September 6, 2019

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

RE: Proposed Adaptations to the ICER Value Assessment Framework: Value Assessment Methods for "Single or Short-Term Transformative Therapies" (SSTs)

Submitted electronically: publiccomments@icer-review.org

Dear Dr. Pearson,

Haystack Project and the Rare Cancer Policy Coalition (RCPC) appreciates the opportunity to respond to the Institute for Clinical and Economic Review's (ICER's) proposed value framework adaptations for single or short-term transformative therapies (SSTs).

Haystack Project is a non-profit organization enabling rare and ultra-rare disease patient advocacy organizations to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for all Americans.

The Rare Cancer Policy Coalition (RCPC) is a Haystack Project initiative that brings together rare cancer patient organizations. RCPC gives participants a platform for focusing specifically on systemic reimbursement barriers and emerging landscape changes that impact new product development and treatment access for rare cancer patients. It is the only coalition developed specifically to focus attention on reimbursement, access and value issues across the rare cancer community. Working within the Haystack Project enables RCPC participants and rare and ultra-rare patient advocates to leverage synergies and common goals to optimize advocacy in disease states where unmet need is high and treatment inadequacies can be catastrophic.

We recently provided feedback on ICER's updated value framework, emphasizing many of the challenges patients with rare and ultra-rare diseases face within the context of the ICER value framework and its reliance on population-level indices of quality and value. We appreciate ICER's recognition that traditional cost-effectiveness methodologies do not capture the potential value of emerging therapies that provide enhanced patient outcomes (and/or potential cures) extending well beyond the treatment period.

BACKGROUND ON RARE AND ULTRA-RARE CONDITIONS

Over 35 years ago, Congress recognized that commercial realities associated with research and development discouraged innovation in treating serious medical conditions affecting small populations. Countless lives have been improved, or saved, by new therapies stimulated by the set of statutory incentives for orphan drugs. Although millions of Americans affected by a rare disease are still waiting and hoping for treatment or a cure, there are many for whom treatments that are already available or in the pipeline are out of reach due to the realities of current reimbursement structures.

- Of the approximately 7,000 rare diseases identified to date, 95% have no FDA-approved treatment option;
- 80% of rare diseases are genetic in origin, and present throughout a person's life, even if symptoms are not immediately apparent;
- Approximately 50% of the people affected by rare diseases are children;
- 30% of children affected by a rare disease will not live to see their 5th birthday; and
- Approximately half of identified rare diseases do not have a disease-specific advocacy network or organization supporting research and development.

Foundational assumptions and policy goals driving ICER's framework and proposed adaptations disproportionately disadvantage transformative therapies for rare and ultra-rare disorders

Innovation in how we understand and address disease mechanisms is currently advancing at a previously unthinkable pace. ICER'S proposed framework adaptation seeks to respond to the emergence of targeted cancer treatments, gene therapy and regenerative medicine, and immunologic approaches to rare, serious, and life-threatening conditions that give renewed hope to patients and their caregivers.

We remain concerned that, even with the proposed adaptations, ICER's framework of "willingness-to-pay" thresholds and panel votes to categorize treatments as low, medium or high value in monetary terms is in diametric opposition to the US health care ecosystem's efforts toward a patient-centered perspective on "value." The US health care system is not driven by vertical equity; it is based on the concept that an insured individual is covered for medically-necessary treatments whether their disease is common and its treatment cost low, or their disease is rare with one, costly, available treatment.

Similarly, ICER's reliance on a payer perspective and its operational paradigm of "risk" as a mathematically-derived sum that can be allocated between payers and manufacturers relegates patients to bystander status. It also discounts the ability of commercial and public entities to mitigate and respond to risk over time with price changes (for manufacturers) and marginal premium increases, formulary strategies, and other tools (payers).

Patients unable to access potentially life-saving treatments, or parents and caregivers struggling to ensure that their child receives the only therapy with potential to halt disease progression, bear the true consequences of risk allocation. We urge ICER to ensure that its concerns about

emerging treatments unduly burdening the health care system be resolved in a manner consistent with US healthcare policy, i.e., that patients insured by public or private payers are entitled to the treatment they need regardless of whether their condition is common and treatment costs low, or their disease is extremely rare and treatment costs are very high.

The proposed framework adaptations will not sufficiently address the unique challenges of valuing transformative treatments for extremely rare diseases.

