Oscar Clinical Guideline: Veozah (fezolinetant) (PG215, Ver. 2)

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.

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. 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

"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.

"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:
    a. Hormonal pharmacologic treatments (i.e., estrogen, with progestin if uterus present), such as ANY of the following:
        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); *and*
    b. Nonhormonal pharmacologic treatments, such as ANY 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. Gabapentin; *or*
        iv. Oxybutynin; *AND*
3. The members does NOT have cirrhosis, severe renal impairment, or end-stage renal disease; *AND*
4. The member is NOT prescribed a concomitant CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine); *AND*
5. 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.

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Postmenopausal Women with Vasomotor Symptoms (VMS)

Reauthorization for continued coverage of Veozah (fezolinetant) for up to an additional 12 months may be granted if the member has recent (within the last 3 months) clinical chart documentation indicating ALL of the following criteria:

1. The member continues to experience moderate to severe vasomotor symptoms (VMS, or hot flashes) that warrant ongoing treatment; *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; *AND*
3. The member has not developed any new contraindications to continued therapy with fezolinetant, such as:
    a. Cirrhosis; *or*
    b. Hepatotoxicity (defined as 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); *or*
    c. Severe renal impairment or end-stage renal disease; *or*
    d. Initiation of a concurrent strong or moderate CYP1A2 inhibitor for chronic use.

Experimental or Investigational / Not Medically Necessary

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.

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Clinical Guideline Revision / History Information

Original Date: 06/27/2024

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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 breast cancer XIII. Increased risk of cardiovascular disease XIV. Migraine with aura XV. 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.	