



September 6, 2019

BY ELECTRONIC DELIVERY

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

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

Dear Dr. Pearson:

We are writing on behalf of the Biotechnology Innovation Organization (BIO) to provide comments on the Institute for Clinical and Economic Review's (ICER's) solicitation for input on draft revisions to its Value Assessment Framework for the assessment of "single or short-term transformative therapies" (SSTs). BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology companies, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes, but have also reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

We appreciate ICER's recognition that the burgeoning field of transformative and curative therapies requires serious discussion around how these treatments are valued by not just payors, but society at large. These therapies have the potential to fundamentally change how we view the treatment of disease. Yet as we strive to shift our health care system to one that rewards valuable care, BIO is concerned that the science of value assessment for all therapies – not just those that are curative or transformational – is woefully behind where it should be for these tools to be used in a substantive way.

BIO has commented previously on our concerns with the methodology of ICER's value framework, and we have proposed both substantive and process-related changes that would be needed for these assessments to accurately capture a therapy's value. Although ICER has attempted to incorporate more contextual considerations into its value framework, its fundamentally flawed structure remains the same: a direct cost effectiveness model that does not capture the societal perspective and other critical value components.

As ICER refines and modifies its value assessment framework, we encourage the organization to recognize that the science and methods around value assessment are not settled and broadly agreed upon by all stakeholders. The fact that ICER engages in regular updates to its value framework evidences the dynamic nature of how we understand value assessment. We recommend ICER work to better communicate the fact that the science of value assessment is not static and incorporate *that* as a fundamental aspect of ICER's work. In this way, ICER can be a partner in working with all stakeholders in advancing the science and methods of value assessment, and not simply dictate what those methods should be.

Below, please find our comments on the specific revisions ICER proposes when assessing SSTs. We note that for some of these changes that are proposed for both the SST modifications, as well as ICER's standard value framework methodology update, we may provide additional comments in our subsequent comment letter on the 2020 modifications.

Section 1: Determining those treatments for which adapted assessment methods will be used

1.1 ICER will use an adapted approach to value assessment for "single and short-term transformative therapies" (SSTs). These are defined as therapies that are delivered through a single intervention or a short-term course of treatment that demonstrate a significant potential for substantial and sustained health benefits extending throughout a patients' lifetimes. SSTs include two subcategories:

- *Potential cures that can eradicate a disease or condition; and*
- *Transformative therapies that can produce sustained major health gains or halt the progression of significant illness*
- ICER should provide clear and transparent inclusion/exclusion criteria around how the SST framework will be applied. Terms such as "transformative," "substantial," and "sustained" are inherently subjective. While we understand that whether to apply the adapted approach will be debated during the open input and scoping document process, we believe it should be evidently clear ahead of time when a therapy will be assessed using the modified framework.

Section 2: Assessing and describing uncertainty

2.1: Cure proportion modeling

- We support the adaptation that allows for cure proportion modeling for SSTs. This method better captures patient heterogeneity and is better aligned with the current science of value assessment.
- We also note that while survival data may present an important opportunity to adjust model fit for therapies that cure disease, other patient-relevant outcomes could be used to better predict model fit for non-life-threatening chronic diseases. We encourage ICER to explore ways to expand on this adjustment for these types of conditions.

2.1: Incremental cost effectiveness scenarios at multiple time horizons

- We support the retention of the lifetime horizon as the base case for the value-based price benchmark.
- However, we are concerned that ICER will conduct CEAs using multiple time horizons, and specifically with how ICER will present these analyses to the public.
- This issue illustrates our concerns with ICER conducting assessments of products that have not yet or just recently come to market. The data manufacturers use to

obtain FDA approval of a product serve a very distinct purpose: to demonstrate the product's safety and efficacy. The same data cannot be used in isolation to support the product's value assessment.

- We recommend ICER explore ways to make this distinction clear to avoid confusion. Analyses at the longest follow-up data available, 5, and 10 years may indeed be of interest to stakeholders as a thought experiment. But they should not be misinterpreted as the product's actual value proposition. At a minimum, we recommend limiting these analyses to the body of the report and not include them as part of the Report-at-a-Glance or related summary material.

2.3: Introducing a new economic review section on "Controversies and Uncertainties"

- We support the consolidation and addition of a section in ICER's reports that explores the inherent uncertainty in conducting value assessments – in both assessments for SSTs and for all ICER reports.
- Material in this section should be summarized and included prominently in the Report-at-a-Glance.
- We recommend this section include a discussion around the difficulties in developing a single incremental cost-effectiveness ratio for a treatment, given the many modeling assumptions and uncertainties used to produce the cost-effectiveness and value-based price benchmarks. In this section, we encourage ICER to present multiple plausible incremental cost-effectiveness ratios.
- ICER should provide clarification related to how material will be chosen for this section (e.g. Will appraisal committees vote on what constitutes a "controversy"? Will alternative models from manufacturers whose products are under review be automatically included if submitted?).

