

November 7, 2022

Submitted electronically to publiccomments@icer.org.

Steven D. Pearson, MD, MSc, President
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, MA 02108

Re: Draft Evidence Report on Treatment for Vasomotor Symptoms Associated with Menopause

Dear Dr. Pearson:

The Society for Women's Health Research (SWHR) appreciates the opportunity to provide input to the Institute for Clinical and Economic Review (ICER) on its Draft Evidence Report assessing the comparative clinical effectiveness and value of fezolinetant for the treatment of vasomotor symptoms (VMS) associated with menopause. Given that approximately 1.3 million women transition into menopause each year, at an average age of 51 in the United States¹ and that VMS, or hot flashes and night sweats, can affect quality of life, SWHR recognizes the need for additional treatments and interventions to assist women during this natural life stage.

SWHR, a more than 30-year-old national nonprofit organization based in Washington, D.C., is widely recognized as a thought leader in promoting research on biological sex differences in disease and eliminating imbalances in care for women through our science, policy, and education work. This includes work in menopause. Specifically, SWHR has developed tools and resources to promote the health and wellness of women transitioning to menopause, including the release of a menopause toolkit in 2022, and continues to encourage thought leaders and policymakers to take a lifespan approach when it comes to the health of women—considering how life stages such as puberty, pregnancy, and menopause could affect other aspects of a woman's health.

In its [comments](#) on the Draft Scoping Document, SWHR called attention to the burden of VMS symptoms in menopausal women—including that the majority of women (73%) are not treating their menopause symptoms;² women of different races and ethnicities have different experiences with VMS, with African American women reporting the greatest duration³ and highest incidence of hot flashes;⁴ and that VMS have been strongly associated with reduced health-related quality

¹ Takahashi TA, Johnson KM. Menopause. *Med Clin North Am*. 2015 May;99(3):521–534.

² State of Menopause Survey. Bonafide. <https://hellobonafide.com/pages/state-of-menopause> Accessed 16 June 2022.

³ Avis NE, Crawford SL, Greendale G, et al. Duration of Menopausal Vasomotor Symptoms Over the Menopause Transition. *JAMA Intern Med*. 2015 Apr;175(4):531-539

⁴ Green R, Santoro N. Menopausal Symptoms and Ethnicity: The Study of Women's Health Across the Nation. *Womens Health (Lond)*. 2009 Mar;5(2):127-133

of life, affecting outcomes including sleep, mood, and cognitive function—and commented on the outcomes of interest, scope of comparative value analyses, and evaluation of direct and indirect costs.

Through this particular comment opportunity, SWHR will share a few key points for ICER’s consideration. At the heart of these comments are that access and affordability, the ability to engage in shared decision-making, and scientific innovation should be not just acknowledged, but valued and reflected within ICER’s final conclusions.

Key Considerations in Response to the ICER Draft Evidence Report on Fezolinetant

SWHR raises the following points in response to the Draft Evidence Report:

Choice and Access. Currently, women have extremely limited pharmacologic treatment options for VMS. Those options are even more limited when it comes to non-hormonal therapies. Within its Draft Evidence Report, ICER acknowledges that there are “women who cannot or do not wish to take menopausal hormone therapy (MHT).”

It is essential that women be provided with as much choice as possible when it comes to establishing a treatment plan, especially when considering that menopause is a highly individualized life stage, with no one woman’s symptoms and symptom severity being the same. ICER’s *Patient and Caregiver Perspectives* section within the Draft Evidence Report reiterates this point, citing clinicians’ comments that “depending on the individual patient characteristics as well as the type (e.g., route of administration, dose, combination hormones) and duration of MHT, for some women the risks of MHT may outweigh the benefits.” For example, as shared in an article from *Human Reproduction Update*, “Postmenopausal women are commonly treated with hormone replacement therapy (HRT) to treat climacteric symptoms and prevent bone loss; however, HRT may reactivate endometriosis and stimulate malignant transformation in women with a history of endometriosis.”⁵ Thus, safe and effective non-hormonal treatment options are an important need.”

