



June 10, 2019

Institute for Clinical and Economic Review
Two Liberty Square
Ninth Floor
Boston, MA 02109

Re: ICER Seeks Public Input for 2020 Value Assessment Framework

Dear Dr. Pearson:

On behalf of the 25 to 30 million Americans with one of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Institute for Clinical and Economic Review (ICER or the Institute) for the opportunity to provide comments on the Institute's call for suggestions and feedback on how to improve its value assessment framework for 2020 and beyond.

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

NORD is also committed to fostering a health care ecosystem that encourages the development of, and affordable access to, safe and effective therapies for rare disease patients. In May 2019, NORD issued a document entitled "[Principles for Assessing Proposals Designed to Lower the Cost of Prescription Drugs in the United States](#)." These principles are intended to provide transparency around NORD's evaluation of proposed public policies for lowering the cost of therapies for our patients. They illustrate NORD's commitment to ensuring our patients can access innovative therapies.

In general, NORD believes that therapies should be priced based upon the value that they bring to patients, their families, and our health system as a whole. However, NORD further believes that the sustainability of the health care system and the existing social and economic inequities that could be exacerbated by high medical costs must also be considered. ICER and other similar entities serve a valuable function in ensuring these goals are achieved. These organizations conduct empirical analyses to assess the value a particular product brings to insurers, patients, and our society as a whole, yet these analyses are only beneficial if they fully incorporate patient perspectives and experiences.

We are pleased to oblige ICER's call for comments on their general value assessment framework, ultra-rare value assessment framework, and patient participation guide. Overall, we acknowledge and applaud ICER for the improvements to date in its evaluations and processes. NORD remains concerned about specific aspects of ICER's reviews that could result in detrimental access challenges for our patients.

Definition of an "Ultra-Rare Condition" as any Population of Fewer than 10,000 Individuals:

NORD continues to be concerned with ICER’s approach to subdividing the rare disease community into ultra-rare and non-ultra-rare conditions. As outlined in NORD’s September 2017 comments on the proposed ultra-rare framework, NORD has long opposed efforts to subdivide the rare disease community into smaller subsets of patient populations. For example, we expressed our concern with the Food and Drug Administration (FDA or Agency) when, in a July 2018 draft guidance on “Slowly Progressive Low-Prevalence Rare Diseases with Substrate Deposition That Results from Single Enzyme Defects: Providing Evidence of Effectiveness for Replacement or Corrective Therapies,” the Agency defined a “low-prevalence rare disease” in the context of the guidance as any disease with fewer than 5,000 individuals.¹

Our concerns with subdividing the community stem from the belief that such policies would do more harm to the rare disease patient populations that do not fall within the “ultra-rare” category than good for the rare disease patient populations that do. We fear that those rare diseases that are excluded would be considered no differently than common diseases and the challenges that arise due to rare, but not “ultra-rare,” patient populations would be ignored and discarded.

In the context of ICER’s assessments, we are concerned that the rare diseases (defined by the Orphan Drug Act as any disease affecting fewer than 200,000 individuals in the United States) that are excluded from the ultra-rare framework will not receive the same flexible and progressive review offered to “ultra-rare” conditions, which could potentially adversely affect their review.

Many of the orphan drugs reviewed by ICER have been reviewed using the “ultra-rare framework.” These include deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy; inotersen and patisiran for amyloidosis; ivacaftor for cystic fibrosis; and Ianadeluman and C1 esterase inhibitors for hereditary angioedema. However, ICER applied its general framework for other rare disease therapies, such as Hemlibra for hemophilia A and therapies for multiple myeloma.

NORD once again requests that ICER consider using its ultra-rare framework not just for diseases with a prevalence of fewer than 10,000 individuals but for all rare diseases. The cut-off of 10,000 individuals is arbitrary, and we disagree with ICER’s original assertion for this cut-off that the “application of adapted methods of value assessment are not needed for the majority of ‘orphan’ drugs as defined by the Orphan Drug Act, as sufficient patient numbers are usually available for ‘routine’ clinical trials, and outcome measures are likely to be relatively standardized and well-documented.”² Clinical trials are often quite difficult for rare diseases of all prevalence levels, and the challenges of developing outcome measures do not disappear at a prevalence of 10,001.

These same concerns also apply to ICER’s disqualification from the ultra-rare framework that occurs when the patient population receiving the therapy is expected to eventually exceed 20,000 individuals. This rationale was initially used to exclude Hemlibra from the ultra-rare framework even though there are fewer than 10,000 individuals currently expected to take the therapy in the United States. However, ICER did end up using the ultra-rare framework in its final report.

¹ Melmeyer, P. (2018, September 25). Retrieved from <https://rare diseases.org/wp-content/uploads/2018/09/NORD-2018-Comments-on-Low-Prevalence-Final.pdf>

² Proposed adaptation of the ICER value framework for the assessment of treatments for ultra-rare conditions. (2017, July 25). Retrieved June 6, 2019, from https://icer-review.org/wp-content/uploads/2017/05/ICER_Proposed_VAF_Adaptations_Orphan_Drugs_072517.pdf

In summary, we strongly encourage ICER to take this opportunity to consider expanding its use of the ultra-rare framework to include all rare diseases, as defined by the Orphan Drug Act.

Willingness-to-Pay Thresholds in the Ultra-Rare Framework:

NORD remains supportive of ICER's approach to increasing the willingness-to-pay threshold up to \$500,000 per QALY within its ultra-rare framework. This higher threshold for willingness-to-pay has been applied appropriately throughout the various ultra-orphan reviews and has resulted in more nuanced and flexible reviews of these therapies.

For these reasons, we encourage ICER to continue to use the willingness-to-pay threshold of \$500,000 per QALY rather than the \$50,000 per QALY employed in the general framework.

