Fezolinetant (VEOZAH)
Criteria for Use
September 2024

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the *PBM INTRAnet* site for further information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive fezolinetant.

- ☐ Known cirrhosis
- ☐ Severe renal impairment (estimated glomerular filtration rate [eGFR] less than 30 ml/min/1.73m^2) ^1
- ☐ Concomitant use of CYP1A2 inhibitors (e.g., cimetidine, mexiletine, fluvoxamine)
- ☐ Baseline AST, ALT, or total bilirubin ≥ 2 times the upper limit of normal ^2

Inclusion Criteria

All of the following criteria must be met.

- ☐ Moderate to severe vasomotor symptoms (VMS) associated with menopause ^3
- ☐ Contraindication or intolerance to menopausal hormone therapy (MHT) or patient preference to avoid
- ☐ Contraindication, intolerance, or insufficient response to one nonhormonal treatment for VMS ^4

1. Patients with serum creatinine of 1.5 times the upper limit of normal or eGFR less than 60 ml/min/1.73m^2 were excluded from clinical trials.
2. Perform baseline liver function testing before initiating fezolinetant (ALT, AST, ALP, total and direct bilirubin). Perform follow-up liver function testing monthly for the first 3 months, then at 6 and 9 months after initiating fezolinetant (and if any signs or symptoms of liver injury occur). ALT=alanine aminotransferase; AST=aspartate aminotransferase; ALP=alkaline phosphatase.
3. Patients studied in clinical trials had an average of 10 to 12 moderate to severe VMS per day at baseline. Fezolinetant reduced hot flashes by about 2.5 per day compared to placebo.
4. Nonhormonal alternatives include selective serotonin reuptake inhibitors (SSRIs) (citalopram, escitalopram, paroxetine); serotonin and norepinephrine reuptake inhibitors (SNRIs) (venlafaxine, desvenlafaxine), gabapentin, and oxybutynin.

Supplemental Information

- **Menopause** is defined as spontaneous amenorrhea for at least 12 consecutive months (or at least 6 consecutive months with follicle stimulating hormone levels of 40 IU/L or greater) or bilateral oophorectomy.
- **VMS severity scale:** mild = sensation of heat without sweating; moderate = sensation of heat with sweating but able to continue activity; severe = sensation of heat with sweating, causing cessation of activity.
- **Pharmacologic Treatments for menopausal VMS:** MHT is the most effective treatment in the management of VMS. The Endocrine Society Guidelines (2015) and the North American Menopause Position Statements (Hormone Therapy 2022 and Nonhormonal Therapy 2023) recommend consideration of MHT in menopausal women younger than 60 years and within 10 years of final menstrual period. Contraindications to MHT include estrogen sensitive cancer, coronary heart disease, myocardial infarction, stroke, venous thromboembolism, and inherited thrombophilia. Alternatively, several nonhormonal treatments have been shown to have modest but significant effects on VMS (SSRIs, SNRIs, gabapentin, oxybutynin, etc.). A large placebo effect has been found in many RCTs, confounding the interpretation of the active treatment effect.
- **Reassessment of continued treatment:** Providers are advised to periodically reassess and discuss the need for continued treatment with patients, given the finite duration of VMS. Consider periodic assessment of liver function during extended treatment.
- **Hepatic transaminase elevation and hepatotoxicity:** Hepatic transaminase elevations and hepatotoxicity have occurred. Perform baseline and follow-up hepatic laboratory tests as recommended in the prescribing information. Do not initiate fezolinetant if AST, ALT, or total bilirubin is 2 times the upper limit of normal or greater. Discontinue fezolinetant if transaminase elevations are greater than 5 times upper limit of normal or if transaminase elevations are greater than 3 times upper limit of normal and the total bilirubin greater than 2 times upper limit of normal. Patients should be advised on signs and symptoms of hepatotoxicity and when to seek medical attention.

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