



Tezepelumab for Severe Asthma: Final Policy Recommendations

December 16, 2021



Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the November 19 Midwest CEPAC public meeting on the use of tezepelumab for the treatment of severe asthma. At the meeting, ICER presented the findings of its revised report on these treatments and the Midwest CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of 2 patient advocates, 1 clinical expert, 2 payers, and 2 representatives from pharmaceutical manufacturers to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed [here](#), and a recording of the voting portion of the meeting can be accessed [here](#). More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found [here](#).

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, President of ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

All Stakeholders

Recommendation 1

All stakeholders have a responsibility and an important role to play in ensuring that effective new treatment options for patients with severe asthma are introduced in a way that will help reduce health inequities.

Asthma disproportionately affects underserved groups in the US including Black, Native American, and Puerto Rican populations. The trials of tezepelumab included mainly patients who were white or Asian. Multiple stakeholders highlighted that the high cost of biologic therapies can worsen disparities in accessing care. This may be due to lack of health insurance that limits access to specialists and the new therapies that they prescribe or high deductible payments that even for those with insurance may result in steep out of pocket costs. Additionally, the lack of research on tezepelumab in Black Americans raises questions about whether the results of clinical trials of

tezepelumab apply to Black populations. We have particular concerns about generalizability to poorer urban settings where air quality may be lower, and we worry that the small numbers of Black Americans in these trials may reflect similarly low levels of people living in poorer urban settings. We also heard from patient groups that only 40% of patients with severe asthma are managed by an asthma specialist.

To address these concerns:

Manufacturers should take the following actions:

- Set the price for new treatments for asthma in fair alignment with added benefits for patients.
- Take steps necessary to include a more diverse patient population in clinical trials, including adequate number of patients with ethnic and racial backgrounds similar to the underlying population in the US with asthma. To accomplish this, manufacturers should engage with patient groups earlier in the design of trials to consider ways to maximize patient diversity.

Regulators:

- The US FDA should develop guidelines requiring that clinical trials have appropriate diversity of the studied population so that manufacturers who work for such diversity are not disadvantaged by additional recruitment time/cost compared with manufacturers who do not seek this diversity.

Payers should take the following actions:

- Create quality measures that assess whether therapies are being equitably distributed across insured patient groups.
- Begin gathering data using these quality measures to inform future quality improvement activities.

Clinical experts and clinical societies:

- Develop expertise in diverse communities in the management of asthma such that providers outside of major medical centers can diagnose and appropriately treat or refer patients with severe asthma.

- Management of severe asthma needs to be broadly improved, perhaps through some combination of centers of excellence and improved technologies to allow telehealth consultations from such centers.

Patient groups:

- Work to expand the involvement of disadvantaged and underrepresented patients in clinical trials either through their own work or in conjunction with PCORI.

Medical journal editors:

- Editors of leading journals should develop policies requiring that trials being considered for publication have adequate diversity of patients.

Payers

Recommendation 1

Payers will need to consider subpopulations of people with severe asthma when designing coverage policies for tezepelumab and other biologics.

For patients with eosinophilic asthma and/or allergic asthma there are a number of biologic therapies with proven efficacy in reducing exacerbations; coverage policies can take this into account when considering preferred initial options. For patients with neither eosinophilic nor allergic asthma who are not on chronic OCS, tezepelumab is the only biologic treatment that has demonstrated efficacy.

Recommendation 2

For tezepelumab and other biologics for severe asthma, payers should meet [criteria for fair access](#), including criteria related to cost sharing, clinical eligibility, step therapy, and provider qualifications. Several key examples of these criteria are shown below:

Cost Sharing

- Patient cost sharing should be based on the net price to the plan sponsor, not the unnegotiated list price.
- At least one drug in every class should be covered at the lowest relevant cost-sharing level unless all drugs are priced higher than an established fair value threshold.

Coverage Criteria: General

- Payers should offer alternatives to prior authorization protocols such as programs that give feedback on prescribing patterns to clinicians or exempt them from prior authorization requirements (“gold carding”) if they demonstrate high fidelity to evidence-based prescribing.
- Payers should document at least once annually that clinical eligibility criteria are based on high quality, up-to-date evidence, with input from clinicians with experience in the same or similar clinical specialty.
- Clinical eligibility criteria should be developed with explicit mechanisms that require payer staff to document using an open and transparent process that is readily accessible to the public that they have:
 - a. Considered limitations of evidence due to systemic under-representation of minority populations; and
 - b. Sought input from clinical experts on whether there are distinctive benefits and harms of treatment that may arise for biological, cultural, or social reasons across different communities; and
 - c. Confirmed that clinical eligibility criteria have not gone beyond reasonable use of clinical trial inclusion/exclusion criteria to interpret or narrow the FDA label language in a way that disadvantages patients with underlying disabilities unrelated to the condition being treated.

