PATIENTS RISING NOW

Guide for Commenting on ICER's Draft Evidence Report on Treatments for Asthma

On September 16, 2021, ICER released its draft evidence report, "Tezepelumab for Severe Asthma: Effectiveness and Value." This guide provides a framework for considering what aspects of the new treatment for asthma are important to patients and their families, and how to consider presenting those perspectives. This guide specifically provides insights about how to read and respond to ICER's draft evidence report, as well as how to request a slot to make comments during ICER's public meeting.

Key Dates

September 16, 2021:	Draft Evidence Report released
October 14, 2021:	Written comments due by 5:00pm ET; deadline to submit request to speak at Public Meeting
November 4, 2021:	Updated Evidence Report released
November 19, 2021:	Public Meeting conducted by ICER's Midwest Comparative Effectiveness Public Advisory Council (CEPAC)
December 16, 2021:	Final Evidence Report and Public Meeting Summary released

Background & How to Participate

The Institute for Clinical and Economic Review (ICER) is a private entity that uses its own analytical process and "value framework" to assess potential new treatments for a variety of diseases. Those assessments often occur before FDA approval, and may result in conclusions that could harm patients by limiting access to new and innovative treatments. You can learn more about ICER here.

There are two primary ways advocates and other stakeholders can give input:

1. **Submit written comments on the draft report, which are due to ICER no later than 5:00pm ET on October 14th.**
2. **Request a slot to make oral comments during ICER's November 19th meeting.**

Submitting written comments on the draft report

Written comments must be submitted to publiccomments@icer.org as a Word document in 12-point Times New Roman font, and are limited to 5 pages, not including references or appendices. The deadline to submit written comments is 5:00pm ET on October 14, 2021.

Requesting a slot to make oral comments

ICER's public meeting on its revised report and discussion by one of its advisory committees is scheduled for November 19th, and will be held virtually. The meeting will have a short period available for public comments. To request a slot to make public comments, an email needs to be sent to publiccomments@icer.org with the person's name, title, and organization. The deadline to make a request to speak is 5:00pm ET on October 14, 2021. Oral comments are limited to no more than five minutes per speaker.

NOTE: Not all requests to make public comments are granted. According to ICER: "We sort through all the requests to make an oral public comment at the meeting. Because we only have a limited time for oral comments at the public meeting, we can only allow a few stakeholders to share their perspective."

Key Points to Consider for Written or Oral Comments

Clinical Effectiveness

- ICER's review of asthma is focused on tezepelumab, a potential medicine that is still pending FDA review. The FDA is expected to make a decision on this treatment during the first three months of 2022.

- Tezepelumab is a potential new treatment for asthma that acts on a different pathway from other treatments for asthma. Tezepelumab acts by blocking thymic stromal lymphopoietin (TSLP), which is earlier in the cascade of inflammatory processes that causes asthma attacks compared to the actions of the other asthma medicines ICER examines in the draft evidence report: dupilumab (Dupixent®) and omalizumab (Xolair®). Because of tezepelumab's novel mechanism of action, the FDA gave it a "breakthrough therapy" designation.

- No studies have compared tezepelumab to either dupilumab (Dupixent®) or omalizumab (Xolair®), so ICER's draft evidence report relied on data from different trials. Thus, in doing its clinical and cost effectiveness "analyses," ICER combined data from multiple trials even though the structure of those trials and the

characteristics of the people varied. Those differences raise serious questions about the accuracy and validity of ICER's alleged findings.

- ICER's review is based on three trials: one large phase 3 trial with 1,061 people over 52 weeks, (529 receiving 210mg of tezepelumab every 4 weeks, and 532 who received placebo); an older, smaller phase 2 trial over 52 weeks with 550 people (138 people who received 70mg of tezepelumab every 4 weeks, 137 received 210mg, 137 received 280mg, and 138 in the placebo group): and an even smaller phase 3 trial of 150 people that lasted 48 weeks looking at reduction in oral steroid use in people receiving tezepelumab who had been taking oral steroids for at least 6 months as well as other medicines to control their asthma.

- The results of the large Phase 3 trial were good, with improvements seen in clinical status with people receiving tezepelumab. Specifically, the study showed that people receiving tezepelumab had fewer exacerbations of their asthma per year compared to people receiving placebo (0.93 v. 2.10). This study also found that people receiving tezepelumab had a longer time before having a first exacerbation (see Figure S5 below). And perhaps most insightfully, 56.3% of the people receiving tezepelumab did not have any asthma exacerbations in the year, compared to only 39.9% of people receiving placebo (see Figure S4 below.) This finding is very important because it highlights how new medicines – such as tezepelumab – often benefit some people more than others.

