

October 15, 2020

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 this opportunity to comment on the Institute for Clinical and Economic Review's (ICER) draft evidence report regarding treatments for bladder cancer. Bladder cancer can present many challenges to a patient's quality of life, and there are currently very few treatment options for patients with high-risk non-muscle invasive bladder cancer that is unresponsive to BCG, so it is critical that new treatments are evaluated carefully when there is appropriate available evidence. PIPC asks ICER to consider the following comments as it moves forward with its assessment.

### **ICER continues to conduct studies prematurely**

PIPC echoes the Cancer Support Community and other stakeholders in the belief that this report is being undertaken prematurely. ICER has chosen again, in the absence of sufficient evidence, to prematurely assess the value-based price of these drugs. No respected health technology assessment agency anywhere in the world evaluates new drugs before phase III data is available and the relevant drug regulation agency has approved its use. Despite this, ICER has made it common practice to prematurely assess the cost-effectiveness of drugs. Without a drug being approved and a price established, it is irresponsible to evaluate its cost-effectiveness.

### **PIPC has concerns about the sources and construction of ICER's health state utility inputs**

The health state utility values for the model seem to be taken from a single study undertaken in the UK where quality of life data was collected as part of the BOXIT trial.<sup>1</sup> The approach taken in this study was to estimate utility loss increments, not to actually estimate utility values of certain health states. This method is a valuable way to capture variance in disease states and comorbidities, but it must be approached correctly.

The problem with ICER's use of these utility values is that these incremental utilities have been applied individually to create proxy health states for the ICER model. In reality, many of these utility loss increments will be relevant to most, if not all, patients, so the use of individual utility loss increments – rather than combinations of utility loss increments is likely to significantly overestimate the health utility levels of people in more severe states of disease. For example, in the ICER model, patients with inoperable advanced metastatic bladder cancer seem to have an

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<sup>1</sup> Cox E, Saramago P, Kelly J, et al. Effects of Bladder Cancer on UK Healthcare Costs and Patient Health-Related Quality of Life: Evidence From the BOXIT Trial. *Clin Genitourin Cancer*. 2019.

HSUV of 0.7. This is a magnitude of quality life higher than people with arthritis<sup>2</sup>, dermatitis<sup>3</sup> or migraine.<sup>4</sup> It is highly unlikely that this an accurate summation of quality of life for people suffering the late stages of incurable cancer, and further demonstrates the flawed logic of a QALY-based model. The result of this overestimation is that the value of reducing time spent in these health states – the stated goal of most new treatments for any disease – will be undervalued.

### **Mixed data sources for measures of effectiveness are likely to lead to biased estimates in the ICER model**

ICER chooses to compare retrospective data to randomized clinical trial data in order to compare effectiveness across drugs. Whenever possible, ICER should compare equivalent data sets for consistency.

The review of the phase II and III trials shows a complete response (CR) for gemcitabine ± docetaxel of no greater than 39%, and HGFRS at 12 months ranging from 21-28% in populations with a high proportion of CIS ±HIG Ta/T1. Yet the ICER model uses a much higher figure that comes from a retrospective chart review of selected patients of 60-69%, and a figure of 75.2% for complete response. ICER acknowledges that these response rates are peculiarly high yet still chooses to use this data instead of comparable source data from trials.

Retrospective data is incredibly valuable when used correctly,<sup>5</sup> but the issue here is that there are not equivalent data sets for new drugs or therapeutic approaches. There is strong empirical evidence that the relative effectiveness of new therapies tend to improve over time, as physicians and providers develop better understanding of when, to whom and how to incorporate therapies into everyday treatment plans.<sup>6</sup> This learning-by-doing leads to a rise in effectiveness, as has been shown to exist in oncology for multiple tumors.<sup>7</sup> Comparing efficacy rates from a phase II or III trial with a retrospective case review is not a reasonable comparison.

### **ICER uses the discriminatory Quality-Adjusted Life Year (QALY)**

As PIPC has voiced many times in the past, we are concerned with ICER's continued use of the Quality-Adjusted Life Year (QALY). The QALY is known to discriminate by devaluing

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<sup>2</sup> Van den Hout WB, Goekoop-Ruiterman YP, Allaart CF, De Vries-Bouwstra JK, M. Hazes JM, Kerstens PJ, Van Zeben D, Hulsmans HM, De Jonge-Bok JM, De Sonnaville PB, Dijkmans BA. Cost-utility analysis of treatment strategies in patients with recent-onset rheumatoid arthritis. *Arthritis Care & Research*. 2009 Mar 15;61(3):291-9.

<sup>3</sup> Sonya Kahn MP. Economic evaluation of dupilumab for moderate-to-severe atopic dermatitis: a cost-utility analysis. *Journal of Drugs in Dermatology*. 2018 Jul;17(7):750-6.

<sup>4</sup> Xu R, Insinga RP, Golden W, Hu XH. EuroQol (EQ-5D) health utility scores for patients with migraine. *Quality of life research*. 2011 May 1;20(4):601-8.

<sup>5</sup> Bowrin K, Briere JB, Levy P, Millier A, Clay E, Toumi M. Cost-effectiveness analyses using real-world data: an overview of the literature. *Journal of medical economics*. 2019 Jun 3;22(6):545-53.

<sup>6</sup> Gaynor M, Seider H, Vogt WB. The volume-outcome effect, scale economics, and learning-by-doing. *American Economic Review*. 2005 May;95(2):243-7.

<sup>7</sup> Stevens W, Incerti D, et al. An empirical investigation of time-varying cost-effectiveness across the product life cycle. *Health Economics*. 2020 May;29(5):580-90.

treatments designed for individuals with disabilities and chronic illnesses. In a 2019 report, the National Council on Disability, an independent federal agency, found that use of the QALY is contrary to United States civil rights laws and due to its implications for disability discrimination.<sup>8</sup> The report specifically focuses on the United Kingdom's use of the QALY, highlighting cancer patients' lack of access to novel treatments and worse outcomes. PIPC encourages ICER to abandon the use of the QALY for this assessment and all those moving forward.

## Conclusion

PIPC has a strong interest in the evolution of patient-centric methods of value assessments so they serve as a usable tool for patients and providers in their decision making. We appreciate ICER's review of our comments on this assessment and are happy to offer further assistance if necessary.

Sincerely,



Tony Coelho

Chairman, Partnership to Improve Patient Care

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<sup>8</sup> National Council on Disability. (November 16, 2019). Quality-Adjusted Life Years and the Devaluation of Life with Disability. [https://ncd.gov/sites/default/files/NCD\\_Quality\\_Adjusted\\_Life\\_Report\\_508.pdf](https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf).