Oscar Clinical Guideline: Veozah (fezolinetant) (PG215, Ver. 3)

Veozah (fezolinetant)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Vasomotor symptoms (VMS), including hot flashes and night sweats, are common symptoms of menopause that can significantly impact quality of life. They are caused by the decline in estrogen levels during the menopausal transition. Systemic menopausal hormone therapy (MHT) with estrogen, with or without progestin, is the most effective treatment for VMS. However, MHT may not be appropriate for all women, such as those with a history of breast cancer, cardiovascular disease, venous thromboembolism, a history of stroke, or active liver disease. In November, 2025, the FDA released that they would be beginning the process of removing several boxed warnings from MHT estrogen products - including references to risks of cardiovascular disease, breast cancer and probable dementia.

Nonhormonal treatment options for VMS include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and other medications like gabapentin, clonidine and oxybutynin. Veozah (fezolinetant) is a non-hormonal once-daily oral neurokinin-3 receptor antagonist approved for the treatment of moderate to severe VMS associated with menopause. It provides an additional nonhormonal treatment option for women who cannot or choose not to use MHT.

In December of 2024, Veozah (fezolinetant) received a boxed warning for the risk of hepatotoxicity. It is recommended to perform hepatic laboratory tests prior to initiation of treatment to evaluate for hepatic function and injury. Do not start Veozah (fezolinetant) if either aminotransferase is greater than or equal to (≥) 2 times the upper limit of normal (ULN) or if the total bilirubin is ≥ 2 times the ULN for the evaluating laboratory. It is recommended that providers perform follow-up hepatic laboratory testing monthly for the first 3 months, at 6 months, and 9 months of treatment. Those are Veozah (fezolinetant) should discontinue therapy 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). Providers should discontinue Veozah (fezolinetant) if transaminase elevations are greater than (>) 5 x ULN, or if transaminase elevations are > 3 x ULN and the total bilirubin level is > 2 x ULN.

Definitions

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Menopause" refers to the point in time 12 months after a woman's last menstrual period, marking the end of the menopausal transition.

"Perimenopause" is the menopausal transition, a span of time starting when a woman begins experiencing menstrual irregularity through 12 months after the final menstrual period.

"Postmenopause" refers to the time after menopause has occurred, starting 12 months after the final menstrual period.

"[s]" indicates state mandates may apply.

"Vasomotor symptoms (VMS)" refer to hot flashes (sensations of heat, sweating, flushing) and night sweats associated with the menopausal transition.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Postmenopausal Women with Vasomotor Symptoms (VMS)

The Plan considers Veozah (fezolinetant) medically necessary when ALL of the following criteria are met:

1. The member is a postmenopausal woman with moderate to severe vasomotor symptoms (VMS); *AND*
2. The member is unable to use, or has tried and failed an 8-week trial of BOTH of the following:[s]
    a. Hormonal pharmacologic treatments (i.e., estrogen, with progestin if uterus present), such as ONE (1) of the following (see Appendix A, Table 1):
        i. Oral estrogens - e.g., estradiol, conjugated estrogens (Cenestin, Enjuvia, Premarin), esterified estrogens (Menest); *or*
        ii. Transdermal estrogens - e.g., estradiol patch (Alora, Climara, Estraderm, VivelleDot, Minivelle); *or*
        iii. Topical Products - e.g., estradiol gel (Divigel, Elestrin, EstroGel), estradiol emulsion (Estrasorb), estradiol transdermal spray (Evamist); *or*
        iv. Oral estrogen/progestin combinations - e.g., Prempro or Premphase (conjugated estrogens/medroxyprogesterone), Activella or Mimvey (estradiol/norethindrone), Angeliq (estradiol/drospirenone), Bijuva (estradiol/progesterone); *or*
        v. Transdermal estrogen/progestin combinations - e.g., CombiPatch (estradiol/norethindrone), Climara Pro (estradiol/levonorgestrel); *or*
        vi. Duavee (conjugated estrogens, bazedoxifene); *or*
        vii. Oral estrogens/methyltestosterone combinations - e.g., Esterified estrogens/methyltestosterone (Covaryx, EEMT HS, Estratest); *or*
        viii. Progesterone only oral therapy - e.g., Prometrium (progesterone), Provera (medroxyprogesterone); *or*
        ix. Intrauterine systems - e.g., Femring (estradiol) or progesterone only intrauterine devices (e.g., levonorgestrel [Kyleena, Liletta, Mirena, Skyla); *and*
    b. Nonhormonal pharmacologic treatments, such as ONE of the following:

i. SSRIs (selective serotonin reuptake inhibitors) - e.g., paroxetine (Paxil, Brisdelle), citalopram (Celexa), escitalopram (Lexapro); *or*
ii. SNRIs (serotonin norepinephrine reuptake inhibitors) - e.g., venlafaxine (Effexor), desvenlafaxine (Pristiq); *or*
iii. Gabapentinoid (e.g., gabapentin or pregabalin); *or*
iv. Oxybutynin;
v. Clonidine; *AND*

3. The member meets ALL of the following:
    a. No evidence of cirrhosis, severe renal impairment, or end-stage renal disease; *AND*
    b. No evidence of concomitant CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine); *AND*
4. The requested medication is being used within the Plan's Quantity Limit of 1 tablet daily.