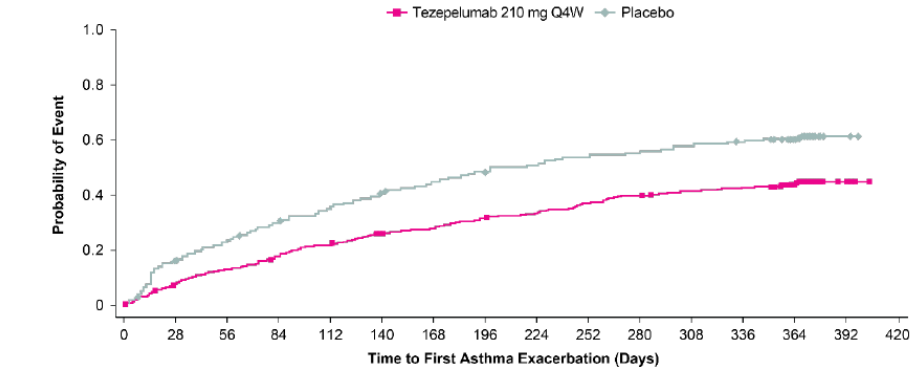

Figure S5. Time to First Exacerbation.

Q4W, every 4 weeks.

[Source: Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med, May 13, 2021 – Supplemental Appendix]

Table S4. Number of Asthma Exacerbations Experienced by Patients and Total Time at Risk of Exacerbation.

	Tezepelumab 210 mg Q4W (N=528)	Placebo (N=531)
No. of exacerbations		
0	297 (56.3)	212 (39.9)
1	135 (25.6)	126 (23.7)
2	48 (9.1)	70 (13.2)
3	27 (5.1)	36 (6.8)
4	7 (1.3)	32 (6.0)
5	9 (1.7)	18 (3.4)
≥6	5 (0.9)	37 (7.0)
Total time at-risk — yr	504.0	482.1

Data are no. (%) unless otherwise stated.

Q4W, every 4 weeks.

[Source: Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med, May 13, 2021 – Supplemental Appendix]

- The large phase 3 trial also showed that the people with asthma receiving Tezepelumab were quickly able to exhale better, which is a key measure for asthma since the disease causes inflammation and constriction of the airways that makes beathing out more difficult (see Figure S5 below).

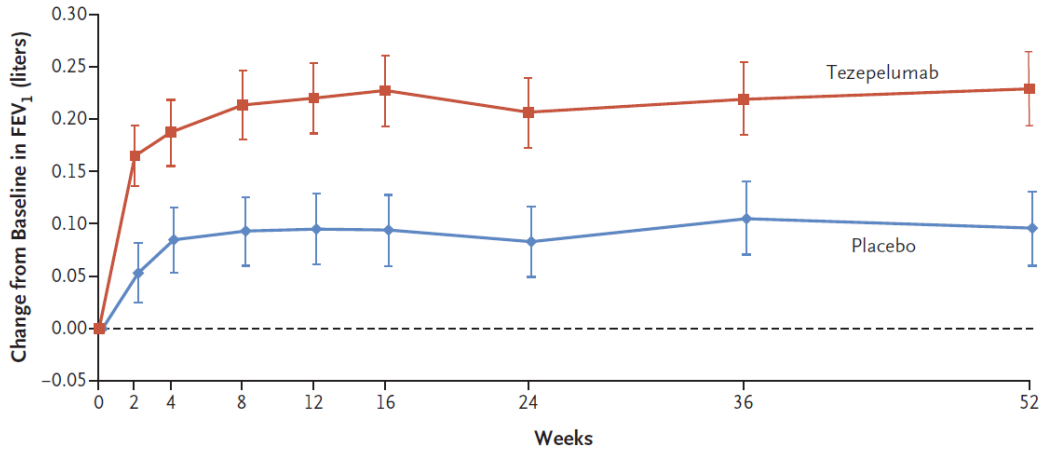

Figure 2. Change from Baseline to Week 52 in Prebronchodilator FEV_1.

I bars indicate 95% confidence intervals. FEV_1 denotes forced expiratory volume in 1 second.