Fezolinetant is a first-in-class, once daily, non-hormonal treatment option for menopause-related VMS. As such, fezolinetant can add to the scope of treatment options available for women seeking to treat menopause-related VMS. This consideration will be critical for both ICER and the U.S. Food and Drug Administration (FDA) as they make future decisions related to fezolinetant. Patient values—including individualized treatment options based on a woman’s unique circumstances and the ability to contribute to shared decision-making between women and their health care providers—should be acknowledged and valued.

Clinical Analysis. Throughout the Draft Evidence Report, ICER recognizes the uncertainty within its analysis. For example, with respect to comparability of outcomes, ICER notes, “While

⁵ Gemmell LC, Webster KE, Kirtley S, Vincent K, Zondervan KT, Becker CM. The management of menopause in women with a history of endometriosis: a systematic review. *Hum Reprod Update*. 2017 Jul 1;23(4):481-500. doi: 10.1093/humupd/dmx011. PMID: 28498913; PMCID: PMC5850813.

the population characteristics were largely comparable across trials, the definitions of our primary outcomes of VMS frequency and severity differed across trials, making cross-trial comparisons more difficult.” Further, ICER shares that there have not been any head-to-head trials with active comparators and that fezolinetant was not compared to selective serotonin reuptake inhibitors (SSRIs)/serotonin–norepinephrine reuptake inhibitors (SNRIs), gabapentin, or pregabalin.

SWHR is concerned that these acknowledgements, while helpful for those reading the report, create uncertainty about the conclusions presented by ICER and leave much room for interpretation for creating coverage and access decisions.

Allowing Room for Scientific Innovation. Fezolinetant, as a first-in-class, non-hormonal treatment option for menopause-related VMS, represents an important step forward in scientific innovation for menopausal women. Within the Draft Evidence Report for reviewing cost-effectiveness, ICER notes that there is “considerable uncertainty about efficacy and long-term safety” of fezolinetant in the treatment of VMS, though it “appears promising.”

Science and evidence development is ever-evolving. Fezolinetant is not a systemic hormone treatment; it is a new and unique treatment mechanism that has the potential to evolve and improve over time and, notably, can provide new and beneficial treatment options for menopausal women. As with all scientific innovation, we must look toward the future and the promise of new scientific discoveries. The current Draft Evidence Report does not account for this evolution or the possibility for fezolinetant to be used in combination with other menopause treatments.

Finally, SWHR calls attention to a point made in a recent blog post by the [Patient Access & Affordability Project](#) on cost effectiveness:

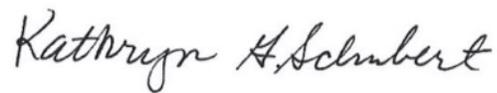
“In the draft report, ICER assesses the clinical effectiveness of different hormone treatments – as well as antidepressants and neurological pain treatments – all of which are available in generic forms. While such options expand choices for patients and clinicians in shared decision making, ICER cost-effectiveness analysis only compares fezolinetant to generic hormone treatments. With that approach, ICER sends clear signals to insurance companies and other payers that, regardless of clinical effectiveness or shared decision making to develop the best care plan for an individual patient, generic medicines, as the cheaper option (for the insurance company), should be given priority in any benefit structure through patient cost-sharing and prior authorization barriers.”

SWHR is concerned that the Draft Evidence Report presented by ICER discounts the potential benefit of fezolinetant by citing the lack of long-term data available and remarks that the cost-effectiveness of the drug “will depend upon its price and whether it is considered an alternative treatment to MHT for all women or whether it will primarily be used by women who cannot or will not take MHT.”

SWHR encourages the Institute to keep in mind that additional choice is a valuable outcome for a significant portion of this population. Further, fezolinetant has the potential to meet the direct needs of women who are not going to take other treatments; if other treatments on the market were sufficient to meet women's needs, the need for fezolinetant would be moot.

Thank you for your consideration of the above comments. SWHR looks forward to engaging with ICER during this assessment and on other future topics affecting women's health. If you have questions or need any additional information that would be helpful to inform ICER's value assessment, please contact me at kathryn@swhr.org or Lindsey Horan, Chief Advocacy Officer, at lindsey@swhr.org.

Sincerely,

A handwritten signature in cursive script that reads "Kathryn G. Schubert".

Kathryn G. Schubert, MPP, CAE
President and CEO
Society for Women's Health Research