PATIENTS RISING NOW

February 18, 2021

Steven D. Pearson, MD, MSc, FRCP
President, Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

RE: Draft Evidence Report "Belimumab and Voclosporin for Lupus Nephritis"

Dear Dr. Pearson:

Patients Rising Now advocates for patients with serious and chronic conditions to have access to life-improving and life-saving therapies and services. Access to such treatments and services is essential, and it spans affordability, insurance coverage and physical access. To support improved access, we are committed to engaging patients, caregivers, clinicians, media, health policy experts, payers, providers and others to foster people-centered discussions about the entire U.S. health care system. That is, our goal is a balanced dialogue that illuminates the truth about health care innovations and advancements in a just and equitable way.

We appreciate the opportunity to provide our comments on ICER's January 22nd Draft Evidence Report, "Belimumab and Voclosporin for Lupus Nephritis: Effectiveness and Value." Our comments about the draft report are organized below into sections about People-Centered Perspectives; and Modeling, Projections and Assumptions.

**Before presenting our comments in those areas, now that voclosporin has been approved by the FDA, and important pieces of information accompanied that approval are available – including some black box warnings – we strongly recommend that ICER redo and reissue its draft report to allow for additional public comment before moving to hold a meeting with its advisory committee, and finalizing a report.**

People-Centered Perspectives

We appreciate the outreach that ICER made to patient groups and the information shared in the draft report's Section 2: "Patient and Caregiver Perspectives." And we share ICER's frustration that the clinical trials on the two specific medicines newly approved for treating nephritis in people with lupus did not include evaluations of quality of life or other real-world metrics important to patients. We believe that those deficits highlight the need for additional discussion and advocacy for inclusion of such metrics in all critical trials, rather than potentially leaving that to follow-on studies. We also agree with ICER's observation that having an oral treatment option may be of significant value to patients, particularly those with travel or mobility limitations.

We note that ICER didn't reference its own very recent work on chronic kidney disease[i] to bring some context about how this condition can affect overall quality of life. We find this omission disappointing. If ICER is so compartmentalized that it cannot recognize its own related reports, then we must question if ICER understands and is capable of promoting team-based care, value-

based systems of care, and reimbursement mechanisms to promote those advances that are widely seen as potentially benefitting both patients and the overall U.S. health care system.

As we consider the scope of the draft report, we are disappointed in ICER's overall presentation of lupus nephritis as a clinical condition. Like too many clinicians, researchers and analysts, the draft report is too tightly focused on nephritis as a sequela of lupus. We are very concerned about this very narrow scope because people with lupus who may develop nephritis as part of their myriad manifestations from having lupus are not – and should not be seen as – "kidneys who have lupus."

The importance of this type of whole-person focus is clearly stated in the Lupus Patient's Voice report that was conducted in parallel with the FDA's Patient-Focused Drug Development Initiative. The Report "was created by the FDA to allow regulators to more effectively understand, in a systematic manner, the unique perspective of people with diseases such as lupus to better assess the risks and benefits of drugs under review."[ii] As that report states, "Lupus is a chronic, **systemic**, and often disabling autoimmune disease **with an unpredictable course and inadequate treatment options**."[iii] (emphasis added) The report also discussed the high incidence of other autoimmune diseases in people with lupus, underscoring the need for whole-person considerations in their clinical care.

ICER needs to do a much better job of encompassing the whole-person concept of value into its work beyond the discussion in Section 2 of the draft report related to symptoms such as fatigue, and life choices that may be limited because of disease progression. Those discussions are most useful when ICER incorporates those very important issues in its analysis. Unfortunately, in this case, ICER did not do so. We realize that without data, inclusion of such factors is difficult, but that cannot be an excuse for disregarding those factors entirely. And for important issues where there is limited data, that uncertainty should be incorporated into the draft report's analyses, conclusions, and discussions to a much greater extent than ICER has been doing.

And lastly, given that the FDA approved label for voclosporin contains a black box warning, ICER should include a discussion of the significance of such a warning for patients, and how that information should be considered as part of patients' shared decision-making with their clinicians.