Coverage Criteria: Specific Considerations

- **Age:** Age criteria are likely to follow the FDA label for tezepelumab. Tezepelumab is likely to be approved for those 12 years of age and older. Payers should have efficient mechanisms for clinicians to seek coverage exceptions for patients with serious unmet need who are near the cutoff for the age necessary for coverage.
- **Clinical eligibility:** Payers will likely use some combination of objective measures of disease severity and/or utilization of services for asthma derived from clinical guidelines or the eligibility criteria in pivotal clinical trials in determining who is eligible for tezepelumab. We did not hear concerns from clinical experts or the patient community about payers utilizing guidelines in making such determinations as long as they were using the most updated guidelines (typically GINA).

For example, with currently available biologics, some payers have defined moderate-severe asthma using FEV1 criteria:

If the member is 12 to 17 years of age, they have a pretreatment FEV1 \leq 90% predicted; if the member is 18 years of age or older, they have a pretreatment FEV1 of \leq 80%

and

FEV1 reversibility of at least 12% and 200 milliliters after albuterol (salbutamol) administration.

Other payers have looked at utilization criteria to define the eligible patient population:

Member has inadequate asthma control (e.g. hospitalization or emergency medical care visit within the past year) despite current treatment with both of the following medications at optimized doses:

- a. High-dose inhaled corticosteroid*
- b. Additional controller, or sustained-release theophylline*

- As noted above, repeated or prolonged need for oral corticosteroids suggests that it may be appropriate to initiate biologic therapy for asthma. Clinical experts advised that three months of frequent OCS treatment, such as on 50% of days, rather than six months as appears in some existing coverage policies, should be considered adequate to initiate biologic therapy.
- **Exclusion criteria:** Although smoking was an exclusion criterion in clinical trials of tezepelumab, clinical experts advised that patients who smoke may also benefit from biologics and should not be excluded from coverage.
- **Duration of coverage and renewal criteria:** It is not unreasonable for payers to seek attestation of benefit of expensive medications prior to renewing coverage for extended time periods. The first renewal is frequently required at six months. Renewal documentation procedures should be streamlined so that patients face no risk of interruption of their medication. Some payers may choose not to require any attestation given that patients and clinicians are likely to discontinue therapy that is not working.
- **Required switching:** Biologic treatments are not easily interchangeable in an individual patient. Clinical experts therefore advised it is not clinically reasonable to require patients with severe asthma to switch biologic therapies when they change insurance plans.
- **Provider restrictions:** Payers are likely to restrict prescribing of tezepelumab to asthma specialists such as pulmonologists and allergists. We heard from clinical experts that this is reasonable given frequent misdiagnosis and poor clinical management of severe asthma by non-specialists. However, to reduce disparities where access to specialists may be limited,

payers should consider allowing prescribing by other providers in consultation with asthma specialists.

Step Therapy

In order to justify step therapy policies extending beyond FDA labeling as appropriate, payers should ensure that:

- 1. The first-step therapy is clinically appropriate for all or nearly all patients and does not pose a greater risk of any significant side effect or harm;***
- 2. Patients will have a reasonable chance to meet their clinical goals with first-step therapy;***
- 3. Failure of the first-step drug and the resulting delay in beginning the second-step agent will not lead to long-term harm for patients;***
- 4. Patients are not required to retry a first-line drug with which they have previously had adverse side effects or an inadequate response at a reasonable dose and duration.***

Payers should recognize that step therapy has generally not been used for biologic therapy in asthma. Individual biologic therapies frequently fail and so all options using different mechanisms of action should be available to patients with asthma.

There are important subpopulations of patients with severe asthma for which certain treatments have clear indications. Only dupilumab has demonstrated reduction in steroid dose in OCS-dependent asthma, and only tezepelumab has shown efficacy in patients with severe asthma with an eosinophil count below 150 cells/ μ L. However, for eosinophilic asthma, there is no strong clinical rationale for first treatment among the available biologic treatment options or tezepelumab. Therefore, if large pricing differentials emerge among these agents, payers may have clinical justification to institute step therapy, as they have done in autoimmune conditions. If considered, such policies must meet all criteria for fair access, including those related to transparency and efficiency of implementation.

