TOOLS FOR PRACTICE #399 | October 14, 2025

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Turn Down the Heat, Part II! Can fezolinetant improve vasomotor symptoms in menopause?

CLINICAL QUESTION

How safe and effective is fezolinetant for vasomotor symptoms?

BOTTOM LINE

At 12 weeks, more women with moderate-severe hot flashes reported feeling "much better" with fezolinetant compared to placebo (48% versus 24%). Additionally, ~60% achieved ≥50% reduction in symptoms versus 36% on placebo. Sleep also improved. Adverse events similar to placebo. Cost may limit use.

EVIDENCE

- Results statistically significant unless indicated.
- Three key industry-funded randomized controlled trials (RCTs), women with spontaneous or surgical menopause (mean age: 55).[1-5] Pooled RCT analyses included.[6-7] Focusing on fezolinetant 45mg versus placebo (334-453 patients) at 12 weeks:
- Moderate-severe vasomotor symptoms:
    - Proportion of patients reporting symptoms “much better:” 48% versus 24% (placebo),[6] number needed to treat (NNT)=5.
    - Proportion with ≥50% reduction in symptom frequency: 59% versus 36% (placebo),[1-2] NNT=5 (PEER calculation).
    - Frequency (daily): Baseline: 10-12.
        - Fezolinetant: 2-3 fewer than placebo.[1-2] Example:[1] Placebo decreased to 7/day versus 4/day (fezolinetant).

- Sleep:
    - Patients reporting "much/moderately better:" 51% versus 34% (placebo),[7] NNT=6.
    - Sleep disturbance questionnaire (range 8-40, higher=worse, baseline: 26-28):
        - 1.5-point mean improvement over placebo.[7]
        - Example:[7] Placebo decreased to 24 versus 22 (fezolinetant).
- Quality of life score. Range 1-8, higher=worse; baseline: 4:
    - 0.5-point mean improvement over placebo.[6] Clinical significance unknown.
        - Example:[6] Placebo decreased to 3.5 versus 3 (fezolinetant).
- 24-week outcomes: Similar to above.[3,5]
- Adverse Events: Four systematic reviews (5 RCTs, 3025-3302 patients). Fezolinetant 45mg:[8-11]
    - Overall or serious adverse effects: Similar to placebo (including headache, abnormal liver function tests, uterine bleeding, endometrial hyperplasia/tumors).
- Limitations: clinical relevance of multiple scale results unclear; not all patients completed questionnaires; short follow-up periods would not capture long-term harms, if any.

CONTEXT

- No RCTs versus other agents. Indirect comparisons suggest fezolinetant may be:
    - Less/similarly effective to hormone therapy.[12]
    - At least as good as non-hormonal agents (examples: SSRIs/SNRIs).[13]
- Symptom improvement: As early as 1-4 weeks.[1,2]
- Notable RCT exclusions: Blood pressure >130/80, endometrial hyperplasia, unexplained uterine bleeding, ALT or AST >1.5x upper limit of normal.[1-2]
- Monitoring: Liver enzymes monthly for 3 months, then at 6 and 9 months.[13] However, no hepatotoxicity reported in RCTs.
- Fezolinentant, cost (30-day):[13] ~$210.
    - Estrogen: $16-60; progesterone: $15-35, other non-hormonals: $15-90.

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