

April 12, 2019

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

Dear Dr. Pearson:

Multiple sclerosis (MS) is an unpredictable and frequently disabling disease of the central nervous system. It disrupts the flow of information within the brain and between the brain and body. The most common disease course is relapsing remitting MS (RRMS), which is characterized by attacks of new or increasing neurological symptoms followed by periods of recovery. Secondary progressive MS (SPMS), which often follows RRMS, results in progressively worsening neurological function and disability and has very limited treatment options available to combat this debilitating disease.<sup>1</sup>

The Institute for Clinical and Economic Review (ICER) recently released its draft evidence report for a treatment specifically for SPMS. We strongly agree with the National Multiple Sclerosis Society that ICER should discontinue the current review for siponimod due to the FDA approval for siponimod and the subsequent approval for cladribine for “relapsing forms of MS to include relapsing-remitting and active secondary progressive MS,” which means that ICER’s scope of the report is no longer sufficient. Additionally, the draft report, which was conducted at too early a point to have sufficient evidence on the treatment, also suffers from two other key shortcomings: the assessment does not consider patient and caregiver preferences and relies on outdated studies and data, calling ICER’s findings into further question.

### **ICER Data Suggests there are Health States Worse Than Death**

ICER’s model includes data from a study that uses “negative utilities” *which implies ICER is assuming there are health states worse than death*. It is widely accepted that the logic of having negative utilities for any health state would lead to the contradictory goal of the premature death of a patient resulting in both health gain and being considered a cost-effective intervention. The use of these utilities shows a callous disregard for patients and an instinct to prioritize cost above all else, even with patient lives at stake. The use of such utilities, while failing to have comprehensive conversations with patients and caregivers about their preferences and what matters most to them in treatment, would skew how decision-makers value treatments and harm patient access to care.

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<sup>1</sup> National MS Society. What is MS? Available at: <https://www.nationalmssociety.org/What-is-MS>

## **ICER's Assessment of MS Treatments is Premature**

In what is becoming a concerning pattern for ICER, this study assessing the value of siponimod was conducted far too early and consequently is based on insufficient and limited data. There are no studies comparing siponimod to currently-available MS disease-modifying therapies (DMTs) or showing long-term outcomes. Due to this limited evidence, the study focuses on a small subset of patient outcomes, completely disregarding patient preference and outcomes that matter to patients. The Consortium of Multiple Sclerosis Centers cites this as a main concern in their comment letter saying, "The decision to focus the review on siponimod appears biased and premature."

## **The Study Fails to Capture Patient and Caregiver Preference**

ICER's assessment fails to appropriately capture MS patient preferences, ignoring the voice and needs of those who are most directly impacted by this disabling disease. Instead of attempting to remedy this gap through patient engagement, ICER's strict timeline and inflexible methods for collecting stakeholder input place additional barriers in front of patient advocates. In their comment letter to ICER, the MS Coalition urged "ICER to consider ways to make the comment periods friendlier to patients by offering companion draft reports at an appropriate health literacy level for the general MS population." Failing to do so means important outcomes that matter to patients and their familiars will continue to be ignored. The MS Coalition focuses on this in their comment letter to ICER offering to partner with them on patient engagement endeavors and saying "it is critical that the review reflect the real life experiences, perspectives, hopes and concerns of people living with MS."

## **The Study Relies on Outdated and Faulty Data**

In evaluating mortality rates for Expanded Disability Status Scale (EDSS) stages, ICER selected a study from 1997<sup>2</sup> over a similar study published in 2018.<sup>3</sup> Whereas the sensitivity analysis of the economic evaluation uses the more recent and more accurate source mortality data, the model ICER uses to develop their value-based price recommendation was based on data from the 1997 study. Similarly, ICER chose to utilize data on health state utility published in a 2007 study rather than a comparable study published in 2016 because they "have been cited extensively in previous economic models." The choice of an older source because it has been cited more extensively indicates strong selection bias. It is obvious that a study published 12

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<sup>2</sup> Pokorski RJ. Long-term survival experience of patients with multiple sclerosis. JOURNAL OF INSURANCE MEDICINE-NEW YORK-. 1997 Jan;29:101-6.

<sup>3</sup> Harding K, Anderson V, Williams O, Willis M, Butterworth S, Tallantyre E, Joseph F, Wardle M, Pickersgill T, Robertson N. A contemporary study of mortality in the multiple sclerosis population of south east Wales. Multiple sclerosis and related disorders. 2018 Oct 1;25:186-91.

years ago would be more frequently cited than one from 2 years ago. Equally obvious is that fact that more recent publications are likely to have more relevant data.

### **Conclusion**

ICER has once again missed the mark by showing callous disregard for patients. Instead of working to engage with MS patients and taking their preferences and needs into consideration in evaluating a treatment designed for MS patients, ICER instead has chosen to rely on dated studies and mechanisms that are widely considered flawed. We encourage ICER to take a hard look at the tools and timing of its reviews, and prioritize accurate data and patient engagement over speed of reviews. The National Multiple Sclerosis Society's assertion that a review at this time is inappropriate based on the new FDA approvals is a clear example of the risk inherent in ICER's rush to judgment on value. We especially and strongly oppose the use of negative utilities that would suggest patients with MS experience a state worse than death. We urge ICER to heed the Society's call to discontinue the current review.

Sincerely,



Tony Coelho  
Chairman, Partnership to Improve Patient Care