September 25, 2017

Steven D. Pearson, MD, MSc, FRCP
President, Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

Dear Dr. Pearson,

We, members of the rare disease community, including patients with melanoma, rare liver diseases, liver-mediated diseases, and liver cancers, appreciate the opportunity to comment on the proposed adaptation of the ICER "Value Framework Assessment for Treatments That Represent a Potential Major Advance for Serious Ultra-Rare Conditions".

We are highly concerned that the premise for this exercise is as evidenced in the quote by Hughes in the conclusion, "whether . . . funding should support the provision of ultra-orphan drugs" and further " that ultra-orphan drugs are reimbursed at all" to call into question the appropriateness of developing and paying for the treatments for patients with rare conditions. For any to have confidence in any value framework developed the essential dignity of patients with rare diseases and right to a chance for optimal health equal to patients with other diseases must be affirmed. Resource allocations for health are choices, they are neither fixed nor finite, nor should they be viewed as zero sum games pitting people against each other.

Ultra-rare is an arbitrary category designation

ICER's first proposal establishes a novel category of disease: the "ultra-rare" diseases. This category is arbitrary and undermines the Orphan Drug Act of 1983 which has proven to be a successful driver of innovative, life-changing and life-saving treatments for patients in the United States. Also, under ICER's proposed amendment, patients who have a disease that affects between 10,000 and 200,000 individuals will be effectively lumped into the "common diseases" category, and the complexities of clinical trial recruitment, study design, evidence generation, and relevant elements to value calculation involving rare diseases that fall in that category will be essentially ignored.

The ICER proposed amendments do not demonstrate the practical differences between either the R&D challenges or the value of a treatment for 9,000 patients and 11, 000 patients or 21, 000 patients. The basis for the criterion of "little chance of future expansion of indication or population that would extend the size of the treated population above 20,000 individuals is unclear. Many factors, not the least

of which are scientific discovery accelerating in a disease state once a treatment is available, may expand use. Also, major gain is a vague term.

Use of QALYs are methodologically undersound and misrepresents value of interventions for people with disabilities and chronic diseases

ICER proposals to use QALYs make any determinations out of concordance with federal policy since by law "the Secretary [for Health and Human Services] shall not utilize such an adjusted life year (or similar measure) as a threshold to determine coverage, reimbursement, or incentive programs" in the Medicare Program.

As so well articulated in the Partnership to Improve Patient Care's white paper, "Measuring Value in Medicine: Uses and Misuses of the QALY", the disconnect in using an academic tool to influence real-life policy based on a presumed ability to quantify the quality of individual patients' lives can be seen in how QALYs are measured and calculated. Many individuals included in population-based surveys can only imagine their response to theoretical scenarios and may be unable to realistically answer how much they value their lives in a particular state of health or what they are willing to trade to treat a hypothetical health condition or symptom.

The seminal Second National Panel on Cost Effectiveness notes that the "quality and usefulness of QALYs depends on the quality and validity of the utility scores used to calculate them" (Neumann, Sanders, Russell, Siegel, & Ganiats, 2017). The methodological difficulty in measuring patient preferences becomes clear when examining the sheer number of survey instruments and methods to measure QALYs. There is no one, single accepted way to determine how to best quantify the value of a particular health state or intervention (Gafni, 1994; Ryan & Farrar, 2000).

The way in which conventional QALYs assign value to health gains from an intervention prioritizes care to individuals with a higher baseline health status, which may result in individuals with disabilities or chronic conditions being disadvantaged.

Perhaps the most concerning of all, in the eyes of a patient advocacy organization, is ICER's plan to not vote on ultra-rare treatments that exceed $175,000 cost per QALY threshold. Preemptively declaring a pricing cap without debate means that ICER will assess treatments without input from patients or caregivers. Eliminating the patient and caregiver narratives from an evaluation of treatment value takes away an opportunity for patients and caregivers to advocate for themselves and their own health. It is imperative that, in assessing the value of any treatment, especially for rare diseases, the patient and caregiver experience be heard.

Proposals would discourage innovation for patients with rare diseases

Discounting the very real practical challenges of clinical research and development in all rare diseases and sending categorical price caps for consideration will greatly reduce investment in therapies for rare diseases, a landscape that only has 625 FDA approved orphan drug approved treatments for 7,000 conditions. Adoption of these proposals could have a profound negative impact on patients with both so-called "ultra-rare" and rare conditions such as, autoimmune hepatitis, primary sclerosing cholangitis primary biliary cholangitis (PBC) and fibrolamellar cancer, rare hepato-biliary diseases which require more, not fewer, incentives for research as they have no cures.

In conclusion, we ask that ICER assess what it means to be the patient or the caregiver of a loved one with a rare disease. Facing barriers to diagnosis, support, research, treatment, and coverage for a variety of interventions and services, they do not need additional disadvantages. Rare disease patients, whether their disease affects 200 or 200,000, deserve equal and fair access to a market that promotes innovation. Patients deserve the chance to advocate for themselves, and caregivers deserve their narratives to be heard. We strongly urge ICER to reevaluate the proposed amendments to the Value Framework Assessment of Treatments for Ultra-Rare Conditions.

Sincerely,

Global Liver Institute

Fibrolamellar Cancer Foundation

Melanoma Research Foundation

Patients Rising