Tezepelumab for Severe Asthma: Effectiveness and Value

Midwest Comparative Effectiveness Public Advisory Council (CEPAC)

Public Meeting — November 19, 2021

Meeting materials available at: https://icer.org/asthma-2021/#timeline
Patient and Clinical Experts

Melanie Carver, Chief Mission Officer, Asthma and Allergy Foundation of America
• AAFA receives funding from Pharmaceutical manufacturers, PhRMA, and PCMA.

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.

Jonathan Corren, MD, Medicine and Pediatrics, UCLA School of Medicine
• Dr. Jonathan Corren has received honoraria from AstraZeneca, Genentech, Regeneron, and Sanofi. Dr. Corren has equity interests in Allakos in excess of $10,000, and received research funding from AstraZeneca, Genentech, Novartis, Optinose, Regeneron, and Sanofi, and is an advisory board member and speaker board member for AstraZeneca.

Michael E. Wechsler, MD, Professor of Medicine, Director of NJH Cohen Family Asthma Institute, National Jewish Health
• Dr. Michael Wechsler has received consulting fees and honoraria from the following health care companies: AstraZeneca, Amgen, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Regeneron, and Sanofi.
“When Julia is having asthma exacerbations it affects her days, her sleep at night. In fact, I always sleep next to her when she is having difficulty breathing so I can be right there to give her her medication… Asthma is the number one reason she misses school.”
Why Are We Here Today?

• What happens the day these treatments are approved by the FDA?
• Patients can have difficulty accessing drugs
  • Coverage eligibility
  • Costs (out-of-pocket and insurance premiums)
• What happens to others in the health care “system”? 
The Impact of Rising Health Care Costs

Leonard Edloe
Richmond, Virginia

The Whitman family
Bird City, Alaska

The Maccoux family
Brooklyn Park, Minnesota
Organizational Overview

• Midwest Comparative Effectiveness Public Advisory Council (CEPAC)

• The Institute for Clinical and Economic Review (ICER)
Sources of Funding, 2021
https://icer.org/who-we-are/independent-funding/

ICER Policy Summit and non-report activities only
*Individual / matching contributions and speech stipends
How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Colorado cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Kaharu Sumino, MD, MPH**, Associate Professor of Medicine, Washington University School of Medicine
    - No relevant conflicts of interest to disclose, defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.
  - **Michael E. Wechsler, MD**, Professor of Medicine, Director NJH Cohen Family Asthma Institute, National Jewish Health
    - Dr. Michael Wechsler has received consulting fees and honoraria from the following health care companies: AstraZeneca, Amgen, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Regeneron, and Sanofi.
- How is the evidence report structured to support CEPAC voting and policy discussion?
Value Assessment Framework: Long-Term Value for Money

- **Special Social/Ethical Priorities**
- **Benefits Beyond “Health”**
- **Total Cost Overall**
  - Including Cost Offsets
- **Health Benefits:**
  - Return of Function, Fewer Side Effects
- **Health Benefits:**
  - Longer Life
## Agenda

<table>
<thead>
<tr>
<th>Time (CT)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00am – 10:20am</td>
<td>Meeting Convened and Opening Remarks</td>
</tr>
<tr>
<td>10:20am – 11:00am</td>
<td>Presentation of the Clinical Evidence</td>
</tr>
<tr>
<td>11:00am – 11:40am</td>
<td>Presentation of the Economic Model</td>
</tr>
<tr>
<td>11:40am – 12:05pm</td>
<td>Public Comments and Discussion</td>
</tr>
<tr>
<td>12:05pm – 12:45pm</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>12:45pm – 2:00pm</td>
<td>Midwest CEPAC Vote on Clinical Effectiveness and Value</td>
</tr>
<tr>
<td>2:00pm – 2:10pm</td>
<td>Break</td>
</tr>
<tr>
<td>2:10pm – 3:30pm</td>
<td>Policy Roundtable</td>
</tr>
<tr>
<td>3:30pm – 4:00pm</td>
<td>Reflections from Midwest CEPAC</td>
</tr>
<tr>
<td>4:00pm</td>
<td>Meeting Adjourned</td>
</tr>
</tbody>
</table>
Presentation of the Clinical Evidence

David M. Rind, MD, MSc
Chief Medical Officer
Institute for Clinical and Economic Review
Key Collaborators

• Belén Herce-Hagiwara, BA
  Research Assistant, ICER

• Serina Herron-Smith, BA
  Senior Research Assistant, ICER

Disclosures:

We have no conflicts of interest relevant to this report
Asthma

• 25 million Americans, including 5 million children

• 1.6 million ER visits, 180,000 hospitalizations, and 3,500 deaths each year in the US

• Asthma is more than twice as common among Black children as among White children and remains somewhat more common among Black adults

• About half of patients with mild-to-moderate asthma exhibit type 2 phenotype; proportion is higher in severe asthma
Severe Asthma