If the above prior authorization criteria are met, the requested product will be authorized for up to 6-months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Postmenopausal Women with Vasomotor Symptoms (VMS)

The Plan considers Veozah (fezolinetant) medically necessary when ALL of the following criteria are met (within the last 3 months):

1. The member continues to meet the above applicable Medical Necessity Criteria; *AND*
2. Clinically significant reduction in the frequency and/or severity of VMS from baseline, such as:
    a. Reduction in the frequency of moderate to severe hot flashes; *or*
    b. Reduction in the symptomatic severity of hot flashes; *or*
    c. Improvement in VMS-related quality of life, sleep, or other member-reported outcomes.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Experimental or Investigational / Not Medically Necessary[s]

Veozah (fezolinetant) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Use in perimenopausal women (before menopause has been reached), as efficacy and safety have not been established in this population.
- Use for treatment of mild VMS, as pivotal trials only included women with moderate to severe VMS defined as ≥7 moderate to severe hot flashes per day or ≥50 per week.

- Use for non-menopausal VMS associated with breast cancer treatment, prostate cancer treatment, polycystic ovary syndrome or other causes, as efficacy and safety for these indications are unknown.Trials assessing the efficacy of Zeovah (fezolinetant) are undergoing and not yet complete and/or published.

References

1. "The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2023 nonhormone therapy position statement of The North American Menopause Society. Menopause. 2023 Jun 1;30(6):573-590. doi: 10.1097/GME.0000000000002200. PMID: 37252752.
2. "The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022 Jul 1;29(7):767-794. doi: 10.1097/GME.0000000000002028. PMID: 35797481.
3. ACOG committee opinion no. 556: Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. Obstet Gynecol. 2013 Apr;121(4):887-890. doi: 10.1097/01.AOG.0000428645.90795.d9. PMID: 23635705.
4. ACOG Practice Bulletin No. 141: management of menopausal symptoms. Obstet Gynecol. 2014 Jan;123(1):202-216. doi: 10.1097/01.AOG.0000441353.20693.78. Erratum in: Obstet Gynecol. 2016 Jan;127(1):166. doi: 10.1097/AOG.0000000000001230. Erratum in: Obstet Gynecol. 2018 Mar;131(3):604. doi: 10.1097/AOG.0000000000002513.
5. Arinkan, S.A. and Gunacti, M. (2021), Factors influencing age at natural menopause. J. Obstet. Gynaecol. Res., 47: 913-920. https://doi.org/10.1111/jog.14614.
6. Baber RJ, Panay N, Fenton A; IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016 Apr;19(2):109-50. doi: 10.3109/13697137.2015.1129166. Epub 2016 Feb 12.
7. British Menopause Society. Non-homonal-based treatments for menopausal symptoms. November 2025. Available at: https://thebms.org.uk/wp-content/uploads/2025/11/04-BMS-ConsensusStatement-Non-hormonal-based-treatments-for-menopausal-symptoms-NOV2025-C.pdf. Accessed 22 December 2025.
8. Cano A, Nappi RE, Santoro N, et al. Fezolinetant impact on health-related quality of life for vasomotor symptoms due to the menopause: Pooled data from SKYLIGHT 1 and SKYLIGHT 2 randomised controlled trials. BJOG. 2024 Aug;131(9):1296-1305. doi: 10.1111/1471-0528.17773. Epub 2024 Feb 6.
9. Cobin RH, Goodman NF; AACE Reproductive Endocrinology Scientific Committee. American Association Of Clinical Endocrinologists And American College Of Endocrinology Position Statement On Menopause-2017 Update. Endocr Pract. 2017 Jul;23(7):869-880. doi: 10.4158/EP171828.PS. Erratum in: Endocr Pract. 2017 Dec;23 (12):1488. PMID: 28703650.
10. Drugs for Menopausal Symptoms. JAMA. 2021;325(23):2394–2395. doi:10.1001/jama.2020.15592
11. Flores VA, Pal L, Manson JE. Hormone Therapy in Menopause: Concepts, Controversies, and Approach to Treatment. Endocr Rev. 2021 Nov 16;42(6):720-752. doi: 10.1210/endrev/bnab011. PMID: 33858012.
12. 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. 2023 Jul 14;108(8):1981-1997. doi: 10.1210/clinem/dgad058.
13. Kagan R, Cano A, Nappi RE, et al. Safety of Fezolinetant for Treatment of Moderate to Severe Vasomotor Symptoms Due to Menopause: Pooled Analysis of Three Randomized Phase 3 Studies. Adv Ther. 2025 Feb;42(2):1147-1164. doi: 10.1007/s12325-024-03073-8. Epub 2024 Dec 30.