Modeling, Projections and Assumptions

The draft report makes an assumption about the price of voclosporin that was based on a single report's four-years old guestimate.[iv] That assumption was clearly very significantly wrong, and for very predictable reasons: The old assumption that voclosporin would be priced at a 10% discount to belimumab, (which was four years away from getting a secondary approval for lupus nephritis), was clearly a broad swath "placeholder" that was the same as three other potential treatments in the report, and apparently based on the premise that later entrants in a treatment area would be priced at a discount to gain market share. This type of "placeholder" may be appropriate when there is no information about the clinical (and other) benefits of each treatment. HOWEVER, the draft report's Figures E5 and E8 (copied below) clearly show the QALY benefits of voclosporin being separated from standard of care to a greater extent than is the case for belimumab.

**Figure E5. Cost-Effectiveness Clouds for Belimumab and Standard Care**

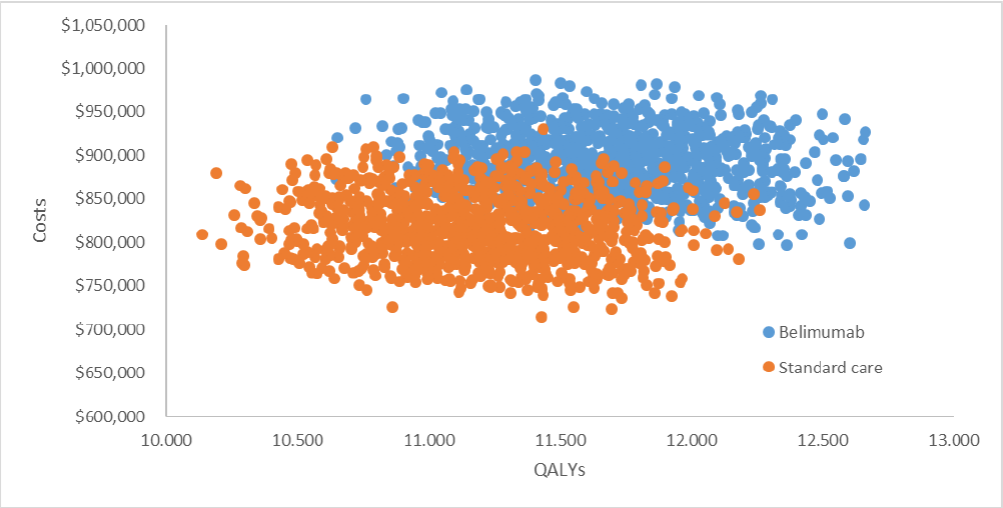
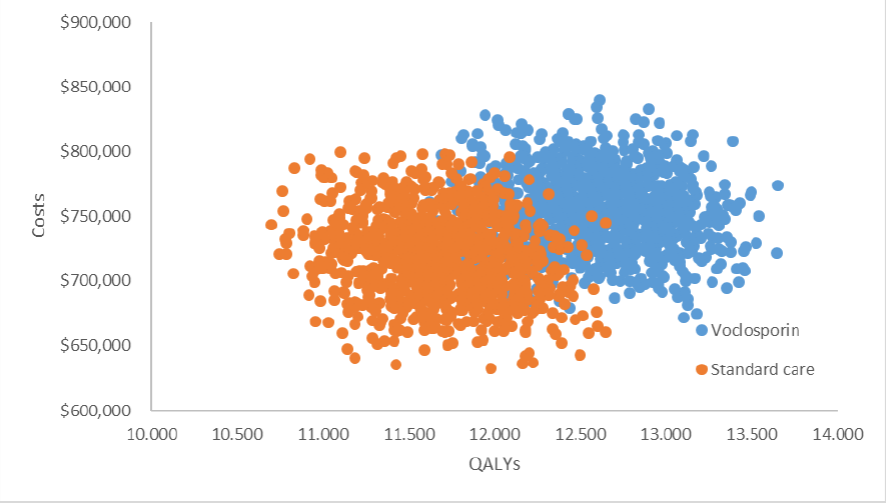



**Figure E8. Cost-Effectiveness Clouds for Voclosporin and Standard Care**




We also note the different QALY scales on the x-axes in those Figures, and their size in the draft report. (The figures above are the actual size as in the draft report.) Using the same x-axis scale in both Figures and making each Figure the same size in the draft report would have been a much better, clearer representation of the data.