[Source: Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med, May 13, 2021]

- The large phase 3 trial also reported improved quality of life based on three different patient reported measures – although the extent of those quality of life measures was

complicated because people receiving placebo also reported significant improvements (see Figure S3 at end of this guide). Unfortunately, ICER only chose to look at the AQLQ measure in its "analysis," and because of the significant improvements seen in the placebo group, it found only limited improvements in quality of life years gained with the use of tezepelumab and thus a low "value" for this potential new treatment. It is important to note that improvements for people taking placebos may be due to their receiving better care while in a clinical trial.

- ICER's analysis is critical of the lack of lack of long-term data. This is a common theme for ICER since it typically conducts its reviews before FDA approval so it can influence insurance companies and others who pay for health care to restrict access to new treatments that ICER believes are overpriced or would "bust" a fictional budget – see below. It should be noted that there is an ongoing follow-up study of the people in the phase 3 study to gather more long-term data.

Recommendation: Advocates for better treatments for asthma should consider making the following points in their written or oral comments:

- Not only has tezepelumab been found to provide clinical benefits, but it improves patients' quality of life and overall wellbeing.

- Provide your personal perspectives and insights as someone with asthma (or as a family member or friend of someone with asthma) about the importance of having more and better treatments – particularly for people who are unable to control their asthma episodes or exacerbations with existing medicines.

- Discuss how asthma that is not well controlled with current treatment options affects the daily lives and productivity of people and their families. As was noted in the New England Journal of Medicine's article about the phase 3 study, "current biologic agents are unsuitable for many patients with severe asthma, particularly those with nonallergic or noneosinophilic phenotypes."

- For patients who have trouble controlling their asthma outbreaks, steroids (including oral steroids) are often a main part of their treatment plan. Oral steroids, especially when taken long-term, can have significant side effects such as diabetes, heart attacks, stroke, cataracts, and osteoporosis. ICER also notes that long-term oral steroid use increases health care costs by more than $8,300/year per person.

- While the 3 trials were only for 52 (or 48) weeks, there is an "extension" study enrolling people who had been in the 3 trials. This study will provide additional long-term information – particularly about safety. This will help clinicians and patients understand how to best use this potential new medicine in real-world situations. ICER should recognize this trial, and be prepared to update its findings with new data – or delay releasing its report until the FDA approves tezepelumab and more long-term and real-world data is available.

- While tezepelumab may not benefit every patient with serious asthma to the same extent, it certainly will provide another important option for patients and their clinicians to consider. Joint decision-making by patients and their clinicians about how tezepelumab fits into their individual treatment plan is critical for quality health care that fits the particular situations of specific patients. ICER's homogenized population-wide assessments may make sense for insurance companies and academics, but ICER also needs to recognize the rights and priorities of individuals in the real world where people live and receive actual clinical care.

Cost Effectiveness

- ICER's economic modeling and analysis has at its core the concept of Quality Adjusted Life Years (QALYs). The use of QALYs for making decisions about payment, coverage and rationing of care has been widely criticized because QALY calculations assume that people with less than perfect health have diminished quality of life, so QALYs discriminate against people with chronic conditions and disabilities.

- In the case of tezepelumab, ICER's draft report concludes that it provides little or no cost-effectiveness benefit. Specifically, ICER concludes it only increases QALYs by about 1.09 over standard care even while it notes a 12% increase in the number of people who reported significant response to tezepelumab. (See chart below)

Table 4.4. Results for the Base Case for Tezepelumab plus SoC Compared to SoC Alone

Treatment	Intervention Cost	Other Non-intervention Costs	Total Cost	QALY's	LYs	evLYs	% Responder†
Tezepelumab plus SoC*	$657,000	$40,000	$697,000	15.00	19.11	15.02	82%
SoC Alone	$122,000	$106,000	$228,000	13.91	18.80	13.91	70%

*Price is a placeholder based on net pricing of dupilumab

† response defined as change from baseline in Asthma Control Questionnaire-6 score of ≥ 0.5

[Source: ICER's Tezepelumab for Severe Asthma; Draft Evidence Report. Institute for Clinical and Economic Review, September 16, 2021, p. 21.]

- ICER's reports includes a "placeholder price" for potential treatments that have not been approved by the FDA. ICER does this because its "value framework" is focused on determining a cost-per-change-in-QALY, which is the fundamental final number that ICER uses to determine "value" as well as to determine what it believes is a "fair price." (ICER typically highlights its "fair price" in press releases and other materials, and the difference between what it has determined to be a "fair price" and the "placeholder price" – or later the actual list price of a treatment once it is approved by the FDA.) For tezepelumab, ICER is using as a "placeholder price" the average net price in the U.S. of dupilumab, which is reported to be $27,860 per year.