Haystack Project supports efforts to expand equitable access to quality health care. Unfortunately, ICER's efforts to date suggest that, even with its proposed framework adaptions for transformative therapies and ultra-rare disorders, ICER evaluations of emerging ultra-rare disease treatments will likely function only to impede access and inject sufficient uncertainty to chill future innovation.

We reiterate our recommendation that ICER approach review of new treatments for rare and ultra-rare diseases, including those that are transformative or potentially curative, with cautious consideration of both the inherent uncertainties in quantifying "value" of these treatments within a more general population health paradigm and the potential that the risk associated with these uncertainties will fall on rare patients denied access.

A recent example is ICER's review of Spinraza and Zolgensma for Spinal Muscular Atrophy (SMA), which yielded the dire statement that "[t]he US health care system cannot sustain paying prices far above traditional cost-effectiveness levels for the growing tide of treatments for ultra-rare disorders." It appears, from ICER's SMA example in its technical brief, that the framework adaptations proposed would have little, if any impact on review of high-cost transformative treatments for ultra-rare disorders. We see this SMA example as providing a clear barometer on the threshold issue of whether or not ICER's adaptations may be a sufficient accommodation for curative or transformative ultra-rare disease treatments because:

- SMA is a catastrophic disorder with some subtypes sufficiently severe to make it unlikely that a baby will survive to age two.
- ICER's New England CEPAC acknowledged "the remarkable effectiveness and many additional potential benefits and contextual considerations of Spinraza and Zolgensma."
- ICER lauded Biogen for its randomized, controlled clinical trial design and its robust enrollment, noting that "their efforts to generate such high-quality evidence sets a standard of excellence which other manufacturers should follow."
- Despite the catastrophic nature of the disease, and the high quality of evidence demonstrating efficacy, ICER's framework drove a unanimous panel vote that Spinraza - until very recently, the only SMA treatment available - represented *low long-term value for the* money due to its *high price.* Spinraza was introduced to the market in 2016, but Zolgensma was not even commercially available at the time of ICER's review.

We believe that it is highly likely that novel approaches to ultra-rare conditions and many rare cancers will similarly fail to clear ICER's hurdles, even with the proposed framework adaptations, until they have been used in clinical practice for a sufficient number of years to establish that the value demonstrated in FDA pivotal trials translates to ICER's view of value

over the long-term. Even then, the treatments we need – existing and yet-to-be-developed – will not demonstrate "value" unless that concept is relevant to the disease and its small patient population, and the model reflects the values of the US health care system.

We urge ICER to refocus its proposed framework adaptations toward refinements that can be integrated quantitatively into ICER assessments.

Haystack Project and the RCPC support efforts to identify disease-specific indicia of value from the patient perspective and appreciate ICER's acknowledgement that additional domains of value exist. Unfortunately, ICER's concerns that quantifying these additional benefits is "exploratory" and without consensus among academic health economists ignores the fundamental reality that by **not** substantively incorporating a quantified value, ICER is erroneously setting the value at zero. For patients with rare and ultra-rare disorders, each ICER decision to approach unknown or novel considerations by reverting to a "gold standard" applied to common conditions with multiple treatment options places an additional layer of distortion on the disease-specific value of a specific therapy.

Haystack Project and RCPC had hoped that ICER would rise to the challenge of placing patients, including those with disabilities and rare conditions, at the center of the value equation. We firmly believe that QALY limitations and deficiencies are most pronounced when applied to rare and ultra-rare conditions. A comprehensive study on the use of incremental cost per QALY gained in ultra-rare disorders by Schlander et al., discussed that a growing body of literature considers cost per QALY economic evaluations in ultra-rare diseases as flawed, and likely to set inequitable benchmarks that treatments for ultra-rare diseases cannot meet.

Despite the shortcomings in utilizing QALY for the diverse set of rare and ultra-rare conditions with emerging treatment options, ICER continues to rely on its use and relegate the disease-specific considerations that are more closely aligned with value to sidebar discussions that are likely to be ignored as extraneous or irrelevant. Patients in countries with technology assessment approaches that use QALY and rigid willingness-to-pay criteria experience treatment delays, coverage denials, and decreased associated survival rates.

We strongly believe that patients and their caregivers deserve innovation in health care economics and value assessments that rise to meet the innovations we are seeing in treating diseases that have long been untreatable and incurable. When ICER articulated these framework adaptations for ultra-rare conditions, it stated :

> When there are challenges translating the outcome measures used in clinical trials and available patient-reported data into QALYs, ICER will conduct a search for "mapping" studies that may allow translation of surrogate outcomes into quality of life measures. The validity of these mapping studies will be discussed with manufacturers, clinical experts, the patient community, and other stakeholders in order to get their input on the most feasible way to translate these other measures of patient outcome into QALYs.

