



**Institute for
Patient Access**

October 22, 2018

Submitted electronically to: publiccomments@icer-review.org

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

Re: Draft evidence report for severe asthma therapies

Dear Dr. Pearson:

On behalf of the Institute for Patient Access and the partner organizations signed herein, I thank you for the opportunity to provide comments regarding ICER's draft evidence report for severe asthma therapies.

About the Institute for Patient Access

The Institute for Patient Access (IfPA) is a physician-led policy research organization dedicated to maintaining the primacy of the physician-patient relationship in the provision of quality health care. IfPA was established in 2012 by the leadership of the Alliance for Patient Access, a national network of more than 800 physician advocates committed to patient access. IfPA is a 501(c)(3) public charity nonprofit organization.

Impact of Severe Asthma

As detailed in ICER's draft evidence report, severe asthma is a challenging lung disease that afflicts millions of Americans. The report explicitly notes the costs that severe asthma imposes on patients, explaining that:

- Severe asthma leads to approximately 14.2 million office visits, 1.8 million emergency room visits, and 440,000 hospitalizations each year in the United States.
- Severe asthma costs society an estimated \$82 billion, including \$50 billion in direct medical costs, \$29 billion from asthma-related mortality, and \$3 billion from missed work and school.

- Individuals with severe asthma represent fewer than 5-10% of all individuals with asthma but account for approximately 50% of all costs.

Access to Clinically Effective Medicine for Severe Asthma

Mitigating the high cost of severe asthma requires, in part, access to the appropriate medications. Those include the five monoclonal antibodies indicated for the treatment of patients with moderate to severe asthma that were reviewed in this draft evidence report.

These medicines are clinically effective, as the report notes. Specifically, the report cites that the five therapies reduce asthma exacerbation rates by 50 percent.

Nevertheless, the report still finds that the drugs are not cost-effective at their current prices.

We urge ICER to reconsider this conclusion for two reasons:

- 1.) The draft evidence report has significant shortcomings, including data and methodological limitations, the inability to incorporate significant unquantifiable costs associated with severe asthma, and analyses performed in the draft evidence report that are still incomplete.
- 2.) **ICER's conclusion could inappropriately restrict patients' access** to appropriate and effective medications.

Exclusion of Quality-of-Life Factors

Many costs that are disproportionately borne by the uncontrolled asthma population are difficult to quantify. Yet, the methodological challenges of valuating these costs do not reduce the burden they place on patients. Ignoring many of these costs, as the draft evidence report does, significantly underestimates the benefits provided by the medicines reviewed.

Link between Uncontrolled Asthma and Comorbidities

Some of the costs that are difficult to quantify include the links between uncontrolled asthma and other comorbidities, such as psychiatric diseases and cardiac diseases that are particularly problematic for seniors with asthma. The estimated benefits from the medications do not account for a potential reduction in comorbidities.

Reduced Quality of Life

Other costs are due to the reduced quality of life that severe asthma imposes on patients living with the disease. These unquantifiable costs include the inability to engage in typical daily activities, the inability to exercise, inability to sleep, and increased student absences from school. While the report mentions several of these costs, the value of these costs is not included in the analysis.

Similarly, the ICER review considered the financial losses associated with work absences (such as lost earnings) for adults with uncontrolled asthma, but the study did not consider the losses associated with people with severe asthma being less productive while at work; nor the problems of people with severe asthma obtaining less education or requiring more social and legal services.

Lifelong Impact on Children

In section 5.2, the review acknowledges that "asthma is a life-long disease and for children suffering from severe, poorly controlled asthma, the disease may impact the entire trajectory of their lives." Yet, the costs of such impact on children are not considered in the review. With uncontrolled asthma making up 34 percent of all children with asthma, it is imperative to consider the unique costs of uncontrolled asthma in children.