14. Khan AA, Alrob HA, Ali DS, et al. Guideline No. 422g: Menopause and Osteoporosis. J Obstet Gynaecol Can. 2022 May;44(5):527-536.e5. doi: 10.1016/j.jogc.2021.09.013.
15. Langer, R. D., Hodis, H. N., Lobo, R. A., & Allison, M. A. (2021). Hormone replacement therapy – where are we now? Climacteric, 24(1), 3–10. https://doi.org/10.1080/13697137.2020.1851183.
16. Lederman S, Ottery FD, Cano A, et al. Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (SKYLIGHT 1): a phase 3 randomised controlled study. Lancet. 2023 Apr 1;401(10382):1091-1102. doi: 10.1016/S0140-6736(23)00085-5. Epub 2023 Mar 13.
17. Melissa A. McNeil, Sarah B. Merriam. Menopause. Ann Intern Med.2021;174:ITC97-ITC112. [Epub 13 July 2021]. doi:10.7326/AITC202107200.
18. Menopause: identification and management: Evidence review G. London: National Institute for Health and Care Excellence (NICE); 2024 Nov.
19. National Institute for Health and Care Excellence (NICE). Menopause: identification and management: Evidence review G. London: National Institute for Health and Care Excellence (NICE); 2024 Nov. PMID: 39652683. Available at: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#managing-symptoms-associated-with-menopause-in-people-aged-40-or-over. Accessed 22 December 2025.
20. Neal-Perry G, Cano A, Lederman S, et al. Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial. Obstet Gynecol. 2023 Apr 1;141(4):737-747. doi: 10.1097/AOG.0000000000005114. Epub 2023 Mar 9.
21. Rees M, Abernethy K, Bachmann G, et al. The essential menopause curriculum for healthcare professionals: A European Menopause and Andropause Society (EMAS) position statement. Maturitas. 2022 Apr;158:70-77. doi: 10.1016/j.maturitas.2021.12.001. Epub 2022 Feb 1.
22. Ryom L, De Miguel R, Cotter AG, et al. Major revision version 11.0 of the European AIDS Clinical Society Guidelines 2021. HIV Med. 2022 Sep;23(8):849-858. doi: 10.1111/hiv.13268. Epub 2022 Mar 25.
23. Salvatore, S., Benini, V., Ruffolo, A. F., Degliuomini, R. S., Redaelli, A., Casiraghi, A., & Candiani, M. (2023). Current challenges in the pharmacological management of genitourinary syndrome of menopause. Expert Opinion on Pharmacotherapy, 24(1), 23–28. https://doi.org/10.1080/14656566.2022.2152326.
24. Shapiro C M M, Cano A, Nappi RE, et al. Effect of fezolinetant on sleep disturbance and impairment during treatment of vasomotor symptoms due to menopause. Maturitas. 2024 Aug;186:107999. doi: 10.1016/j.maturitas.2024.107999. Epub 2024 May 15.
25. Shea AK, Wolfman W, Fortier M, Soares CN. Guideline No. 422c: Menopause: Mood, Sleep, and Cognition. J Obstet Gynaecol Can. 2021 Nov;43(11):1316-1323.e1. doi: 10.1016/j.jogc.2021.08.009. Epub 2021 Nov 4.
26. Stuenkel CA, Davis SR, Gompel A, et AL. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015 Nov;100(11):3975-4011. doi: 10.1210/jc.2015-2236. Epub 2015 Oct 7.
27. US Preventive Services Task Force. Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2022;328(17):1740–1746. doi:10.1001/jama.2022.18625
28. Veozah (fezolinetant) [prescribing information]. Northbrook, IL: Astellas Pharma US, Inc; December 2024.
29. 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 Oct;43(10):1188-1204.e1. doi: 10.1016/j.jogc.2021.08.003. Epub 2021 Aug 11. Erratum in: J Obstet Gynaecol Can. 2022 Feb;44(2):227. doi: 10.1016/j.jogc.2021.12.005.

Appendix

Table 1: Generally Recognized Absolute and Relative Contraindications to Estrogen-based Menopausal Hormone Therapy (MHT)

Absolute contraindications (Generally recommended to Avoid Estrogen Therapy)	Relative contraindications (Caution Should be Exercised)
I. Acute cardiovascular disease II. Acute or decompensated liver disease III. History of breast cancer IV. History of cardiovascular disease (coronary artery disease or stroke) V. History of estrogen-dependent neoplasia including endometrial cancer VI. History of venous thromboembolism Hypertriglyceridemia VII. Pregnancy VIII. Protein C, protein S, or antithrombin deficiency or other known thrombophilic IX. Prolonged immobilization X. Unexplained vaginal bleeding	XI. Active gallbladder disease XII. Increased risk of cardiovascular disease* XIII. Migraine with aura XIV. Hypertriglyceridemia
There are no agreed upon guideline-defining absolute and relative contraindications. The above are based on the Endocrine Society Clinical Guideline on the Treatment of Symptoms of Menopause (2015). Provider discretion should guide therapeutic appropriateness for the individual being treated. **As of November 2025, the FDA has recommended removal of the boxed warning in reference to the increased risk of cardiovascular disease, breast cancer, and probable dementia from package labeling of hormone replacement therapy; however package inserts have not yet all been updated to reflect this change.*	

Clinical Guideline Revision / History Information

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