Society for Women's Health Research

June 21, 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 Background and Scope: Fezolinetant for Moderate to Severe 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 Scoping Document outlining how it plans to conduct the clinical effectiveness and value assessment of fezolinetant for the vasomotor symptoms (VMS) associated with menopause.

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 science, policy, and education.

Through this comment opportunity, SWHR will share a few key points for ICER's consideration. Chiefly, given that menopause exclusively affects women, it will be vital that this assessment take a female-centered approach that reflects this life stage's unique patient experience, including indirect burdens, availability of current and necessary treatment options, and quality of life.

The Burden of VMS Symptoms in Menopausal Women

Approximately 1.3 million women transition into menopause each year, at an average age of 51 in the United States.[1] Each woman's menopause experience is different. Some are likely to experience the transition to menopause with few symptoms, while others may have a variety of symptoms at differencing levels of severity and that last for different periods of time.

Among the most common symptoms associated with menopause is VMS, or hot flashes and night sweats, which are "episodes of profuse heat accompanied by sweating and flushing, experienced predominately around the head, neck, chest, and upper back."[2]

[1] Takahashi TA, Johnson KM. Menopause. Med Clin North Am. 2015 May;99(3):521–534.
[2] Thurston RC, Joffe H. Vasomotor symptoms and menopause: findings from the Study of Women's Health across the Nation. *Obstet Gynecol Clin North Am*. 2011;38(3):489-501. doi:10.1016/j.ogc.2011.05.006

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- **The majority of women (73%) are not treating their menopause symptoms**.[3] Despite the fact that VMS occur during the menopause transition for up to 80% of women in the United States, most are not treating those symptoms.

- **Women of different races and ethnicities may have different experiences with VMS.** The Study of Women's Health Across the Nation (SWAN) reported variations in how long VMS usually last across populations.[4] Time spans ranged from 4.8 years among Japanese women to 10.1 years for African American women. African American women also often report the highest incidence of hot flashes.[5] Research also indicates that Native American women may experience the worst perimenopausal hot flashes of all.

- **There are important quality of life considerations for women experiencing VMS**. Based on SWAN analyses, VMS have been strongly associated with reduced health-related quality-of-life, affecting outcomes including sleep, mood, and cognitive function, and the association was strongest in those with more frequent VMS. Notably, the association did not apply to menopause itself.

Key Considerations in Response to the Fezolinetant Assessment Draft Scoping Document

Menopause is a life stage that exclusively affects women—and one that can have implications for a woman's overall quality of life. Further, it is a highly individualized process; no one woman's symptoms and symptom severity are the same.

Currently, women have extremely limited treatment options for VMS. Those options are even more limited when it comes to non-hormonal therapies. Therefore, it is essential that women be provided with as much choice as possible when it comes to establishing a treatment plan. Given that fezolinetant would be a first-in-class, non-hormonal treatment option for menopause-related VMS, as ICER conducts this assessment, SWHR would encourage the Institute to keep in mind that additional choice alone could be a valuable outcome for a significant portion of this population.

Additionally, SWHR would raise the following points in response to items included in the Draft Scoping Document:

- **Outcomes**. Within the outcomes of interest listed in the Draft Scoping Document are "Other menopausal symptoms," including vaginal symptoms, urinary tract symptoms, sexual function, and "Other patient-reported outcomes," including mood changes. While SWHR appreciates that ICER is thinking about these symptoms—as they are all relevant outcomes in a woman's menopause journey—it has not been suggested that fezolinetant could be used to treat any of these symptoms. Fezolinetant is only being investigated for the treatment of moderate to severe VMS associated with menopause and its long-term safety, as reiterated early in the Draft Scoping Document. Measuring the drug's value against symptoms on

[3] . State of Menopause Survey. Bonafide. https://hellobonafide.com/pages/state-of-menopause Accessed 16 June 2022.

[4] . 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.

[5] 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

which it does not claim to work could skew the assessment of the drug and take attention away from the drug's intended purpose.

- **Scope of Comparative Value Analyses**. SWHR is glad that key economic model inputs will include clinical probabilities, quality of life values, and health care costs along with productivity impacts and indirect costs, data permitting.

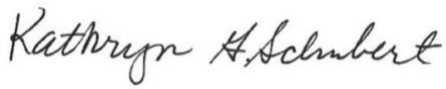
  However, SWHR would note that ICER includes, among the health outcomes against which it is evaluating interventions, quality-adjusted life years (QALYs) and life-years gained. SWHR would again remind ICER that menopause itself is a life stage, not a life-threatening disease or condition, and that fezolinetant is not meant to, nor does it claim to, add years to one's life; its goal is to reduce menopause-related VMS. While research has been conducted into menopause's effect on life expectancy (research shows that age-adjusted mortality is reduced 2% with each year of age at menopause[6]), that research shows life expectancy is related to the menopause stage and not to its symptoms.

- **Direct and Indirect Costs**. SWHR appreciates that ICER will aim to evaluate productivity impacts and other indirect costs of VMS. A 2015 study found that untreated VMS are associated with higher health care utilization, work loss, and cost burden.[7] With respect to productivity, one research study looking at presenteeism (attending work while sick) among peri and postmenopausal women revealed that among women experiencing VMS, women with severe and moderate symptoms had presenteeism rates of 24.28% and 14.3% versus 4.33% in women with mild symptoms. While VMS are not life-threatening, they are disruptive across multiple areas of a woman's life. Considering the patient experience and overall quality of life will be of the utmost importance.

Thank you for your consideration of the above comments. SWHR looks forward to engaging with ICER during this assessment and on future other 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,



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[6] Ossewaarde ME, Bots ML, Verbeek AL, Peeters PH, van der Graaf Y, Grobbee DE, van der Schouw YT. Age at menopause, cause-specific mortality and total life expectancy. Epidemiology. 2005 Jul;16(4):556-62. doi: 10.1097/01.ede.0000165392.35273.d4. PMID: 15951675.

[7] Sarrel P, Portman D, Lefebvre P, Lafeuille MH, Grittner AM, Fortier J, Gravel J, Duh MS, Aupperle PM. Incremental direct and indirect costs of untreated vasomotor symptoms. Menopause. 2015 Mar;22(3):260-6. doi: 10.1097/GME.0000000000000320. PMID: 25714236.