March 2, 2022

Steven D. Pearson, MD, MSc
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, MA 02108
Email: publiccomments@icer.org

RE: Public Comments ICER Draft Evidence Report for COVID Treatments

Dear Dr. Pearson:

The Innovation and Value Initiative (IVI) appreciates the opportunity to provide comments on the Institute for Clinical and Economic Review (ICER) Draft Evidence Report for Treatments for COVID-19.

IVI is a 501(c)(3) nonprofit research organization committed to advancing the science, practice, and use of value assessment in healthcare to make it more meaningful to those who receive, provide, and pay for care. Founded in 2017, the organization includes members from the research, patient, payer, purchaser, clinician, and innovator stakeholder communities. IVI's work emphasizes collaboration and exploration of new solutions that address our common values of patient-centricity, transparency, and vigorous enhancement of economic evaluation methods.

The COVID-19 pandemic has highlighted the uncertainties associated with evaluating the clinical and economic value of novel treatments. We agree with ICER that it is important to assess the health and economic outcomes of drugs for the treatment of mild-to-moderate newly diagnosed COVID-19. After review of the Draft Report, however, we have several concerns about the process and substance of the analyses.

IVI supports value assessment approaches that produce credible and relevant information to support decision making that maximizes benefits to patients with the greatest efficiency for the health system. To that end, IVI encourages ICER to conduct analyses that reflect and align with several key principles for value assessment:

Sustains Authentic Patient Centricity
- The Draft Report includes qualitative input from only three patients, which may not be seen as a representative sample for the purposes of this assessment.
    - Given the differential impacts of COVID on different subgroups in our society, it is crucial to engage with patients from diverse communities in the conceptualization of an economic model.

- Some of the key model inputs might not fully account for the impacts of COVID-19 and its treatments on patients.
    - Long-term sequelae after a COVID-19 infection and its disutility are sourced from an earlier paper (Sheinson et al.) that may not adequately reflect the long-term impacts of COVID hospitalization/recovery on patients.
    - This report should acknowledge how little we know here, and that this is an area where patient engagement is crucial.
- Several highlighted factors of importance to patients may not be adequately accounted for – specifically impacts on work and productivity. More robust estimates of costs for lost work for individuals and caregivers should be estimated as part of such analyses given evidence of impact.
    - This is particularly important from an equity standpoint, as impacts on career salaried employees are likely markedly different than impacts on hourly wage or service industry employees where loss of employment may be a factor.

Advances Transparency
- IVI believes that full access to the methodologies, calculations, and functioning of the model should be standard.
- By undertaking this analysis, ICER is endeavoring to contribute real-time learning in an evolving pandemic. More complete transparency of the model concepts and functioning would align with this commitment to common shared learning in the health economics and outcomes research (HEOR) space.
    - This transparency and model access are especially important here, given the evolving evidence base and need to continually update inputs and uncertain assumptions.

Focuses Value Discussion Across Treatment Interventions
- While the scope of this assessment is clearly focused on treatment interventions for mild to moderate COVID-19, IVI sees a missed opportunity by not addressing an obvious comparator: prevention measures, including masks and vaccination.
- As this assessment concludes that cost-effectiveness is similar for all available treatments and efficacy among sub-populations is established by ever-evolving evidence, there is limited utility for the findings to change practice or policy. Comparison with preventive measures – which could substantially change the trajectory of both the pandemic and its economic impact – could contribute important context and science-based insight to ongoing policy debates about resource allocation to prevention policies compared to treatment and mitigation.

Improves Clinical and Real-World Data
- As acknowledged by ICER, the model relies heavily on sparse clinical trial data, which could limit its applicability in the real world, especially in an environment where the virus is mutating rapidly and the treatment strategies to treat and/or prevent COVID are also rapidly evolving.
- To ensure this analysis delivers meaningful and accurate insights, IVI recommends that ICER postpone finalization of the report until more detailed clinical and real-world data

are available, or that explicit plans for ongoing updating of analyses be developed and followed.

Facilitates Customizable Decision-Making
- As stated above, allowing more open access to the cost-effectiveness model would allow interested stakeholders to customize analyses to match relevant populations more closely, to test different assumptions, or to include alternative or updated inputs as they become available.
- An "open-source", flexible, and transparent approach to model development, would allow stakeholders to work together as new evidence comes in, making the model more relevant and credible to various stakeholders.

Adapts To and With Evolving Evidence
- The report rightly acknowledges the ongoing evolution of evidence related to the pandemic and treatment strategies. Given the uncertainty of both treatment impacts and societal impacts, a more transparent and collaborative approach to this model's future development is warranted.
- ICER's draft report notes the many limitations of the evidence base but may not fully convey the inherent uncertainty from these limitations. Additional scenario analyses would help outline the potential magnitude of changes if uncertain assumptions are varied.

Supports Health Equity
- Subgroup analyses to consider and account for lack of representativeness in data should be clearly articulated.
- ICER noted that they reached out to manufacturers to ask for additional data by subgroup "such as race, vaccination status, variant of concern, time since randomization, serum antibody status, and individual risk factors for progression to severe disease" and stated that "data was [sic] either not available or insufficient to assess differential effectiveness in these populations". ICER also noted the "lower proportion of Black populations in the Phase III trials for molnupiravir and Paxlovid".
- Where clinical trial data might not reflect disparities in effectiveness or treatment outcomes in the real world, some indication of the likely impacts on under-represented subgroups (even if qualitative) could be useful to readers.
- Data inputs derived from a sample not representative of the target population might also result in model insights that could further exacerbate disparities.

Fosters Long Run Innovation
- A limited societal perspective was included as a scenario analysis, but it does not account for the full range of benefits potential treatments could have in the broader economy. This could lead to an under-estimate of the value of these therapies, which may be not only cost-effective, but also cost saving. Reimbursement and coverage decisions based on incomplete estimates could also deter long-run incentives for innovation.

Cultivates Modernized Methods

- Given the prevalence of COVID-19 and its profound societal impacts on a global scale, this is an opportunity for us to advance methods to incorporate some of the additional elements of value from the "value flower" developed by the [ISPOR special task force](#) (e.g., fear of contagion, equity considerations) and patient input/perspectives.

We appreciate the opportunity to provide input to ICER's Draft Evidence Report for Treatments for COVID-19. Please do not hesitate to contact us for further discussion.

Sincerely,

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