



September 25, 2017

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

**Re: ICER Proposed adaptation of the ICER value framework for the assessment of treatments for ultra-rare conditions**

Dear Dr. Pearson:

On behalf of the 30 million Americans with one of the nearly 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Institute for Clinical and Economic Review (ICER) for the opportunity to provide comments on the Institute's "Proposed adaptation of the ICER value framework for the assessment of treatments for ultra-rare conditions."

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.

We are committed to fostering an ecosystem that encourages the development and accessibility of safe and effective therapies for rare disease patients. We are excited by the advent of value frameworks, and believe that value frameworks, if developed collaboratively and used responsibly, can provide objective analysis for assessing the value of therapeutic interventions.

Rare diseases are largely understudied, misunderstood, and ignored due to the inherently small patient populations of each rare disease. It is for these reasons that Congress, state legislatures, and Federal and state regulatory bodies have recognized that rare diseases require a specialized, unique approach. Congress passed the Orphan Drug Act of 1983 and the Rare Diseases Act of 2002. Further, state legislatures across the country are creating Rare Disease Advisory Councils to advise state governmental bodies on the unique needs of the rare disease patient community. Finally, the Food and Drug Administration (FDA) and the National Institutes of Health (NIH) have created offices dedicated to rare disease research and drug development.

We applaud ICER for continuing this institutional recognition and adaptation by putting forward an amended value assessment framework for rare disease healthcare interventions. However, while we support several of the proposed changes ICER outlines within its adapted framework, we are very concerned with other approaches ICER has decided to pursue.

The following comments are structured using the outline of ICER's proposed adapted framework.

**1.1 ICER will consider using an adapted approach to value assessment for treatments that will be called a “potential major advance for a serious ultra-rare condition” if the three following criteria apply:**

- **The treatment is envisaged for a patient population of fewer than 10,000 individuals**
- **There is little chance of future expansion of indication or population that would extend the size of the treated population above 20,000 individuals**
- **The treatment potentially offers a major gain in improved quality of life and/or length of life**

NORD is very concerned with ICER’s proposed division of rare diseases into ultra-rare and non-ultra-rare conditions, and opposes this proposal. For decades, NORD has opposed efforts to create an ultra-rare category in various settings. For example, NORD has opposed creating an ultra-orphan category within FDA regulatory review of orphan therapies, public and private reimbursement policy for orphan therapies, and incentives for orphan drug development. Invariably we have asserted that creating an ultra-orphan subcategory will do more harm to the rare diseases that do not fall within that category than good for the rare diseases that do.

In addition, we are not convinced by ICER’s rationale that,

“only when patient populations near a smaller size of approximately 10,000 individuals does it seem that assessment methods might need to change in some way to recognize the distinctive practical challenges to evidence generation, and to give special consideration to value in the context of the price X volume needed to provide adequate rewards for risk and innovation.”

We find this claim baseless and unfounded, and the lack of any citation or outside justification only furthers our conviction. There are many factors that contribute to the difficulty in evidence generation for orphan therapies, and we are confident they do not start and stop at the 10,000 prevalence number. For example, many diseases with prevalences above 10,000 are even more difficult to develop therapies for due to the heterogeneity of the manifestation, progression, and severity of the diseases, as well as the variability of treatment effects.

We also strongly disagree with ICER’s assertion that “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.” Again, we disagree with this unsubstantiated claim. Congress and FDA have long recognized the unique challenges of developing orphan therapies above population sizes of 10,000 individuals by enacting and implementing various incentives and regulatory practices that do not disqualify diseases with over 10,000 individuals. For ICER to make this claim, it is directly in contrast with every other institution in the United States that sets policy for the rare disease community.

It also makes little sense to us to require the unlikelihood of future expansion of indications in order to qualify for the adapted framework. The future prospects of a therapy’s use have nothing to do with the current evidence that FDA or ICER have to consider. If a therapy is approved for a very small patient population, it is accompanied with all of the characteristics that ICER itself identifies as requiring an

adapted approach regardless of future expansion of indications. To apply this arbitrary requirement goes against ICER's very own logic and reasoning.

We strongly urge ICER to reconsider this approach outlined within this section. We encourage ICER to abandon use of an arbitrarily created subdivision of the rare disease patient community, and instead use the well-recognized and established definition for a rare disease already in existence: 200,000 or fewer individuals with the disease in the U.S.

**2.1 For assessment of the comparative clinical effectiveness of potential major advances for serious ultra-rare conditions, ICER will not change its approach to rating evidence according to the ICER EBM matrix, nor will there be different “standards” of evidence. Instead, ICER will provide specific context regarding the potential challenges of generating evidence for these treatments, including considerations of challenges to conducting RCTs, to validating surrogate outcome measures, and for obtaining long-term data on safety and on the durability of clinical benefit. The commonly used approach of evaluating major advances for severe ultrarare conditions against historical controls will be highlighted.**

We again are concerned with the approach enumerated within this section. We appreciate ICER's recognition of the “potential challenges of generating evidence for [ultra-orphan] treatments.” But we are concerned that ICER is relegating these unique circumstances to merely “context” within their reports, without any integration into the methodology of the value assessment framework, will demote these critical considerations to a lower standard of evidence, and result in coverage decision makers ignoring them altogether.

After attending the Orphan Drug Assessment and Pricing Summit on May 31, 2017, it became clear to us that many of the stakeholders representing the insurance industry simply wanted a final number to base their coverage decisions on. By not including these crucial considerations into the methodology, ICER is allowing insurers to ignore these considerations by providing them with an assessment that does not include them.

Providing context within the final report is insufficient. Instead, ICER should integrate these considerations into the quantitative methodology of the comparative clinical effectiveness assessment.

**3.2 For [serious ultra-orphan] treatments ICER will adapt its analyses to provide willingness-to-pay threshold results for a broader range, from \$50,000 per QALY to \$500,000 per QALY. No special quantitative weighting system will be applied to different magnitudes of QALY gains or to baseline severity of the condition.**

We support ICER's decision to expand its willingness-to-pay threshold from \$50,000 per QALY to \$500,000 per QALY. This is a valid method to incorporate the well-established higher societal valuation of therapies for rare diseases. However, we again request that this adjustment is made for all orphan therapies, not just a small ultra-orphan subset.

**3.3 ICER will calculate a value-based price benchmark for these treatments using the standard range from \$100,000 to \$150,000 per QALY, but will add language in all report formats indicating that decision-makers in the US and in international settings often give special**

**weighting to other benefits and to contextual considerations that lead to coverage and funding decisions at higher prices, and thus higher cost-effectiveness ratios, than applied to decisions about other treatments.**

We are disappointed that ICER has chosen against amending its standard value-based price benchmark for orphan therapies. Again, ICER elects to use “language in all report formats” to inform decision makers rather than incorporating these critical considerations into the quantitative methodology.

Once again, we are concerned with ICER relegating the special circumstances in which orphan drugs are developed to easily-ignored qualitative report language. We again urge ICER to incorporate these considerations into the methodology itself. It was the insurance industry’s input during the Orphan Summit that, “suggested that it would be preferable to remain consistent in the use of \$100,000 to \$150,000 per QALY.” This preference did not originate from the patient or provider community.

ICER’s preference for simplicity and consistency over accuracy and inclusion of nuance is concerning. Even though amending the value-based price benchmark to consider the unique circumstances of orphan drug development and reimbursement is difficult, we urge ICER to pursue this nonetheless.

**3.4 When ICER 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. Instead, ICER will provide a crosswalk to a cost consequence price for a treatment and condition pair that is the closest clinical analogue that can be found.**

We hope that ICER can provide additional information on when and how this determination would be made, and how exactly it plans to “provide a crosswalk to a cost consequence price for a treatment and condition pair that is the closest clinical analogue that can be found.” At this time, we do not feel that we have enough information on this method to adequately comment.

**4.1 For report sections on “other benefits and disadvantages” and “contextual considerations,” ICER will include a broader frame to seek evidence and perspective on the potential for these treatments to affect positively the family, school, and community. Information will also be sought on the potential impact of new treatments on the infrastructure for screening and care of the affected individuals.**

We commend ICER for its plan to “include a broader frame to seek evidence and perspective on the potential for these treatments to affect positively the family, school, and community. NORD has long held that the societal benefits of an orphan therapy should be included within any assessment of its value. While we prefer these values to be included quantitatively within the assessment of the therapy, we are encouraged that ICER is broadening its focus to include as many of the therapy’s positive impacts as possible.

We are particularly pleased that,

“ICER reports will seek input from patients and clinical experts on the potential impact of a new treatment on the entire “infrastructure” of care, including effects on screening for affected

patients, on the sensitization of clinicians, and on the dissemination of understanding about the condition that may revolutionize how patients are cared for in many ways that extend beyond the treatment itself.”

We thank ICER for this important step forward. However, we ask that ICER reexamine their patient participation guide and amend it appropriately to ensure this information can be adequately collected. As it currently stands, ICER’s process for including the patient community is far too expedited for many patients and patient organizations to participate. Three-week comment periods for dense and esoteric ICER documents is far too short a time for a small rare disease patient organization to contribute. If ICER intends on making a concerted effort to include as many “other benefits and disadvantages” as possible, it must account for the limitations of the small communities that can offer such data and expertise.

**5.1 ICER will conduct over the coming year a collaborative process through which it will seek to develop a template for providing information in its reports on the research, development, and other relevant costs related to new treatments for serious ultra-rare conditions. Until this template is completed, ICER will work with individual manufacturers of treatments under review to determine what, if any, information related to the costs of development can be shared as part of the public deliberation regarding the value of these treatments and their appropriate pricing.**

While we are not opposed to this effort moving forward, we are concerned with how it may impact the valuation of orphan therapies. More specifically, we believe a “fair price” and a “price that reflects the value of the treatment” are two different concepts. Assessing a therapy’s value should rest solely on the benefits it brings to the individual, the healthcare system, and society as a whole with the consideration of the unique nature of rare diseases and orphan drugs integrated within. We are unsure how the financial investment a company makes into developing the therapy impacts the value it then offers to society.

We encourage ICER not to conflate the two topics, and to focus on the valuation of therapies rather than expand its scope into issues of fairness.

**6.1 During public meetings of ICER’s independent appraisal committees, votes on the “long-term value for money” of treatments for serious ultra-rare conditions will be done according to the same procedures for other interventions, i.e. if the base case estimate falls between \$50,000-\$175,000 per QALY. However, for treatments of ultra-rare conditions, ICER will not assign any designation of value if the base case cost-effectiveness ratio is above \$175,000 per QALY.**

While we are appreciative of ICER’s proposal to “not assign any value rating to ultra-rare treatments if the base-case cost-effectiveness ratio exceeds \$175,000 per QALY,” we are concerned that ICER will be using the same cost-effectiveness range as they do with all other therapies. This is another circumstance where we request ICER to consider changing its quantitative methodology for determining value rather than depending on qualitative conjecture.

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 [pmelmeyer@rarediseases.org](mailto:pmelmeyer@rarediseases.org) or (202) 545-3828.

Thank you in advance for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'P. Melmeyer', with a long horizontal flourish extending to the right.

Paul Melmeyer  
Director of Federal Policy