October 12, 2021

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 on Tezepelumab for Severe Asthma

Dear Dr. Pearson:

On behalf of the Institute for Patient Access and Allergy & Asthma Network, we thank you for the opportunity to provide comments regarding ICER's *Draft Evidence Report on Tezepelumab for Severe Asthma*.

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. To further that mission, IfPA produces educational materials and programming designed to promote informed discussion about patient-centered care. IfPA was established in 2012 by the leadership of the Alliance for Patient Access, a national network of health care providers committed to shaping a patient-centered health care system. IfPA is a 501(c)(3) public charity nonprofit organization.

About the Allergy & Asthma Network

Allergy & Asthma Network is the leading national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy & research. The Network specializes in sharing patient-friendly, medically accurate information through its award-winning magazine Allergy & Asthma Today, E-newsletter, AllergyAsthmaNetwork.org and numerous community outreach programs.

Draft Evidence Report Comments

As ICER finalizes its evidence report, IfPA and AAN urge you to consider several important points.

Clinical Data Shows Tezepelumab to Be an Efficacious Treatment

As the draft evidence report notes, clinical trials indicate that tezepelumab is an efficacious treatment that uses a different mechanism of action. As reported in Allergic Living:

> in a large Phase 3 clinical trial, the biologic drug tezepelumab was able to reduce asthma exacerbations by 56% over a year in adult and teen patients with severe, uncontrolled disease. The rate of reduction is considered clinically meaningful.[1]

While reporting on the results of its Phase III trial, AstraZeneca noted that tezepelumab is "the only biologic medicine to consistently and significantly reduce AAER [annualized asthma exacerbation rate] in a broad population of severe asthma patients irrespective of baseline eosinophil count."[2]

Based on these positive clinical results, tezepelumab is a new and valued treatment option for patients, especially for patients living with severe uncontrolled asthma.

More Treatment Options & New Mechanisms of Action are Valuable to the Asthma Community

Just as asthma impacts people differently, existing treatment options serve some patients better than others. Some people's asthma conditions are mild or moderate, and intermittent symptoms may be well controlled by the current standard of care. Others live with severe asthma, which may or may not respond to the current standard of care. For those who don't respond to existing treatments, their asthma may progress to a more severe or uncontrolled state. And, while asthma symptoms have an impact on patients' lives regardless of severity or frequency, severe asthma in particular can reduce quality of life and hamper patients' ability to sleep, maintain mental health, exercise, stay focused at work or school, or participate in social or extracurricular activities.

These considerations are complicated by the reality that asthma is a chronic disease that will often impact people over their entire lives. The severity of the disease tends to worsen as people age, which can be complicated by waning efficacy of patients' current treatments over time. The fact that current treatments are controlling patients' asthma symptoms today does not guarantee that their symptoms will be well controlled tomorrow.

Existing medications, including targeted biologic therapies, prove valuable and effective for many asthma patients. Through increasing efficacious treatment options by introducing a new mechanism of action, tezepelumab increases the likelihood that patients and their clinicians can find an effective regimen to control the disease and its symptoms – reducing dangerous or expensive exacerbations, added physician appointments and visits to the ER.

As a new medicine with a novel mechanism of action, tezepelumab represents an important addition to the asthma community's treatment options. While the value of expanding treatment

[1] Goodwin J and Smith G "Dupilumab Remission; Tezepelumab in Severe Asthma" Allergic Living, March 2, 2021, https://www.allergicliving.com/2021/03/02/aaaai-news-dupilumab-remission-tezepelumab-in-severe-asthma-palforzia-safety/.

[2] https://www.astrazeneca.com/media-centre/press-releases/2021/tezepelumab-is-the-first-biologic-to-consistently-and-significantly-reduce-exacerbations-in-broad-population-of-severe-asthma-patients.html.

options is difficult to quantify, it is imperative that these considerations be documented in the final evidence report.

Severe Uncontrolled Asthma Exacts a High Cost

These considerations are particularly important for people living with severe asthma and for whom the current standard of care is ineffective, including people with severe uncontrolled asthma. As noted in the draft evidence report, the CDC estimates that 25 million Americans are living with asthma, and that patients with severe uncontrolled asthma represent an estimated 5-10% of total asthma cases.[3] These figures suggest that there are currently between 1.3 million and 2.5 million people in the United States living with severe uncontrolled asthma.

Severe uncontrolled asthma meaningfully reduces patients' quality of life and, in extreme cases, can even be fatal. In fact, severe uncontrolled asthma is recognized as a "major unmet medical need" by the medical community.[4] Based on the current clinical trial results, tezepelumab will help fill this major unmet medical need. If properly applied to the small share of patients with severe uncontrolled asthma, the total societal cost estimates cited in the draft evidence report provide a useful benchmark for understanding the potential value of tezepelumab.

As the draft evidence report documents, the total societal costs are an estimated $82 billion, inclusive of direct medical costs, asthma-related mortality, and missed work and school. As with most diseases, however, these societal costs are not evenly distributed across all patients. Instead, a small minority of patients bear a disproportionate share of these costs. In the case of asthma, it is the patients living with severe uncontrolled asthma who bear a disproportionate share of the costs.