- In developing its economic model for cost effectiveness, ICER makes many wide-ranging assumptions, but does not consider how treatments will improve over time – including the possibility of new treatments that are in development – or how people with certain types of asthma may benefit more from tezepelumab.

Recommendation: Advocates for better treatments for asthma should consider making the following points in their written or oral comments:

- Question ICER's use of QALYs as a fundamental basis for its cost effectiveness evaluation, and refute the concept that someone with a chronic health condition has a reduced quality of life since the concept of "perfect health" is fictional – everyone has health issues and challenges. While asthma may be seen by the general public as not a very significant health issue, people with asthma recognize that it not only is life-altering, but it can be life-threatening with about 3,500 people in the U.S. dying from asthma every year. In addition, among the five million children with asthma in the U.S., it is twice as common among Black children than White children, which is another example of disparities in U.S. health and health care.

- Present the patient perspective that what is important for patients is what they have to pay for treatments they need, i.e., co-payments and other forms of cost-sharing based upon their specific health insurance plans. Most people in the U.S. with health insurance (except those with Medicare who do not have supplemental insurance, a.k.a. Medigap) have an annual out-of-pocket spending limit of $8,550 for individual coverage or $17,100 for family coverage. That means that after spending that much for their healthcare services and treatments (such as biologics for asthma), they would not have to pay more. ICER's concerns about costs and prices are clearly focused on health insurance company spending rather than patient costs, access, and quality of care.

- Insurance companies should not establish very high co-payments, or erect cost-based barriers – such as prior authorization or similar policies – that restrict access to medicines. Advocates should raise concerns that ICER's cost-effectiveness analysis will cause insurance companies to create such higher co-payments and other access barriers for people with serious asthma, which can include difficult authorization forms designed to burden patients and their clinicians in order to prevent patients from obtaining tezepelumab.

Budget Impact

- One of the more controversial aspects of ICER's reports looking at potential new treatments is their development of a fictional "budget impact" that assumes the U.S. healthcare system is a monolithic single payer entity. ICER's budget impact process asserts that in any year, all new medicines shouldn't receive more than a certain amount of money in total – regardless of how much they benefit patients. In addition, because this "budget impact" calculation encompasses all medicines that could be introduced in a year, and it allocates the same dollar amount to each medicine based upon a formula that uses how many new treatments the FDA had approved in recent years, ICER's model provides a feedback loop that if adhered to would be a disincentive for developing new treatments. That is, if many new medicines are approved by the FDA, then in future years, ICER's "budget limit" for every new medicine would be lower – which is exactly what happened when ICER updated its "budget impact" formula in July 2021: ICER lowered its budget impact threshold per new medicine by $85 million largely because the FDA approved more medicines in recent years. (ICER's formula is based on its assertion that health care spending – particularly for new medicines – should be tied to GDP growth.)

- In doing its budget impact assessment, ICER does not consider other treatment options that have been developed or are in development, such as devices or surgical interventions.

- If ICER's "budget impact" concept seems bizarre or confusing, that's because it is both bizarre and confusing.

Recommendation: Advocates for better treatments for asthma should consider making the following points in their written or oral comments:

- **Similar to the fictional cost-effectiveness analysis, ICER's budget impact assessment does not represent patients' perspectives.** Rather, real people are concerned about what they have to pay for the treatments they need. In contrast, ICER's "budget impact" assessments and "fair price" provide rationale for insurance companies to deny coverage and erect access barriers. In particular, the budget impact "assessment" may be used by government health care programs like the Department of Veterans' Affairs (VA), Medicare, and state Medicaid programs to create barriers or extend administrative delays for making new medicines available.

- Criticize ICER for presenting fictional, somewhat arbitrary numbers based on so many assumptions that they are essentially meaningless. Advocates should express concern that ICER's faulty numbers will be used by insurance companies to justify denying patients access to medicines that could improve their health and lives.

- Advocates should point out the inconsistency of ICER's analytical methods that penalize future medicines if there are more medicines approved by the FDA in previous years. **Under ICER's scheme, future medicines would face greater pricing and access restrictions irrespective of their clinical (and economic) benefits if they are developed in years after many other new treatments become available, which would reduce incentives for all manner of future biomedical research and development spending.**

Conclusions

- Summarize and restate your thoughts and provide overall recommendations for what ICER should do – or not do – particularly related to the harm that ICER's conclusions could cause by limiting access to this potential new treatment for asthma by empowering health insurance companies and government programs to deny payment or create barriers for patients receiving the treatments their physicians recommend.

