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May 8, 2018

Submitted electronically to: publiccomments@icer-review.org

Steven D. Pearson, MD, MSc, President
Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

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 a range of chronic, debilitating, painful conditions disproportionately or exclusively affecting women.

SWHR, a nonprofit organization based in Washington, DC, is widely recognized as a thought leader in promoting research on biological differences in disease and eliminating imbalances in care for women through science, policy, and education.

SWHR appreciated the opportunity to submit an open input letter on migraine to ICER on November 30, 2017, and continues to closely follow the methodology ICER is employing to assess the effectiveness and value of calcitonin gene-related peptide (CGRP) inhibitors, the new class of preventive therapies for episodic and chronic migraine.

As we stated in our previous letter, because women are disproportionately affected by migraine, any value assessment of new therapies for migraine, including ICER's, must take into account sex and gender differences as well as the unique patient experience, disease burden, and impact to society.

Current preventive treatment options are suboptimal for many patients, and there has been no real innovation in the past two decades in migraine prevention. No preventive drug class currently available has been designed to specifically prevent migraine. New treatment options are long overdue.

The Burden of Migraine on Women

Migraine is one example of a chronic, debilitating, painful condition that affects women differently than men.¹ Migraine is three times more common in women than men, and the pathophysiology, presentation, and management of the disease is different in women and men. Migraine ranks as the second leading cause of global burden of disability, making it a serious public health issue with social and economic consequences. SWHR urges ICER to consider the burden of migraine on women as it prepares to finalize its model and valuation of CGRP inhibitors:

- 1) **Peak prevalence for women with migraine occurs during one of the most active stages of their lives.** The peak occurs between 30 and 39 years of age, a time when many women are at the height of their careers and balancing work, family, and social obligations.²
- 2) **Women experience migraine differently than men.** Women are more likely than men to experience longer and more intense migraines, report more migraine-associated symptoms such as nausea and visual aura, and have higher levels of headache-related disability.^{3,4}
- 3) **Women with migraine have more comorbid conditions than men with migraine, with an average of 11 and 5 comorbid conditions, respectively.**⁵ In addition, certain comorbid conditions are more prevalent in women and others more prevalent in men. For example, research shows women are more likely to have comorbid psychiatric conditions such as depression and anxiety, whereas men are more likely to have comorbid somatic symptoms such as obesity and blurred vision.^{6,7} Restless leg syndrome is comorbid with migraine and is approximately twice as prevalent in women.^{8,9,10,11}
- 4) **Female sex hormones play a large role in the development of migraine and are likely contributors to observed differences between women and men in this disease.** Nearly two-thirds of all people with migraine have hormonal triggers, and these factors are part of what makes migraine more common in women.^{12,13,14}
- 5) **Women account for 80 percent of direct and indirect costs associated with migraine in the United States, which are upwards of \$78 billion each year.**^{15,16,17} Migraine can be disabling and costly for patients, employers, and society as a whole.¹⁸ Most of these costs are indirect, with lost productivity (presenteeism and absenteeism) playing a large role.¹⁹
- 6) **Seeking and receiving care for migraine varies by gender.** Women are more likely than men to receive a migraine diagnosis, but less likely than men to receive appropriate treatment.^{20,21}

Key Issues and Recommendations on ICER Migraine Draft Evidence Report

SWHR has the following concerns about the methodology ICER employed to analyze the potential budget impact of CGRP inhibitors.

- 1) **Because migraine is more common in women and affects women differently than men, data should be stratified by sex.** In previous reports, ICER has shown a willingness to stratify the cost-effectiveness results by subpopulation. Given the ways that migraine and migraine treatments affect women differently than men (as described above), we strongly encourage ICER to stratify the final results of its cost-effectiveness analysis (CEA) by sex.
- 2) **Migraine quality of life data used in ICER's analysis may not adequately capture the disproportionate effect this disease has on women.** The Headache Impact Test 6 (HIT-6) and Migraine Disability Assessment Test (MIDAS) are two of the most commonly used quality of life questionnaires for migraine, but they are not without flaws.^{22,23,24} For example, the HIT-6 and MIDAS ask about the quality of life from the past four weeks and three months, respectively, which may not appropriately capture lost productivity and missed work that occurred *prior to* these windows of time. Importantly, these instruments only evaluate the effects on the person with migraine and only *during* attacks, meaning the burden of migraine on the family is not adequately captured, nor is the burden of disease *in between* attacks. Individuals with migraine may have lost productivity and/or miss family or social obligations in between migraine attacks because of prodromal symptoms or anxiety about the uncertainty of the next attack.

Limitations in the current quality of life measures for migraine are important for ICER to recognize and account for in its analysis given the significant effects migraine has on physical, emotional, and social aspects of daily life for women.

- 3) **CEA based on quality-adjusted life years (QALY) may not adequately capture the differences in preferences and clinical characteristics of women with migraine.** While we recognize that ICER has committed to using CEA as the basis for its value framework, we would strongly encourage ICER to develop novel approaches to assessing value. Many stakeholders have acknowledged the limitations of QALY-based CEA, particularly in accounting for heterogeneity.^{25,26} Women with migraine vary in age, employment, caregiver status and socioeconomic status. A simple cost-effectiveness ratio cannot capture those differences.
- 4) **Flawed assumptions used by ICER regarding the price of migraine treatments may have significant implications for a woman's access to care.** ICER's estimation of the budget impact of migraine treatments (and therefore the number of women and men who can access treatment) is based on the wholesale acquisition cost (WAC) of a drug. Not taking the rebates and discounts frequently negotiated between payers and pharmaceutical manufacturers into account may lead to inaccurate estimations of the budget impact of these

treatments. Similarly, the CEA appears to be based on a placeholder WAC estimate, which is likely to result in incorrect estimates for the value of these treatments.

If payers rely on flawed estimates, it could have significant implications for women's access to important treatments for migraine. We encourage ICER to consider accounting for likely rebates and discounts in its estimates.

5) **ICER's analysis should accurately reflect the direct health care costs of migraine.**


Emergency department visits, hospitalization, and therapeutics are the main direct cost drivers of migraine. An underestimation of their combined costs will result in an incorrect valuation of CGRP treatments. We urge ICER to conduct robust sensitivity analysis around medical resource use and direct cost estimates using published sources.

Migraine prevention with appropriate treatments has the potential to improve health quality significantly and thus reduce the burden of migraine on individuals, families, and employers. We urge ICER to refine its methodology so model estimates can fully reflect improvements in a woman's quality of life and work productivity as a result of CGRP inhibitor intervention. Recognizing the full potential of this new class of preventive treatment options for migraine sends a strong signal to payers to scrutinize patient access to innovations that may correct suboptimal care for many women.

Thank you for considering the above input as ICER finalizes its evidence report of therapies for migraine. We look forward to serving as a resource on this and other topics affecting women's health.

If you have questions or if we can provide further information to inform ICER's value assessment, please contact Sarah Wells Kocsis, Vice President of Public Policy, at 202.496.5003 or swellskocsis@swhr.org.

Sincerely,



Amy Miller, PhD
President and Chief Executive Officer
Society for Women's Health Research

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- ²⁶ PIPC White Paper: Uses and Misuses of the QALY-Ethical Issues and Alternative Measures of Value. June 21, 2017. <http://www.pipcpatients.org/resources/white-paper-uses-and-misuses-of-the-qaly-ethical-issues-and-alternative-measures-of-value>