• Some overlap in definitions

• 5-10% of all asthma

• Global Initiative for Asthma (GINA):

  A subset of difficult-to-treat asthma that is uncontrolled despite adherence with maximal optimized high dose ICS/LABA treatment and management of contributory factors, or that worsens when high dose treatment is decreased
Patient Experience of Severe Asthma

• Most patients report having daily symptoms and are scared and burdened by their symptoms

• Interferes with living the life they want to live

• Burdens family and caregivers

• Fear systemic corticosteroid side effects

• Daily symptom control is more important than reducing asthma exacerbations
Type 2 Phenotype

• Phenotypes not clearly defined and can overlap
• Increases in type 2 helper cells
• Response to antigens/allergens
• Allergic asthma and eosinophilic asthma are generally considered type 2 asthma
  • All the biologics currently available are for allergic asthma (omalizumab) or eosinophilic asthma (mepolizumab, reslizumab, benralizumab, dupilumab)
• Thymic stromal lymphopoietin (TSLP) sits early in pathway
Modified with permission from Israel et al. 2017, Copyright Massachusetts Medical Society.
Tezepelumab

• Monoclonal antibody targeting TSLP
• Subcutaneous injection every four weeks
• FDA decision expected early next year
Scope of Review

• Intervention: Tezepelumab for severe asthma

• Comparators
  • All patients: usual care alone (placebo arm of clinical trials)
  • Eosinophilic asthma: dupilumab + usual care
  • Allergic asthma: omalizumab + usual care
  • Steroid dependent asthma: dupilumab + usual care
Clinical Evidence
Tezepelumab: Clinical Evidence

• Phase 2 (dose finding) “PATHWAY” trial in 550 adults with uncontrolled asthma

• Phase 3 “NAVIGATOR” trial in 1061 adults and adolescents with severe, uncontrolled asthma

• Phase 3 “SOURCE” trial in 150 adults with OCS-dependent asthma; limited reporting to date
Outcomes

• Annualized asthma exacerbation rate (AAER): Primary outcome of most trials, but not most patient-important outcome

• Improvement in daily symptoms (ACQ and AQLQ measure symptoms and QoL) most important to patients; MCID 0.5 points

• Subgroups
  
  • Most drugs had only worked in eosinophilic asthma so stratification by eosinophil count is particularly important
  
  • Omalizumab used in allergic asthma so can compare that subgroup as well
# Tezepelumab and Dupilumab in All Patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>AAER Rate Ratio Range vs. Placebo</th>
<th>Difference in ACQ* vs. Placebo</th>
<th>Difference in AQLQ vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab 210 mg</td>
<td>0.29 to 0.44</td>
<td>Δ = 0.29 to 0.33</td>
<td>Δ = 0.20 to 0.34</td>
</tr>
<tr>
<td>Dupilumab 200 &amp; 300 mg</td>
<td>0.30 to 0.54</td>
<td>Δ = 0.22 to 0.39</td>
<td>Δ = 0.26 to 0.36</td>
</tr>
</tbody>
</table>

AAER: annualized asthma exacerbation rate, ACQ: Asthma Control Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, mg: milligram

* ACQ-5 used for dupilumab trials. ACQ-6 used for tezepelumab trials.
# Tezepelumab and Dupilumab by Eosinophil Count

<table>
<thead>
<tr>
<th>Drug</th>
<th>Blood Eosinophil Count (cells/µL)</th>
<th>AAER Rate Ratio Range vs. Placebo</th>
<th>Difference in ACQ* vs. Placebo</th>
<th>Difference in AQLQ vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>210 mg</td>
<td>≥150</td>
<td>0.34 to 0.39</td>
<td>Δ = 0.35 to 0.41</td>
<td>Δ = 0.29 to 0.41</td>
</tr>
<tr>
<td></td>
<td>&lt;150</td>
<td>0.17 to 0.61</td>
<td>Δ = 0.09 to 0.30</td>
<td>Δ = 0.11 to 0.44</td>
</tr>
<tr>
<td>Dupilumab†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 &amp; 300 mg</td>
<td>≥150</td>
<td>0.44</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>&lt;150</td>
<td>0.93 to 1.15</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

AAER: annualized asthma exacerbation rate, ACQ: Asthma Control Questionnaire, AQLQ: Asthma Quality of Life Questionnaire, mg: milligram

* ACQ-5 used for dupilumab trials. ACQ-6 used for tezepelumab trials.
† Data from LIBERTY ASTHMA QUEST only, not reported for the phase 2b study
# Tezepelumab and Omalizumab in Allergic Asthma

