

KEY FINDINGS

	tezepelumab (Amgen, AstraZeneca)
Evidence Rating	C++: the evidence provides high certainty that tezepelumab is at least comparable to standard of care alone (without biologics), with the possibility of delivering either a small or substantial net health benefit
Estimated Annual Price	Placeholder price: \$28,000
Annual Health-Benefit Price Benchmark	\$9,000-\$12,100
Change from Annual Price Required to Reach Threshold Price	N/A: discounts not presented due to placeholder price

“ICER previously reviewed biologic therapies for moderate-to-severe asthma, and none of these were effective in patients without allergic or eosinophilic asthma. Tezepelumab has a new mechanism of action and does reduce exacerbations even in patients without eosinophilia who really have not had good options for treatment until now. For other asthma patients for whom biologics are available, tezepelumab is not clearly superior to those options, and it may be less effective at getting patients off oral steroids than dupilumab.”

– ICER’s Chief Medical Officer, David Rind, MD

THEMES AND RECOMMENDATIONS

- 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.
- Payers will need to consider subpopulations of people with severe asthma when designing coverage policies for tezepelumab and other biologics. 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.
- 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.
- Biologic therapies for asthma are expensive; prices should be reduced.
- Researchers looking at real world evidence in treatments of asthma should be aware of potential threats to validity, including selection bias.

## Clinical Analyses

### KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

The Centers for Disease Control and Prevention (CDC) estimates that 25 million Americans, including 5 million children, have asthma. Asthma leads to approximately 1.6 million emergency room visits, 180,000 hospitalizations, and 3,500 deaths each year in the US. The societal costs are estimated to be \$82 billion, including \$50 billion in direct medical costs, \$29 billion from asthma-related mortality, and \$3 billion from missed work and school. In the US, asthma is more than twice as common among Black children as among White children (13.5% and 6.4%, respectively), and remains somewhat more common among Black adults.

Patients with severe asthma represent fewer than 5-10% of all individuals with asthma. Asthma has been divided into different phenotypes with some overlap. About half of individuals with mild-to-moderate asthma exhibit the type 2 phenotype, and the proportion is believed to be larger in severe asthma. Allergic asthma and eosinophilic asthma are generally forms of type 2 asthma. None of the five biologic therapies that ICER reviewed in 2018 appeared to be effective for patients who had neither allergic asthma nor eosinophilia.

Tezepelumab is a new monoclonal antibody that targets thymic stromal lymphopoietin (TSLP). It is administered by subcutaneous injection every four weeks. In this report, we review the clinical effectiveness of tezepelumab for severe asthma and also compare it with agents indicated for certain subpopulations: 1) omalizumab for patients with allergic asthma; and 2) dupilumab for patients with eosinophilic asthma. We also compare the efficacy of tezepelumab and dupilumab in patients dependent on chronic oral corticosteroids.

Patients, patient groups, and clinicians have emphasized the need for treatments that allow

patients to return to their usual activities of daily living. Symptom relief, asthma control, and quality of life matter much more to patients than a reduction in asthma exacerbations.

In two randomized trials in a broad population of patients with severe asthma, tezepelumab improved symptom scores compared with placebo, but these improvements (0.20 to 0.34) were smaller than the minimal clinically important differences (MCIDs) of 0.5 on these scales.<sup>6,7</sup> However, in both trials, tezepelumab substantially reduced annualized asthma exacerbation rate (AAER) compared with placebo (RR 0.29 to 0.44).

For patients with eosinophilic asthma, improvements in symptom scores and reductions in AAER were similar to the results seen with dupilumab. For patients with allergic asthma, improvements in symptoms were similar to those seen in older trials of omalizumab while reductions in AAER were somewhat greater than with omalizumab. Patients with non-eosinophilic asthma treated with tezepelumab showed similar improvements in symptom scores to patients with eosinophilic asthma in one of the two randomized trials, and only minimal improvement in the other trial. In one of the two randomized trials, patients with non-eosinophilic asthma had larger reductions in AAER than those with eosinophilic asthma, while in the other randomized trial, reductions in AAER were smaller in such patients, but still appeared to be clinically meaningful.

In a separate randomized trial of tezepelumab in patients with steroid-dependent asthma, patients treated with tezepelumab were not more likely to reduce their oral corticosteroid (OCS) dose at week 48 than patients treated with placebo (odds ratio [OR] 1.28, 95% CI 0.69 to 2.35). In contrast, a randomized trial of dupilumab found a greater reduction in OCS

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dose compared with placebo (70% vs 42%;  $p < 0.001$ ), and more patients had a reduction of OCS dose of at least 50% (80% vs. 50%;  $p < 0.001$ ).

