

July 29, 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 Ulcerative Colitis. Ulcerative Colitis (UC) is a painful and, at times debilitating, chronic illness that does not currently have a cure. UC patients are more likely than people without UC to experience other health conditions like cardiovascular disease and arthritis. Given the complications and comorbidities associated with UC, it is imperative to deliver more options of efficacious treatments to patients. With this in mind, PIPC asks ICER to consider the following comments:

ICER neglects to account for heterogeneity of patient population

UC is a highly heterogeneous condition. The presentation of symptoms and disease course can vary substantially among patients. In some, the disease course may reflect periods of active disease and remission, while in others the symptoms are persistent despite increased use of medical therapy. In addition, there are noted but currently poorly understood differences in how racial and ethnic minorities experience UC. The Crohn's & Colitis Foundation highlighted this heterogeneity in their initial letter to ICER, noting that treatment needs may vary greatly based on the specific patient's presentation of the disease: "UC is heterogeneous and the needs of each patient unique...Because each patient is unique and UC is a chronic and generally progressive disease, optimal care for the UC patient requires timely access to the full suite of treatments currently available."

Though ICER acknowledges the reality that UC patients are heterogeneous in their report, they neglect to represent this in their base case for cost-effectiveness and continue to base these judgements off of an "average" patient. Reliance on averages in cost-effectiveness analyses has shown to be illogicalⁱ and unscientific.ⁱⁱ It also results in very real harm for many patients whose experiences do not sit conveniently close to the averages portrayed in these sampling-based summaries of widely varying sets of outcomes.ⁱⁱⁱ As a result, new therapies that are likely to have significant impacts on the lives of patients with life-altering levels of discomfort and pain

will not be made available – or will have their access restricted – simply because other patients deemed to fall into the same disease category experience far less of such pain and discomfort, or experience it infrequently rather than constantly, diluting the effects of the former group.

ICER’s use of the QALY is inappropriate

PIPC would like to reiterate the point it has made to ICER in past comment letters that the use of the Quality-Adjusted Life Year (QALY) is inappropriate in assessing treatments for chronic illnesses. For many UC patients, incremental improvements in health without having to undergo surgery are significantly beneficial to their quality of life, even if they never achieve “perfect health.”

ICER’s use of the QALY in this report is particularly concerning because the utility weights used vary considerably from other published estimates.

ICER uses utility weights for active UC, clinical response without remission, and clinical remission of 0.69, 0.78 and 0.87 respectively.^{iv} Other published estimates of the utility weight of time spent in active UC not only vary considerably from the figure used in the base case for ICER’s report, but they also tend to have multiple figures describing various levels of severity of active disease. For example, Wohel et al^v and Tsai et al^{vi} estimate mild active UC at 0.72, but for moderate and severe disease the utility is estimated at 0.42. Similar estimates have been used in numerous UC treatment models in the last decade.^{vii} This is also the estimate of utility for severe disease that was suggested by the Evidence Review Group of NICE in recent submissions for amongst others vedolizumab.^{viii}

ICER’s choice to use a single “active disease” utility weight that represents an average across all patients with the disease, rather than one which represents the population with moderate to severe disease for which these drugs are indicated, is concerning. As mentioned previously, UC is a disease of significant heterogeneity in terms of severity.^{ix} It is inevitable that the utility weights for patients suffering moderate or severe disease will be lower, as their suffering is more extreme,^x and the use of an artificially higher utility weight for active disease will underestimate the value of any effective treatment as ICER’s model uses the utility weight as the most impactful input variable.

ICER omits outcomes that matter to patients

Patient advocacy groups have voiced concerns to ICER about the narrow scope of symptoms collected in clinical trials, which omit outcomes important to patients, like pain, fatigue, and depression. Published studies confirm the need to incorporate this data. One recent study of nearly 300 Crohn’s and UC patients found that 40% of respondents met criteria for chronic pain and nearly 20% reported opioid use,^{xi} and much of this pain was not directly explained by rate of

incidence of disease activity. Despite this consistent message from patient groups and researchers, it does not appear that these outcomes were incorporated into ICER's economic model.