Incorporation of Contextual and Non-Traditional Benefits and Values:

NORD continues to be appreciative of ICER's inclusion and consideration of contextual and non-traditional benefits of a therapy to the patient, their family, and caregivers. There are many benefits of a therapy that are generally not well-captured within traditional cost effectiveness analyses. These include quality-of-life (QOL) improvements for the patient, such as a better ability to sleep, better management of pain, and the ability to partake in employment and hobbies.

We are also thankful that ICER is specifically requesting feedback from patients and their organizations on how to incorporate patient generated evidence and "methods to integrate dimensions of value not captured by the QALY." Both of these topics are critically important to ensuring patient viewpoints and contextual and non-traditional benefits are incorporated. We hope that disease-specific organizations, particularly those who have already participated in an ICER review, will comment on their experiences and how ICER can improve the process of data collection going forward.

There are many potential ancillary benefits of therapeutic interventions to families and caregivers. Parents of children with rare diseases value the ability to sleep through the night, go back to work, socialize with friends, or take better care of their child. Caregivers also are benefited if their patient is healthier and happier. Further, societal benefits should be considered, including substantial advances in science and medicine.

Consequently, we thank ICER for considering these benefits as it evaluates therapies. However, as explained in our previous comments, we still encourage ICER to find ways to include these contextual and non-traditional benefits into the specific cost-per-QALY outcome of the evaluation. For example, ICER considered patient viewpoints and quality-of-life benefits in its review of treatments for spinal muscular atrophy, amyloidosis, hemophilia, and others. However, as evidenced in each of these reports, these "potential other benefits" were left to a separate, non-quantitative section of each ICER report, thus, allowing these considerations to be siloed away from ICER's final determination.

There are methodologies ICER can employ to incorporate not only non-traditional and contextual benefits to patients but also benefits to family members, caregivers, and society. In fact, ICER employed such methodologies in its assessment of Luxturna for a specific retinal blindness. In this assessment,

ICER evaluated Luxturna from both the health system and societal perspective, thus, allowing readers to ascertain the potential benefit of the therapy outside of strict cost-per-QALY, budgetary, and insurer-oriented structures.

While this is encouraging, and we again applaud ICER for moving in this direction, there were still many additional ways in which ICER could have better incorporated the “potential other benefits” that were again siloed in Luxturna’s report. Consequently, while we applaud ICER for its progress, we still encourage ICER to better incorporate patient, familial, and caregiver experiences and perspectives and the non-traditional value derived from orphan therapies.

Value-based Price Benchmark of \$100,000 to \$150,000 per QALY:

While NORD understands ICER’s desire to apply a uniform value-based price benchmark across all therapies regardless of the framework used, we still encourage ICER to consider either using a higher value-based price benchmark to acknowledge the additional non-traditional and contextual benefits orphan drugs often provide. Alternatively, ICER could keep the same price benchmark but better incorporate these benefits into the cost-per-QALY itself. If ICER chooses to exercise neither of these options, it will once again be ignoring value that patients, family members, and caregivers derive from these therapies.

Patient Participation Process:

NORD continues to be concerned by the arduous, time-consuming, and overly-expedited process in which patient organizations are expected to participate. NORD understands that ICER aims to review therapies on an iterative, thorough, and expedited timeline. Consequently, ICER requests that stakeholders, including those in the patient community, respond to substantial and content-rich documents, such as scoping documents and evidence reports, on a particularly accelerated timeline.

As representatives of the rare disease patient community, we are particularly concerned about the effect this has on rare disease patient organizations that represent communities for which a therapeutic review is being conducted. Many disease-specific organizations dread upcoming ICER reviews for their population as it will cause them to sacrifice work on many other programs and services for their communities. Organizations have had to drop other initiatives to spend a large proportion of their time and resources on participating in ICER reviews.

NORD asks that ICER consider ways to make their patient participation process less burdensome on the community. By doing so, ICER can accomplish one of its goals set forth in “A Patient’s Guide to Open Input” of ensuring that a diversity of patient experiences are collected.³ By requiring an extensive understanding of health economics, as well as substantial time and resources to participate, ICER is potentially excluding patients and patient organizations that could offer important input.

Therefore, NORD encourages ICER to consider ways to capture the voice of all patients and patient organizations in a particular disease space. This includes perhaps extending timelines for commenting (three weeks is often too short for a several-hundred-page document) and proactively reaching out to

³ The 2020 Update to ICER’s Value Assessment Framework: A Patient’s Guide to Open Input. Retrieved from https://icer-review.org/wp-content/uploads/2019/05/ICER_2020VAF_Patient_Guide_05212019.pdf

under-represented communities. We are appreciative that ICER's has viewed NORD as a resource when seeking patient organizations that represent certain populations, and we encourage ICER to continue to reach out if we can be at all helpful in ensuring patient voices are well represented.

Additionally, ICER should find ways to ensure that the patient perspective is adequately represented at public meetings. This includes facilitating remote patient participation for those who are unable to travel to the meeting to attend in-person. For those who are able to attend in-person, ICER should allow for a summary that is longer than 250-words to be submitted by oral presenters. Limiting patients to such a small written summary forces patient to present their experiences in ways they may not feel to be accurate or complete. We invite ICER to consider expanding the total word allowance, if not abolishing it all together, for patients, families, and caregivers.

We thank ICER for the opportunity to comment, and we look forward to working with ICER to accurately and collaboratively assess the values of orphan therapies. For questions regarding NORD or the above comments, please contact me at rsheer@rarediseases.org, or 202-588-5700.

Thank you in advance for your consideration.

Sincerely,

/s/

Rachel Sher
Vice President of Policy and Regulatory Affairs