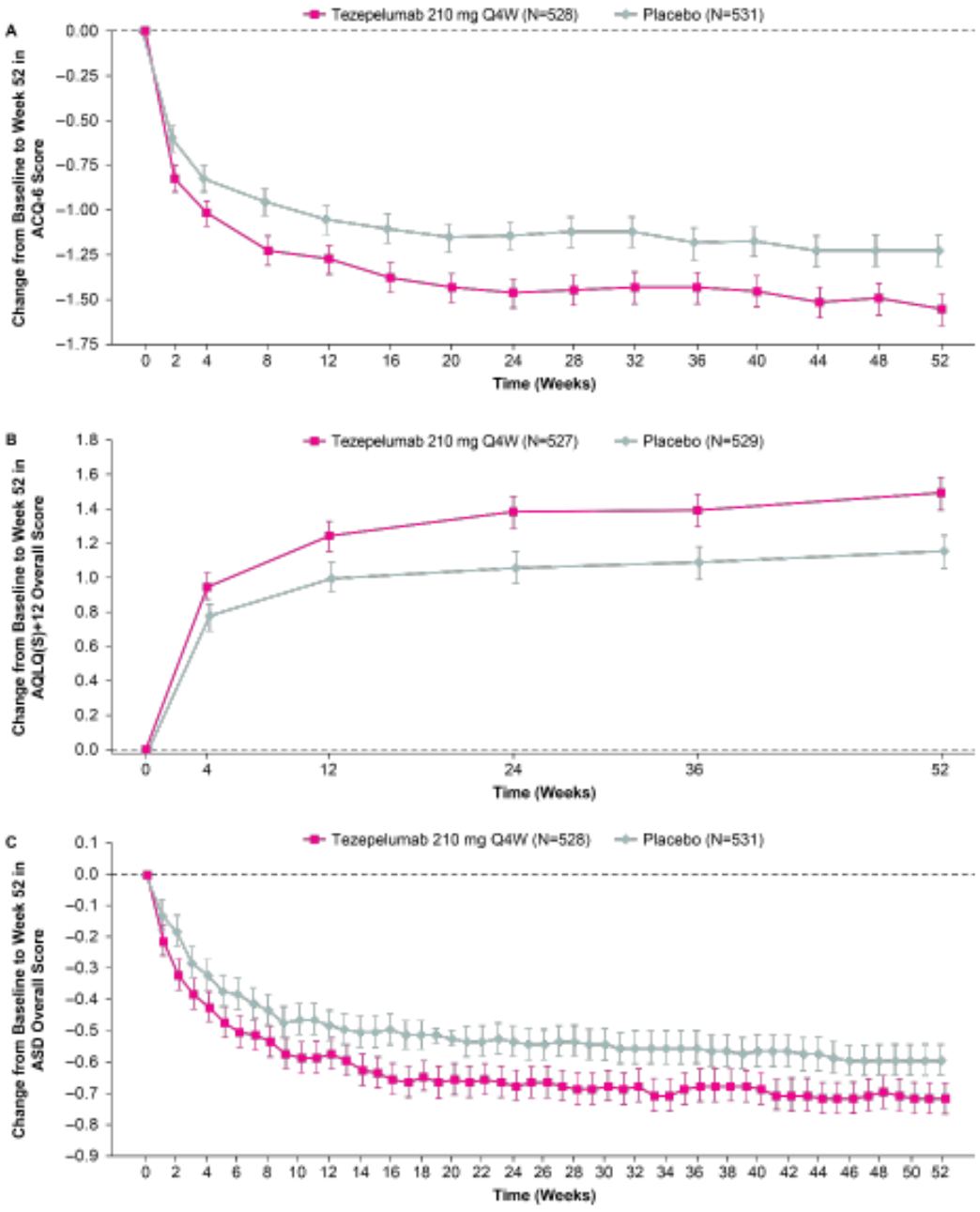

Figure S3. Change over Time from Baseline to Week 52 in: ACQ-6 Score (Panel A); AQLQ(S)+12 Overall Score (Panel B); and ASD Overall Score (Panel C).

Data are LS means with 95% CI. Data are from a model for repeated measures following multiple imputation to complete the follow-up assuming missing-at-random. Treatment, visit, region, age (adolescents or adults), and treatment-by-visit interaction were included as factors in the model.

[Source: Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med, May 13, 2021 – Supplemental Appendix]