ICER defines only three health states for the disease: active UC, response without remission, and response with remission. Even if we assume that a generic patient-reported outcomes (PRO) tool, like the EQ-5D or SF-36, effectively captures all the components of utility in UC including pain, fatigue, anxiety and depression, the fact that many of these will not be directly correlated with disease activity, and that they will vary considerably with severity of active disease, means that ICER's simplistic representation of the disease will have a negative impact across a considerably heterogeneous patient population who are known to show wide variance in terms of treatment effect. That heterogeneous group is currently represented by just one health state when in active disease, which has the detrimental outcome of failing to capture health gains properly for patients with more severe UC.

ICER missed an opportunity to evaluate true “value” to patients

Vedolizumab is a gut-selective biologic agent that is recommended as a potential first-line treatment for both induction and maintenance in UC but is often not covered by insurance until failure of other treatment options. In some cases, patients must try and fail at least two TNF inhibitors before vedolizumab is considered medically necessary and ultimately covered by payers, even despite clinical evidence that many patients do not respond to this biologic class. Patient advocacy organizations highlighted to ICER that one of patients' primary concerns around access to treatment is step-therapy.

ICER's assessments are frequently considered by insurers as they develop arduous step therapy guidelines. Step therapy is primarily used by payers as a utilization management tool to help contain costs, and there is no evidence to suggest the use of step therapy improves health outcomes. Given that ICER's stated goal is to determine true clinical and cost-effectiveness of treatments, and to optimize value in the United States healthcare system, this would have been an opportunity to evaluate the impact of step therapy on clinical outcomes in UC patients. It is a worthy question to determine whether there is any long term 'value' in the payer community's reliance on step therapy,^{xii} which has been shown to result in very real harm to patients.^{xiii} This could have been easily modeled through a scenario analysis to assess the value of treatment pathways with and without step-therapy.

There is evidence that in the case of ulcerative colitis, the vast majority of insurance medical policies around prescribing for UC are incompatible with current American Gastroenterological Association (AGA) clinical pathway recommendations.^{xiv} ICER's UC assessment represents a missed opportunity to develop a comprehensive modeling exercise comparing step therapy to a

system where patients are prescribed the most effective treatment indicated for them based on their physician's expert diagnosis, disease progression, individual patient characteristics, and relevant clinical society guidelines. ICER's decision not to capitalize on this opportunity contradicts its previously stated goal to determine the true value of treatments and is another missed attempt to better account for outcomes that matter most to patients.

Conclusion

UC is a condition that impacts a very heterogeneous patient population, and treatment can vary greatly from patient to patient. For this reason, it is imperative that ICER account for this heterogeneity within its model and consider improving its methods.

Sincerely,



Tony Coelho
Chairman
Partnership to Improve Patient Care

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^{iv} Malinowski KP, Kawalec P. Health utility of patients with Crohn's disease and ulcerative colitis: a systematic review and meta-analysis. *Expert Rev Pharmacoecon Outcomes Res*. 2016;16(4):441- 453.

^v Woehl A, Hawthorne B, Morgan C, Puneekar Y, McEwan P. The epidemiology and healthcare resource use in patients with Crohn's disease: a population based UK study. *Value Health* 2007; **10**: A355.

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^{vii} Chaudhary MA, Fan T. Cost-effectiveness of infliximab for the treatment of acute exacerbations of ulcerative colitis in the Netherlands. *Biologics in therapy*. 2013 Jun 1;3(1):45-60.

^{viii} <https://www.nice.org.uk/guidance/ta342/chapter/3-The-company-submission#cost-effectiveness>

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^x Walmsley RS, Ayres RC, Pounder RE, Allan RN. A simple clinical colitis activity index. *Gut*. 1998 Jul 1;43(1):29-32.

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^{xii} Fischer MA, Avorn J. Step therapy—clinical algorithms, legislation, and optimal prescribing. *Jama*. 2017 Feb 28;317(8):801-2.

^{xiii} Soumerai SB, Zhang F, Ross-Degnan D, Ball DE, LeCates RF, Law MR, Hughes TE, Chapman D, Adams AS. Use Of Atypical Antipsychotic Drugs For Schizophrenia In Maine Medicaid Following A Policy Change: Discontinuities in use of these critical drugs became apparent after Maine Medicaid instituted prior authorization and step therapy. *Health Affairs*. 2008;27(Suppl1):w185-95.

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