In all trials, adverse events with tezepelumab did not appear to be significantly different from placebo. This is also true of dupilumab, and long-term studies of dupilumab provide additional evidence of safety. Adverse events with omalizumab are uncommon, however omalizumab carries a “black box” warning for anaphylaxis.

Important uncertainties include the lack of head-to-head trials of these agents, the lack of longer term data on safety of the new mechanism of action of tezepelumab, and the inability to evaluate subpopulation effects among racial groups given the notable paucity of Black patients in the trials of tezepelumab; at least some trials of dupilumab and omalizumab had participation of Black patients closer to their percentages in the US population. Overall, given the strength of evidence in different patient groups, ICER’s ratings for comparative clinical effectiveness are as shown below.

**Table 1. Evidence Ratings**

Treatment	Comparator	Population	Evidence Rating
Tezepelumab	Standard of care	<i>All Patients With Severe Asthma</i>	C++
	Dupilumab	<i>Eosinophilic Asthma</i>	I
	Omalizumab	<i>Allergic Asthma</i>	I
	Dupilumab	<i>Steroid-Dependent Asthma</i>	C-

## Economic Analyses

### LONG-TERM COST EFFECTIVENESS

We performed an economic analysis of tezepelumab in the broad population of patients with severe asthma. Treatment with tezepelumab results in gains of 1.09 QALYs and 1.12 evLYs. From a health system perspective and using a placeholder net price of approximately \$28,000 per year, we estimate a cost of \$430,000 per QALY gained and \$422,000 per evLY gained, which would exceed usual cost-effectiveness thresholds. Cost-effectiveness is only modestly improved when productivity and other broader effects are included within a modified societal perspective.

The Health Benefit Price Benchmark (HBPB) for a drug is defined as the price range that would achieve incremental cost-effectiveness ratios between \$100,000 and \$150,000 per QALY or per evLY gained. The HBPB of tezepelumab is \$9,000 to \$12,100 per year.

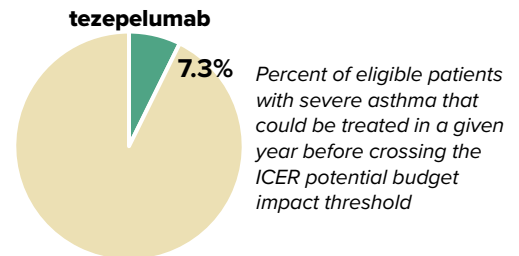
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In summary, tezepelumab reduces exacerbations in patients with severe asthma, including in some types of asthma for which other biologic therapies are not effective. Because severe asthma is more prevalent among Black Americans, health gains from a successful treatment that has consistent benefits across racial subgroups would provide proportionally greater benefit to that racial group on a population basis. As discussed

above, however, studies have not adequately enrolled Black Americans to demonstrate such a consistent effect. Additionally, as with other biologic therapies, improvements in daily symptoms and quality of life are relatively small. Pricing for tezepelumab is not yet known but at anticipated prices, the treatment will not reach traditional thresholds considered cost-effective in the US market.

### POTENTIAL BUDGET IMPACT

Only 7.3% of the roughly 139,000 patients, or approximately 10,200 patients, could be treated each year without crossing the ICER budget impact threshold of \$734 million per year over five years at the annualized placeholder price of \$27,860.



## Public Meeting Deliberations

### VOTING RESULTS

- For treating severe asthma, a majority (10-4) of panelists found that the evidence is **adequate** to demonstrate a net health benefit of tezepelumab added to standard of care when compared to standard of care alone.
- For treating severe allergic asthma or severe eosinophilic asthma, a majority of panelists found that the evidence is **not adequate** to distinguish the net health benefit of tezepelumab from that of omalizumab (13-1) and dupilumab (14-0), respectively.
- For treating steroid-dependent asthma, a majority (14-0) of panelists found that the evidence is **not adequate** to distinguish a net health benefit of tezepelumab from that of dupilumab.

During their deliberations, panel members also weighed the therapies' other potential benefits, disadvantages, and contextual considerations. For tezepelumab voting highlighted the following as particularly important for payers and other policymakers to note:

- The magnitude of the lifetime impact on individuals with severe asthma.

Consistent with ICER's process, the Midwest CEPAC did not vote on long-term value for money because the manufacturer has not yet announced a price for tezepelumab.

## About ICER

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The Institute for Clinical and Economic Review ([ICER](https://www.icer.org)) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public

hearings through three core programs: the California Technology Assessment Forum ([CTAF](https://www.ctaf.org)), the Midwest Comparative Effectiveness Public Advisory Council ([Midwest CEPAC](https://www.midwestcepac.org)) and the New England Comparative Effectiveness Public Advisory Council ([New England CEPAC](https://www.newenglandcepac.org)). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care.

For more information about ICER, please visit ICER's website ([www.icer.org](https://www.icer.org)).