Original Effective Date: 09/06/2023
Current Effective Date: 09/21/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C25593-A

Veozah (fezolinetant)

PRODUCTS AFFECTED

Veozah (fezolinetant)

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. Documentation of 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][2]

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 Veozah (fezolinetant) include: Known cirrhosis, severe renal impairment or end-stage renal disease, and concomitant use with CYP1A2 inhibitors. Do not start Veozah 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 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 Veozah (fezolinetant) include: Known cirrhosis, severe renal impairment or end-stage renal disease, and concomitant use with CYP1A2 inhibitors]

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

None

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

45mg 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 3 (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 and/or night sweats, are the most common symptoms reported with menopause, occurring in approximately 75%–80% of menopausal women. VMS is believed to be caused by changes in estrogen levels and increased neurokinin B (NKB) activity in the hypothalamus, the region of the brain responsible for thermoregulation. Kisspeptin, neurokinin B, dynorphin A (KNDy) neurons contribute to body temperature control in the thermoregulatory center of the hypothalamus. KNDy neurons are inhibited by estrogen and stimulated by NKB at the neurokinin 3 (NK3) receptor. Estrogen decline during menopause leads to uninhibited NKB-mediated stimulation of KNDy neurons, leading to dysregulation of the thermoregulatory center.

Hot flashes 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. Hot flashes 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 VMS duration of approximately 7.4 years. However, 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 and risk and increased risk for low bone density and fractures.

Management of VMS currently includes menopausal hormone therapy (MHT), nonhormonal therapies, and/or non-pharmacologic interventions. According to the 2022 North American Menopause Society (NAMS) hormone therapy position statement, MHT is considered the gold standard of treatment of VMS and the benefits outweigh the risks in healthy women within 10 years of menopause and less than 60 years of age.

Currently available nonhormonal therapies for the management of VMS include selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), gabapentinoids, oxybutynin, and clonidine. Current guidelines recommend nonhormonal therapies for women who want to manage VMS but either cannot take hormone therapy due to significant risk factors or contraindications or prefer not to take hormone therapy. Based on available evidence, the 2023 NAMS nonhormone therapy position statement, recommends SSRIs, SNRIs, gabapentin, Veozah (level 1 evidence) as well as oxybutynin (levels I-II evidence).

The efficacy of Veozah for the treatment of moderate to severe vasomotor symptoms due to menopause was evaluated in the first 12-week, randomized, placebo-controlled, double-blind portion of each of two phase 3

clinical trials. In each of these two trials, after the first 12 weeks, women on placebo were then re-randomized to Veozah for a 40-week extension to evaluate safety for up to 52 weeks total exposure. In Trials 1 (NCT04003155) and 2 (NCT04003142), 1022 women (522 in Trial 1 and 500 in Trial 2) who had a minimum average of 7 moderate to severe vasomotor symptoms per day were randomized to one of two doses of fezolinetant (including the 45 mg dosage strength) or placebo. Randomization was stratified by smoking status. The mean age of the postmenopausal women was 54 years. Women self-identified as Caucasian (81%), African American (17%), Asian (1%), and Hispanic/Latina ethnicity (24%). The study population included menopausal women with one or more of the following: prior hysterectomy (32.1%), prior oophorectomy (21.6%), or prior hormone therapy use (19.9%). Those who were on prior hormone therapy underwent a wash-out period prior to trial participation. The co-primary efficacy endpoints for both trials were the mean change from baseline in moderate to severe vasomotor symptoms frequency and severity to Weeks 4 and 12. Data from each trial demonstrated statistically significant and clinically meaningful (≥ 2 hot flashes over 24 hours) reduction from baseline in the frequency of moderate to severe vasomotor symptoms for Veozah 45 mg compared to placebo at Weeks 4 and 12. Data from each trial also demonstrated a statistically significant reduction from baseline in the severity of moderate to severe vasomotor symptoms (over 24 hours) at Weeks 4 and 12 for Veozah 45 mg compared to placebo.

Table 2: Mean Baseline and Change from Baseline to Weeks 4 and 12 for Mean Frequency of Moderate to Severe Vasomotor Symptoms over 24 Hours in Women Treated with VEOZAH in Trials 1 and 2

Parameter	Trial 1		Trial 2	
	VEOZAH 45 mg (n=174)	Placebo (n=175)	VEOZAH 45 mg (n=167)	Placebo (n=167)
Baseline				
Mean (SD)	10.4 (3.92)	10.5 (3.79)	11.8 (8.26)	11.6 (5.02)
Change from Baseline to Week 4				
LS Mean (SE)	-5.4 (0.30)	-3.3 (0.29)	-6.3 (0.33)	-3.7 (0.33)
Difference vs Placebo (95% CI)	-2.1 (-2.9, -1.3)	--	-2.6 (-3.5, -1.6)	--
P-value	< 0.001[1]	--	< 0.001[1]	--
Change from Baseline to Week 12				
LS Mean (SE)	-6.4 (0.31)	-3.9 (0.31)	-7.5 (0.39)	-5.0 (0.39)
Difference vs Placebo (95% CI)	-2.6 (-3.4, -1.7)	--	-2.5 (-3.6, -1.5)	--
P-value	< 0.001[1]	--	< 0.001[1]	--

1. Statistically significantly superior compared to placebo at the 0.05 level with multiplicity adjustment.
LS Mean: Least Squares Mean estimated from a mixed model for repeated measures analysis of covariance; SD: Standard Deviation; SE: Standard Error.