According to a study in the Journal of Allergy and Clinical Immunology, "retrospective claims research indicates that approximately half of asthma-related direct costs are incurred by patients with severe asthma."[5]

Worth noting, the health and economic burdens of severe and uncontrolled asthma are projected to significantly grow in the future, increasing still further the value of an efficacious treatment. Looking at the costs of uncontrolled asthma over the long-term, Yaghoubi et. al. estimated the 20-year direct costs to be $300.6 billion, or a total economic burden of $963.5 billion when indirect costs are included. The researchers expect American adolescents and adults to "lose an estimated 15.46 million QALYs over this period because of uncontrolled asthma."[6]

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[3] See also, Kupczyk M and Wenzel S. U.S. and European severe asthma cohorts: what can they teach us about severe asthma? J Intern Med 2012; 272:121–32. Wenzel S. Severe Asthma in Adults. Am J Respir Crit Care Med. 2005; 172; 149–60.

[4] Kupczyk M and Wenzel S. U.S. and European severe asthma cohorts: what can they teach us about severe asthma? J Intern Med 2012; 272:121–32.

[5] Hankin CS, Bronstone A, Wang Z, Small MB, and Buck P "Estimated Prevalence and Economic Burden of Severe, Uncontrolled Asthma in the United States" The Journal of Allergy and Clinical Immunology, Volume 131, Issue 2, February 1, 2013, https://www.jacionline.org/article/S0091-6749(12)03119-3/fulltext.

[6] Yaghoubi M, Adibi A, Safari A, FitzGerald JM, and Sadatsafavi M "The Projected Economic and Health Burden of Uncontrolled Asthma in the United States" American Journal of Respiratory and Critical Care Medicine, June 5, 2019.

Per-Patient Costs Better Reflect the Expense of Severe Asthma & the Value of Effective Treatment

Assuming the costs associated with asthma-related mortality and missed work and school are due to severe asthma, patients living with uncontrolled severe asthma account for $57 billion of the total costs of asthma, or per-patient costs up to nearly $44,000. These substantial per-patient costs signify the high value of an efficacious medicine that can control or lessen severe asthma symptoms and help lower the current costs borne by severe asthma patients and their families.

The cost-effectiveness analysis should explicitly account for the $44,000 in per-patient costs due to severe uncontrolled asthma when evaluating the value of tezepelumab. It is, consequently, imperative that the final evidence report incorporate these higher but more applicable per-patient costs estimates and acknowledge the reality that the costs associated with severe uncontrolled asthma will likely increase significantly without access to an effective treatment.

The Cost-Effectiveness Analysis Should Account for Severe Asthma's Demographic Disparities

The draft evidence report should also more fully account for the reality that African American, Hispanic and Native American communities bear a larger burden from asthma than do other demographic groups. Some of the troubling trends include:[7]

- Black Americans are nearly 1.5 times more likely to have asthma, five times more likely to visit the emergency room due to asthma, and three times more likely to die from asthma compared to white Americans
- Puerto Ricans are twice as likely to have asthma and have a nearly three-fold higher rate of asthma-related deaths than the broader Hispanic and white populations in the United States
- Native Americans are nearly twice as likely to experience asthma symptoms every day and have a 10% higher risk of death from chronic lower respiratory diseases relative to white Americans.

In evaluating the value of tezepelumab for people with severe and uncontrolled asthma, the disproportionate impact of asthma on people of color is an important consideration. We urge ICER to account for these impacts in its final report.

Cost Assumptions Do Not Account for the Temporary Nature of Product Exclusivity

The lifetime cost estimates do not appear to account for the temporary nature of product exclusivity. Even if the draft evidence report's assumed price were accurate in the short term, the price for the medicine should be expected to decline over time once product exclusivity expires. For instance, as GoodRx has noted, while the average cash price for branded Advair was $496 in 2018, "the lowest GoodRx price for the most common version of generic Xopenex HFA is around $32.39."[8]

[7] https://www.aafa.org/asthma-disparities-burden-on-minorities.aspx.
[8] Marsh T "Here's Why Asthma Inhalers Are So expensive" GoodRx, June 8, 2020, https://www.goodrx.com/conditions/asthma/heres-why-asthma-inhalers-are-so-expensive.

As with other chronic diseases, the costs of asthma medication will stretch across a lifetime. Since the average market exclusivity period is around 12 years, it is reasonable to expect the price of the tezepelumab to decline over time, which will significantly reduce the expected lifetime treatment costs. Lower lifetime treatment costs will meaningfully alter the cost-effectiveness of tezepelumab, even at the assumed price. The final evidence report could offer a more realistic outlook were it to account for competition's impact on medication costs over the relevant study timeframe.

Conclusion

IfPA and AAN urge ICER to address our concerns related to this draft evidence report. Based on the current iteration, ICER's analysis provides an inaccurate picture of the benefits created by tezepelumab for the treatment of asthma. If IfPA or AAN 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 IfPA at 202-951-7097.

Sincerely,

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Institute for Patient Access

Tonya S. Winders
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Allergy & Asthma Network