Inability to Account for Ethnic Disparities

There are also important income and ethnic disparities with respect to the treatment of asthma that should be noted. For example, asthma prevalence and mortality are highly related to poverty. With respect to ethnicities, African Americans are three times more likely to be hospitalized due to asthma, and three times more likely to die from asthma. African American women have the highest mortality rate due to asthma. Hispanics and Puerto Ricans are also at higher risks to environmental hazards leading to allergic or asthmatic responses.

Since these groups disproportionately suffer asthma-related consequences, they will also disproportionately benefit from medicines that more effectively control asthma symptoms. However, this draft report does not account for the income and ethnic disparities of asthma.

Limited Scope of Studies Reviewed

An important limitation of the results reported in the draft evidence report is the limited scope of the data ICER reviewed. In designing the criteria for the analysis, ICER identified variables that determine the value of medicines designed to treat moderate-to-severe-asthma. These variables included the number of emergency room visits, the number of hospitalizations, and several quality of life indicators typically applied to asthma patients.

In many cases, however, the majority of studies ICER reviewed did not even report on the factors of interest. For example:

- Only two out of the 18 studies collected data on "Change in AQLQ (Asthma Quality of Life Questionnaire) and SGRQ" indicators
- Only three out of the 18 studies collected data on "Reductions in OCS (Oral Corticosteroids) Dose" as key quality of life indicator

- Only seven out of the 18 studies collected data on annual rate of ER visits and hospitalizations
- Only nine out of the 18 studies collected data on change in FEV1 change from baseline pre/post bronchodilator.

Methodological Shortcomings

Beyond its data limitations, the draft evidence report also raises methodological concerns.

Specifically, page 17 of the report states that: “given the residual heterogeneity across studies, we consider this analysis exploratory.” Exploratory data analyses are typically a first step in the data analysis process. Once exploratory data analyses are complete, it is common for researchers to perform more formal statistical analyses on the data set. As the report notes, however, such a formal analysis cannot be performed because of the heterogeneous nature of existing research.

Relying on an exploratory analysis introduces an unacceptable amount of uncertainty into the reported results. Further, since the clinical effectiveness results contain unknown errors, cost calculations that utilize the clinical results will also contain unknown errors. Therefore, the cost effectiveness results reported in the draft evidence report are likely inaccurate.

Timing & Incomplete Analysis

In two instances the draft evidence report notes that the analysis is incomplete, but additional analyses will be performed for the final report.

Specifically, page 26 notes:

We requested data from manufacturers in the subgroup of patients with eosinophils ≥ 300 cells/ μ L and two or more exacerbations in the year prior to randomization, but received data too late for the draft review. **We will update our NMA with the additional data for the final report.** (emphasis added)

And page 28 states:

Because of the residual heterogeneity of the underlying patient populations and the definitions of exacerbations used across trials, we consider this to be an exploratory analysis. **We hope to have more homogenous data from the manufacturers prior to the final report.** (emphasis added)

Additional data and new analyses could materially change the clinical effectiveness and cost effectiveness of these drugs as presented in the final report. Thus, *the opportunity to*

provide input at this stage is perfunctory; it is an opportunity to respond to a draft that could be unrepresentative of the final analysis.

If stakeholders' input bears any weight in this process, ICER would have waited and released the report for public comment after all applicable data was incorporated. Alternately, ICER could offer stakeholders the chance to respond to a more representative, second iteration of the draft.

Conclusion

Based on the current iteration, this analysis provides an inaccurate, incomplete picture of the benefits created by these new biologic medicines for the treatment of asthma. IfPA and the undersigned partner organizations urge ICER to address the concerns related to this draft evidence report.

If IfPA can provide further detail or aid the Institute for Clinical and Economic Review in incorporating any of the above recommendations into its report, please contact Brian Kennedy at 202-499-4114.

Sincerely,

Institute for Patient Access
American Association for Respiratory Care
Allergy & Asthma Network
American College of Allergy, Asthma, & Immunology