Table 3: Mean Baseline and Change from Baseline to Weeks 4 and 12 for Mean Severity of Moderate to Severe Vasomotor Symptoms over 24 Hours in Women Treated with VEOZAH in Trials 1 and 2

Parameter	Trial 1		Trial 2	
	VEOZAH 45 mg (n=174)	Placebo (n=175)	VEOZAH 45 mg (n=167)	Placebo (n=167)
Baseline				
Mean (SD)	2.4 (0.35)	2.4 (0.35)	2.4 (0.34)	2.4 (0.32)
Change from Baseline to Week 4				
LS Mean (SE)	-0.5 (0.04)	-0.3 (0.04)	-0.6 (0.05)	-0.3 (0.05)
Difference vs Placebo (95% CI)	-0.2 (-0.3, -0.1)	--	-0.3 (-0.4, -0.2)	--
P-value	0.002[1]	--	< 0.001[1]	--
Change from Baseline to Week 12				
LS Mean (SE)	-0.6 (0.05)	-0.4 (0.05)	-0.8 (0.06)	-0.5 (0.06)
Difference vs Placebo (95% CI)	-0.2 (-0.4, -0.1)	--	-0.3 (-0.5, -0.1)	--
P-value	0.007[1]	--	< 0.001[1]	--

1. Statistically significantly superior compared to placebo at the 0.05 level with multiplicity adjustment.
LS Mean: Least Squares Mean estimated from a mixed model for repeated measures analysis of covariance; SD: Standard Deviation; SE: Standard Error.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Veozah (fezolinetant) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Veozah (fezolinetant) include: known cirrhosis, severe renal

impairment (eGFR 15 to less than 30 mL/min/1.73 m2) or end-stage renal disease (eGFR less than 15 mL/min/1.73 m2), concomitant use with CYP1A2 inhibitors (e.g., fluvoxamine, mexiletine, cimetidine). Do not start Veozah if ALT or AST is ≥ 2 x ULN or if the total bilirubin is ≥ 2 x ULN for the evaluating laboratory.

Exclusions/Discontinuation:
While using Veozah, perform follow-up hepatic laboratory tests monthly for the first 3 months, at 6 months, and 9 months after 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 (new onset fatigue, decreased appetite, nausea, vomiting, pruritus, jaundice, pale feces, dark urine, or abdominal pain). Discontinue Veozah if transaminase elevations are > 5 x ULN, or if transaminase elevations are > 3 x ULN and the total bilirubin level is > 2 x ULN.

OTHER SPECIAL CONSIDERATIONS:
Veozah (fezolinetant) has a Black Box Warning for risk of hepatotoxicity. Hepatotoxicity has occurred with the use of Veozah in the post-marketing setting. Perform hepatic laboratory tests prior to initiation of treatment to evaluate for hepatic function and injury. Do not start Veozah if either aminotransferase is ≥ 2 x the upper limit of normal (ULN) or if the total bilirubin is ≥ 2 x ULN for the evaluating laboratory.

Veozah (fezolinetant) tablets are to be swallowed whole. Tablets should not be cut, crushed, or chewed.

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:
Veozah TABS 45MG

REFERENCES

1. Veozah (fezolinetant) [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc; December 2024.
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4. Institute for Clinical and Economic Review. January 2023. Accessed June 1, 2023. https://icer.org/wpcontent/uploads/2022/06/ICER_Menopause_FinalReport_01232023.pdf
5. Johnson KA, et al. Efficacy and safety of fezolinetant in moderate-to-severe vasomotor symptoms associated with menopause: a Phase 3 RCT [published online ahead of print, 2023 Feb 3]. J Clin

Endocrinol Metab. 2023;dgad058. doi:10.1210/clinem/dgad058
6. 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. 2023;401(10382):1091-1102. doi:10.1016/S0140- 6736(23)00085-5
7. Neal-Perry G, et al. Safety of fezolinetant for vasomotor symptoms associated with menopause: a randomized controlled trial. Obstet Gynecol. 2023;141(4):737-747. doi:10.1097/AOG.0000000000005114
8. Pinkerton JV, et al. Neurokinin receptor antagonist, fezolinetant, for treatment of menopausal vasomotor symptoms [published online ahead of print, 2023 Apr 25]. J Clin Endocrinol Metab. 2023;dgad209. doi:10.1210/clinem/dgad209

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q3 2025
REVISION- Notable revisions: Continuation of Therapy	Q3 2024
NEW CRITERIA CREATION	Q3 2023