Although ICER has embraced a role in assessing value for each new treatment for an ultra-rare disorder, we are unaware of any instances for which it accommodated the unique circumstances of a specific disease by attempting to translate surrogate outcomes into QALY. We firmly believe that patients with an emerging transformative or potentially curative treatment for their rare or ultra-rare disease present a compelling case for ICER to either quantify patient perspectives on high-value outcomes within its framework or decline review.

Haystack Project and RCPC actively encourage patient advocates to explore and gather data on what outcomes are most important to patients. Patient advocates, armed with sufficient time to devise proactive and meaningful input, can not only improve the validity of ICER's assessments, but increase patient acceptance of and agreement on the results of its reviews. While we appreciate ICER's concern that incorporating patient priorities, preferences and views on outcomes into its QALY framework on a disease-specific basis is new territory, the weight of evidence indicates that general population perceptions of high-value outcomes within QALY have little validity across rare and ultra-rare diseases. We therefore strongly believe that any concerns on validity of cost-effectiveness and value assessments in rare diseases are as, if not more, compelling when ICER adheres to a QALY-based framework that is recognized as a poor fit for these conditions.

To the extent that disease-specific considerations cannot be incorporated in a quantitative manner, we urge ICER to recommit to its position that when it "judges that it is not feasible to translate measures of patient outcome into QALYs, ICER will provide analyses of the potential costs and consequences of treatment, and will not produce a value-based price benchmark." Although ICER did not adhere to these limitations in more recent reviews, for transformative treatments addressing rare and ultra-rare conditions, the analyses would fulfill ICER's goal of supporting informed decisions between patients and their providers.

Conclusion

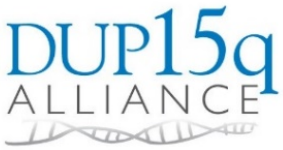
Where providers, patients, and payers have a set of treatment options approved for a specific condition, ICER can play an important role in informing decisions. We are, however, concerned that ICER's proposed changes and adaptations to its framework over time have yielded assessments that judge the novel treatments we hope for and need to live full and productive lives as "low value." Specifically, we believe that ICER's framework(s):

- Inappropriately conflates the impact of a therapy on patient health outcomes, including quality of life, with the potential budget impact to any individual payer or group of payers;
- Fails to consistently and transparently apply standards that are validated for use within the disease state;
- Will have the unintended consequence of discouraging innovation;
- Fails to incorporate real-world data, and pricing decisions; and
- Fails to incorporate patient and caregiver perspectives of value.

While we do not believe the framework adaptations sufficiently address these methodological deficiencies, we appreciate ICER's efforts toward improving the relevance and validity of its assessments. Once again, we appreciate the opportunity to comment on the proposed framework adaptation. As the voice of rare and ultra-rare disease advocates, we look forward to working with you in the future to facilitate patient and caregiver engagement, and to further inform your rare and ultra-rare disease policies, proposals, and frameworks. If you have any questions or would like to discuss our comments and recommendations, please contact Saira Sultan at 202-360-9985.

Sincerely,


ippf
International
Pemphigus&
Pemphigoid
Foundation


DUP15q
ALLIANCE


National
MPS
Society
Support for Families. Research for a Cure.


Lipodystrophy
United


nnpdf
NATIONAL NIEMANN-PICK DISEASE FOUNDATION, INC.


SLC6A1 Connect
SLC6A1 Research & Support


Bridge the Gap
SYNGAP
Education & Research Foundation


SPF
SPASTIC
PARAPLEGIA
FOUNDATION, INC.
Research / Education / Support

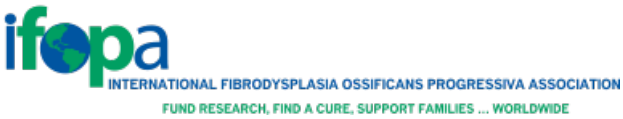

CANCERcare®


Nevus Outreach, Inc.
The Association for Large Nevi & Related Disorders


CURECRPS
FOUNDATION


RNE


Choroideremia
RESEARCH FOUNDATION


ifopa
INTERNATIONAL FIBRODYSPLASIA OSSIFICANS PROGRESSIVA ASSOCIATION
FUND RESEARCH, FIND A CURE, SUPPORT FAMILIES ... WORLDWIDE