PIPC Partnership to Improve Patient Care

October 23, 2023

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

Dear Dr. Pearson,

The Partnership to Improve Patient Care (PIPC) appreciates the opportunity to comment on the Institute for Clinical and Economic Review (ICER) assessment of treatments for Pulmonary Arterial Hypertension (PAH).

PAH is a rare, progressive disorder. Over time, a patient's heart loses the ability to effectively pump blood throughout the body. Even patients with well controlled PAH deal with serious impacts on their quality of life and are often forced to radically alter their lifestyles in order to manage their disease. There is currently no cure for PAH and there is a need for more effective treatments. As ICER conducts its assessment of treatments for PAH, PIPC urges it to consider the following comments.

ICER Continues to Use the Discriminatory QALY

Multiple studies have shown that cost-effectiveness models that use the quality-adjusted life year (QALY) discriminate against patients with chronic conditions[1] and people with disabilities.[2] There is widespread recognition that the use of the QALY is discriminatory. The QALY has historically been opposed by the American public and policy makers. The National Council on Disability (NCD), an independent federal agency, concluded in a 2019 report that QALYs discriminate by placing a lower value on treatments which extend the lives of people with chronic illnesses and disabilities. NCD recommended that policymakers and insurers reject QALYs as a method of measuring value for medical treatments.[3]

ICER's chosen model does not lend itself to consideration of the PAH's heterogeneous patient population.

ICER chose to use a health state transition model (HSTM), which is unable to evaluate heterogeneity of patients and the relative effectiveness of therapies on those populations. Given the heterogeneity of the PAH population, an individual patient simulation model would have been a better choice.

[1] Paulden M. Recent amendments to NICE's value-based assessment of health technologies: implicitly inequitable?. Expert review of pharmacoeconomics & outcomes research. 2017 May 4;17(3):239-42.
[2] Nord E, Pinto JL, Richardson J, Menzel P, Ubel P. Incorporating societal concerns for fairness in numerical valuations of health programmes. Health economics. 1999 Feb;8(1):25-39.
[3] https://www.ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

The model is also based on a single outcome, WHO-FC, which categories PAH into a small number of states. This over-categorization tends to hide marginal effects.[4, 5]

ICER had the ability to categorize health states by any number of outcome measures, and others may have been stronger choices. Specifically, ICER could have chosen to categorize by 6MWD, the primary endpoint in the STELLAR trial. The primary endpoint showed a 390% difference in effect for treated patients versus those on placebo whereas the relative improvement for WHO-FC showed just a 106% difference. It is concerning that ICER chose a secondary endpoint from the trial that had the smallest relative difference between treatment and placebo arms around which to build its model. This is also the outcome with the least sensitive measure of difference for patients with the disease, making an already simplistic model even more immune to relative difference.

ICER excludes transplantation as an outcome of PAH, which leads to an underestimate of the value of effective treatment.

ICER chooses to exclude transplantation as an outcome of PAH from the model. This is a major shortcoming as transplantations are burdensome on the patient and caregiver, of limited availability, and carry a significant cost. With all of this in mind, there is huge value – both economic and in terms of patient preference – to avoid a transplant. ICER's choice to exclude the costs and outcomes associated with transplantation very likely led to underestimation of the true value of treating PAH patients with sotatercept.

The durability assumptions in the model don't adequately reflect the available evidence.

The model makes an assumption that improvement can only occur over the first 24 weeks due to questions of uncertainty around the durability of the treatment beyond that shown in the STELLAR trial, yet subsequent and ongoing studies clearly shown durability to 18 and 24 months. Among patients continuing treatment in the PULSAR open-label extension trial, improvements in pulmonary vascular resistance, 6MWD, and NT-pro BNP were maintained over 18 to 24 months.[6]

ICER assumes a linear relationship between severity of disease and utility increments, which is an approach that is losing validity among entities that practice value assessment.

[4] Naggara O, Raymond J, Guilbert F, Roy D, Weill A, Altman DG. Analysis by categorizing or dichotomizing continuous variables is inadvisable: an example from the natural history of unruptured aneurysms. American Journal of Neuroradiology. 2011 Mar 1;32(3):437-40.
[5] Bennette C, Vickers A. Against quantiles: categorization of continuous variables in epidemiologic research, and its discontents. BMC medical research methodology. 2012 Dec;12:1-5.
[6] Humbert M, McLaughlin V, Gibbs JSR, et al. Sotatercept for the treatment of pulmonary arterial hypertension: PULSAR open-label extension. European Respiratory Journal. 2023;61(1):2201347.

In recent years, there has been widespread reevaluation of several of the assumptions that cost utility analysis is built on.[7] This argument has been most prominent with respect to the reliance on the assumption that every unit of health gain – measured here in health-related quality of life - is equal in value.[8] In other words, a single unit of health generates the same utility whether that health is accrued to someone who is suffering considerable disease burden, or to someone who is suffering minimal disease burden.[9] In fact, several health technology assessment systems in Europe have backed away from direct use of strict cost-per-QALY estimates for this very reason, and incorporate the role of severity adjacent to the results to make a more context-relevant case for, or against, a new technology.[10,11]

PIPC would encourage ICER to follow this model and recognize that diseases that put a larger burden on patients and caregivers, like PAH, should be viewed differently than more common, less burdensome diseases.

Conclusion

PIPC urges ICER to reconsider the use of the QALY along with several of its modeling choices given many of them do not accurately represent the pathway of a PAH patient or convey the potential value of an effective treatment.

Sincerely,

Tony Coelho
Chairman
Partnership to Improve Patient Care

[7] Beresniak A, Medina-Lara A, Auray JP, De Wever A, Praet JC, Tarricone R, Torbica A, Dupont D, Lamure M, Duru G. Validation of the underlying assumptions of the quality-adjusted life-years outcome: results from the ECHOUTCOME European project. Pharmacoeconomics. 2015 Jan 1;33(1):61-9.
[8] Sund B, Svensson M. Estimating a constant WTP for a QALY—a mission impossible? The European Journal of Health Economics. 2018 Jul;19(6):871-80.
[9] MacKillop E, Sheard S. Quantifying life: understanding the history of quality-adjusted life-years (QALYs). Social Science & Medicine. 2018 Aug 1;211:359-66.
[10] Barra, M. and K. Rand-Hendriksen, *A missing cornerstone in the Norwegian Priority Commission's weighting scheme–Sub-treatment balancedness is a necessary property for priority setting criteria.* Nordic Journal of Health Economics, 2016. **4**(2): p. pp. 8-23.
[11] Swedish Parliamentary Priorities Commission, *Priorities in health care: ethics, economy, implementation*. 1995, Stockholm: Swedish Government.