Manufacturers and Payers

Recommendation 1

Biologic therapies for asthma are expensive, prices should be reduced.

At our public meeting, Sanofi expressed interest in aligning prices with benefits across different indications. This is a particular issue with their drug dupilumab, which ICER has judged to be priced fairly when used to treat atopic dermatitis. Systems and regulations in the US interfere with indication-specific pricing, but manufacturers should continue to seek innovative ways to accomplish such alignment.

Manufacturers of other biologic therapies for asthma should reduce their prices to align with their clinical benefits in asthma.

Manufacturers should also continue to work with payers and policymakers to develop options to reduce the role that rebates play in supporting high list prices.

Researchers and Patient Organizations

Recommendation 1

Researchers looking at real world evidence in treatments of asthma should be aware of potential threats to validity, including selection bias.

Since head-to-head trials of biologics are unlikely to be performed, there may be an interest by manufacturers, payers, and independent researchers in examining efficacy through the use of RWE. Given the apparently similar efficacy of biologics seen in randomized trials, issues of selection bias as well as differing comorbidities and other potential confounders are a threat to validity in such studies since biases within a data set could overwhelm small differences in efficacy.

Specific areas require additional research

- As discussed above, additional research is required to demonstrate the efficacy of tezepelumab in underserved and underrepresented populations. To the extent that such populations tend to live in urban settings and be exposed to particulates, the generalizability of the results of the clinical trials of tezepelumab is in doubt.
- Research is needed on the development and use of biomarkers to allow better prediction of which patients will benefit from a given therapy such as tezepelumab. To the extent that manufacturers already have some such data, they should endeavor to promulgate and share their results rather than refusing to do so as occurred for this report when ICER asked for information on a specific subgroup treated with tezepelumab.
- Quality of life instruments have been developed specifically for asthma. If patient groups or others feel that these instruments are not adequately capturing the benefits seen with new therapies, they should work with researchers to develop new measures that they trust. We note, however, that the manufacturer of tezepelumab collected multiple measures of quality of life, some of which have not been made publicly available, and could have analyzed these results in various ways to try to capture quality of life improvements if they felt that the published measures did not reflect the full benefits seen with tezepelumab.

References

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the November 19 Public meeting of the Midwest CEPAC.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

ICER Staff and Consultants*	
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*No relevant conflicts of interest to disclose, defined as more than \$10,000 in healthcare company stock or more than \$5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Appendix Table 2. Midwest Panel Member Participants and COI Disclosures

Participating Members of Midwest CEPAC	
Eric Armbricht, PhD* Associate Professor, Saint Louis University Center for Health Outcomes Research, School of Medicine and College for Public Health & Social Justice	Heather Guidone, BCPA* Program Director, Center for Endometriosis Care (CEC)
Alan Balch, PhD* Chief Executive Officer, Patient Advocate Foundation, National Patient Advocate Foundation	Jill Johnson, PharmD* Professor, Department of Pharmacy Practice, University of Arkansas for Medical Sciences College of Pharmacy
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*No relevant conflicts of interest to disclose, defined as more than \$10,000 in healthcare company stock or more than \$5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Mindy Bauer, PharmD , Associate Director, Clinical Pharmacy, IPD Analytics	Dr. Bauer is a full-time employee of IPD Analytics.
Melanie Carver , Chief Mission Officer, Asthma and Allergy Foundation of America	AAFA receives funding from Pharmaceutical manufacturers, PhRMA, and PCMA.
Kyle Hvidsten, MPH , Head, Health Economics & Value Assessment, Sanofi	Kyle Hvidsten is a full-time employee of Sanofi.
Tony R. Vancauwelaert, MD, FAAFP , Executive Medical Director, Enterprise Medical Operations - Pharmacy, Health Care Services Corporation	Dr. Vancauwelaert is a full-time employee of Health Care Services Corporation.
Michael E. Wechsler, MD , Professor of Medicine, Director of NJH Cohen Family Asthma Institute, National Jewish Health	Dr. Wechsler has received consulting fees and honoraria from the following health care companies: AstraZeneca, Amgen, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Regeneron, and Sanofi.
Tonya Winders, MBA , President & Chief Executive Officer, Allergy & Asthma Network	Tonya Winders serves as a speaker & advisor to AstraZeneca, Amgen, GSK, Novartis, Sanofi, Regeneron & ALK Abello. The Allergy & Asthma Network receives funding from healthcare companies for unbranded disease awareness, education, advocacy & research.
David Zimmer, BS, MBA , Vice President US Value and Access, Amgen	David Zimmer is a full-time employee of Amgen.