Now that voclosporin has been approved by the FDA, its actual list price and reported net revenue per patient have been reported.[v] The estimated revenue of $65,000 per year to the company (which we assume is equivalent to the net price since it is much lower than the reported list price of $144,175 based on $3,950 for a ten-day supply at full dosage),[vi] represents a cost per QALY that – according to our analysis of the information ICER included in the draft report – is approximately 25% less than the cost per QALY for belimumab.[vii]

Given that the definition of value is benefits (which could include clinical, patient, health system, and society benefits) divided by cost, the company's reported pricing for voclosporin seems to be completely appropriate, and since it is orally administered, an even higher net price could be justified. That is, the company's pricing for voclosporin reflects the clinical and other benefits it provides.

It could be asserted that ICER's draft report (which was released on the same day as the FDA's approval of voclosporin) provided data and rationale for the company's pricing decisions. In that vein, some may point to ICER as reason for this new drug having a higher price than previously projected. However, as all good analysts and researchers understand, correlation does not prove causation. We are much more inclined to believe that the company understood their own data, could compare it to that of existing treatment options – including belimumab – and derived a price (including expected rebates and discounts, etc.) to determine a price consistent with its value to the patient, society, and the health care system that would also enable it to have favorable reimbursement and coverage by payers and adoption by clinicians.

And lastly, the newly approved label for voclosporin[viii] includes guidance for lowering the daily dosing for people with reduced kidney or liver function. We did not see that adjustment in ICER's modeling assumptions. We would appreciate ICER providing insights about that clinical situation. For example, did ICER include that reduced dosing into its modeling, did ICER not know about such dosage adjustments in the clinical trials or from the deliberations by the FDA's advisors, or was it assumed that the number of people who would be using such lower dosages was not knowable or would be very small, etc.?

Conclusions

Patients Rising Now is pleased that people with lupus – should they have or develop nephritis – now have two new and better treatment options that are both clinically and cost effective. We are glad that ICER's draft report reached a similar conclusion. However, given that voclosporin has now been approved by the FDA, we strongly urge ICER to redo its work on the draft report based upon the now available FDA label and price information, and reissue an updated draft report for further comment by the entire array of stakeholders – particularly patient groups and clinician experts.

Sincerely,

Terry M. Wilcox

Terry Wilcox
Co-Founder & Executive Director, Patients Rising Now

[i] https://icer.org/assessment/anemia-in-chronic-kidney-disease-2021/#timeline

[ii] "Lupus: Patient Voices," Report on Externally-led Patient-Focused Drug Development Meeting: September 25, 2017, http://lupuspfdd.org/LupusPatientVoicesFINAL.pdf

[iii] "Lupus: Patient Voices," Report on Externally-led Patient-Focused Drug Development Meeting: September 25, 2017, http://lupuspfdd.org/LupusPatientVoicesFINAL.pdf

[iv] "Immunotherapies in Late-Stage Development for Patients With Severe SLE and/or Lupus Nephritis," P T. June 2017;42(6):394-397; citing data source for pricing strategies in Table 1 as: Gehrke SS. PharmaPoint: Systemic Lupus Erythematosus and Lupus Nephritis—Global Drug Forecast and Market Analysis to 2025. New York, New York: GlobalData; December 2016.

[v] "FDA approves first-of-its-kind lupus drug," BioPharma Dive, January 25, 2021, https://www.biopharmadive.com/news/fda-aurinia-approval-lupus-oral-drug/593898/

[vi] "FDA approves first-of-its-kind lupus drug," BioPharma Dive, January 25, 2021, https://www.biopharmadive.com/news/fda-aurinia-approval-lupus-oral-drug/593898/

[vii] Using $65,000/year as the net price to recalculate the Incremental Cost Effectiveness Ratio in the draft report's Figure 4.6 results in an amount of approximately $110,000, which is about 25% less than the Incremental Cost Effectiveness Ratio for belimumab as presented in Figure 4.5.

[viii] https://www.auriniapharma.com/lupkynis-prescribing-information - See Section 2.3 Dosage Recommendations.