2.4: Probabilistic sensitivity analysis linked to policy recommendation for outcomes-based payment

- Including a recommendation related to how payors should finance a product ignores the complex legal and regulatory barriers to executing outcomes-based payments.
- The selection of 25% or more PSAs at or above \$200,000/QALY is arbitrary and has no scientific basis.
- Making these recommendations is outside of ICER's purview. Without policymakers addressing the barriers to these types of payment arrangements, recommending their adoption may needlessly complicate both payors and manufacturers ability to enter into them.
- There are many different potential options for outcomes-based agreements, with implications for cost-effectiveness as well as short and long-term administration and operationalization. ICER is not in a position to make judgements or recommendations about these elements of outcomes-based contracts.

Section 3: Additional elements of value

3.1: Addition of two domains of "potential other benefits and disadvantages" for voting by appraisal committees:

- (1) A potential advantage for therapies that offer special advantages by virtue of having a different balance or timing of risk and benefits versus other treatments; and*
- (2) a potential disadvantage for therapies that, if not successful, could reduce or even preclude the potential effectiveness of future therapies.*

- We are encouraged that ICER has acknowledged the existence of additional domains of value that will be voted on by the appraisal committees. However, we are deeply concerned that these elements will not be integrated quantitatively into the assessment of SSTs or therapies being assessed under ICER's standard value framework.
- ICER's concern with more substantive incorporation of these benefits appears to rest on the opinion that these concepts are "exploratory" and "lack any consensus among academic health economists." However, as an entity engaged in value assessment, ICER has a duty to advance a discussion around methods, not simply throw up its hands in the face of a spirited debate.
- We also note that while there may be ongoing discussion about how these elements of value should be included, concepts such as the value of hope, real option value, insurance value, equity value, etc., have been the subject of significant academic research and peer-review study. The same cannot be said, however, of some of the concepts ICER proposes to introduce in the modification of its framework for SSTs. While ICER offers rationales for its choices of 25% of PSAs above \$200,000/QALY (see comment above) or for the entire concept of its "shared savings" scenario (see comment below), we are not aware of any robust scientific discussion of these concepts' inclusion in value assessment.
- We encourage ICER to further explain why these untested and arbitrary concepts should be included in its SST framework while other, more robust, concepts should be discarded entirely.

Section 4: Time Divergence Between Costs and Benefits

4.1: Discounting: ICER proposes to continue its use of a 3% discount rate as standard for both costs and outcomes

- We believe the nature of these therapies requires a smaller discount rate than is used for traditional therapies, given that the level of analysis will be over the lifetime of the patient.
- Using the same discount rate for traditional therapies underestimates the uncertainty of the outcome for these therapies to make outcomes comparable across disease areas and indications.

- We recommend ICER be more flexible in setting discount rates for these therapies. At a minimum, assessments of SSTs should explore the impact of divergent discounts rates for these versus other therapies so that stakeholders can see the impact and understand its implications.

Section 5: Affordability and Fair Sharing of Economic Surplus

5.1: ICER will develop a "shared savings" scenario analysis for SSTs as an adjunct to the base case. Cost offsets in this scenario will accrue to the innovator for the first 12-year period in the model, and thereafter cost offsets will accrue to the health system generally.

- We are deeply concerned with the inclusion of this new scenario analysis and recommend ICER refrain from including it in the SST framework until further stakeholder input and methodological concerns can be addressed.
- As noted above, the selection of a 12-year exclusivity period is arbitrary. If interpreted strictly by payors, this scenario analysis would penalize manufacturers that develop products with durability of benefit that falls outside of ICER's artificial range.
- Assigning 100% of cost offsets to the health system after 12 years also ignores the incremental, dynamic nature of innovation.
- We note that in its standard framework, ICER declined to make assumptions about the loss of exclusivity, even when there is a level of certainty that the product under evaluation will encounter patent expiry during the model time horizon, asserting that this component is "difficult to estimate." We find it contradictory to make assumptions about the timing of loss of exclusivity and the supposed lack of generic competition for these technologies in the context of this "shared savings" scenario analysis.
- Concepts such as the assignment of economic surplus are political questions that should be resolved openly and transparently through the political process. We believe ICER is an inappropriate venue for such decision-making.

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Conclusion

If you have any questions regarding our comments or if we can be of further assistance, please do not hesitate to contact us at (202) 962-9200.

Sincerely,

/s/

Crystal Kuntz
Vice President
Healthcare Policy and Research