serum transaminase [alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)] levels > 3x the upper limit of normal (ULN) occurred in 2.3% of women receiving VEOZAH and 0.9% of women receiving placebo in three clinical trials. No serum elevations in total bilirubin (> 2x ULN) occurred. Women with ALT or AST elevations were generally asymptomatic. Transaminase levels returned to pretreatment levels (or close to these) without sequelae with dose continuation, and upon dose interruption, or discontinuation. Women with cirrhosis were not studied.

Perform baseline bloodwork to evaluate for hepatic function and injury prior to VEOZAH initiation. Do not start VEOZAH if concentration of ALT or AST is $\ge 2x$ ULN or if the total bilirubin is elevated (e.g., $\ge 2x$ ULN) for the evaluating laboratory. If baseline hepatic transaminase evaluation is < 2x ULN and the total bilirubin is normal, VEOZAH can be started. Perform follow-up evaluations of hepatic transaminase concentration at 3 months, 6 months, and 9 months after initiation of therapy and when symptoms (such as nausea, vomiting, or yellowing of the skin or eyes) suggest liver injury.

ADVERSE REACTIONS

The most common adverse reactions with VEOZAH ≥ 2% and > placebo (VEOZAH % vs. placebo %) are: abdominal pain (4.3% vs. 2.1%), diarrhea (3.9% vs. 2.6%), insomnia (3.9% vs. 1.8%), back pain (3.0% vs. 2.1%), hot flush (2.5% vs. 1.6%), and hepatic transaminase elevation (2.3% vs. 0.8%).

Please see additional Important Safety Information on previous page. Please click here for full Prescribing Information for VEOZAH™ (fezolinetant).

REFERENCES: 1. VEOZAH [package insert]. Northbrook, IL: Astellas Pharma US, Inc. 2. Thurston RC. Vasomotor symptoms. In: Crandall CJ, Bachman GA, Faubion SS, et al., eds. Menopause Practice: A Clinician's Guide. 6th ed. Pepper Pike, OH: The North American Menopause Society, 2019:43-55. 3. Depypere H, Lademacher C, Siddiqui E, Fraser GL. Fezolinetant in the treatment of vasomotor symptoms associated with menopause. Expert Opin Investig Drugs 2021;30(7):681-94. 4. Jayasena CN, Comninos AN, Stefanopoulou E, et al. Neurokinin B administration induces hot flushes in women. Sci Rep (Epub) 02-16-2015. 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.



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