<table>
<thead>
<tr>
<th>Drug</th>
<th>AAER Rate Ratio Range vs. Placebo</th>
<th>Difference in ACQ-6 vs. Placebo</th>
<th>Difference in AQLQ vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab 210 mg</td>
<td>0.20 to 0.42</td>
<td>$\Delta = 0.10$ to $0.29$</td>
<td>$\Delta = 0.07$ to $0.34$</td>
</tr>
<tr>
<td>Omalizumab*</td>
<td>0.52</td>
<td>NR</td>
<td>$\Delta = 0.26$</td>
</tr>
</tbody>
</table>

AAER: annualized asthma exacerbation rate, ACQ-6: Asthma Control Questionnaire-6, AQLQ: Asthma Quality of Life Questionnaire, mg: milligram; NR: not reported

* Data from prior ICER report
Reduction in Systemic Steroids

• Tezepelumab (SOURCE trial)
  • Patients were not more likely to reduce their OCS dose at week 48 with tezepelumab than placebo (OR 1.28, 95% CI 0.69 to 2.35)

• Dupilumab (VENTURE trial)
  • Greater reduction in OCS dose with dupilumab than placebo (70% vs. 42%)
  • More patients had a reduction in dose of at least 50% (80% vs. 50%)
  • More patients had a reduction in dose to below 5 mg/day (69% vs. 33%)
Harms

• Adverse events and serious adverse events are rare with all these drugs

• Omalizumab does carry a “black box” warning for anaphylaxis

• Dupilumab and omalizumab have long-term safety data
Controversies and Uncertainties

• Lack of head-to-head trials (particularly with omalizumab, old trials)
• Very high placebo response rates in randomized trials
• Tezepelumab has a new mechanism of action, so concerns about as-yet-unidentified harms
• We do not have data on the subgroup who have neither eosinophilic asthma nor allergic asthma. We asked the manufacturer for data for this subgroup, but these data were not provided
• Very few Black patients in the tezepelumab trials despite severe asthma being more common in this population in the US
Modified with permission from Israel et al. 2017, Copyright Massachusetts Medical Society.
Potential Other Benefits and Contextual Considerations

• Death from asthma is uncommon, but severe asthma has daily symptoms that interfere with nearly all activities and that markedly reduce quality of life

• Asthma disproportionately affects Black Americans, and they may have a more severe disease course

• The ICER Health Improvement Distribution Index for Black Americans with asthma is 1.21
Public Comments Received

• “The MCID concept is meant to compare a change from baseline in an individual patient (or group of patients), not the difference in response between two populations.”

• “While the report recognizes the efficacy of omalizumab for patients with an allergic phenotype, the dupilumab efficacy in this patient population should also be recognized.”

• “ICER’s reliance on the QALY is of great concern, especially when being used in an evaluation regarding asthma patients. As asthma is a chronic disease, the quality of life of patients, as defined by the QALY, is already diminished. This will lead to lower scores, even for drugs that are clinically effective, as patients with chronic diseases often cannot achieve perfect health.”
Summary

• Tezepelumab is likely effective for a broad group of patients with type 2 asthma and perhaps some with non-type 2 asthma

• This effectiveness, as with other biologics, reflects greater efficacy in reducing exacerbations than improving daily symptoms; therapies that reduce daily symptoms are needed

• We lack long-term safety data, which affects our evidence ratings (as it did for new biologics in the 2018 review)

• Tezepelumab is probably less effective in reducing need for oral corticosteroids than dupilumab
## Evidence Ratings

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Population</th>
<th>Evidence Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab vs.</td>
<td>Standard of care</td>
<td>All Patients With Severe Asthma</td>
<td>C++</td>
</tr>
<tr>
<td>Tezepelumab vs.</td>
<td>Dupilumab</td>
<td>Eosinophilic Asthma</td>
<td>I</td>
</tr>
<tr>
<td>Tezepelumab vs.</td>
<td>Omalizumab</td>
<td>Allergic Asthma</td>
<td>I</td>
</tr>
<tr>
<td>Tezepelumab vs.</td>
<td>Dupilumab</td>
<td>Steroid-Dependent Asthma</td>
<td>C-</td>
</tr>
</tbody>
</table>
Questions?
<table>
<thead>
<tr>
<th></th>
<th>Tezepelumab 210 mg Q4W</th>
<th>Placebo</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N/Estimate</td>
<td>N/Estimate</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>528/0.93</td>
<td>531/2.10</td>
<td>0.44 (0.37, 0.53)</td>
</tr>
<tr>
<td>Age at study entry (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescent (≥12 – &lt;18)</td>
<td>41/0.68</td>
<td>41/0.97</td>
<td>0.70 (0.34, 1.46)</td>
</tr>
<tr>
<td>Adult (≥18 – &lt;65)</td>
<td>391/0.99</td>
<td>416/2.27</td>
<td>0.43 (0.35, 0.54)</td>
</tr>
<tr>
<td>Adult (≥65)</td>
<td>96/0.76</td>
<td>74/1.87</td>
<td>0.41 (0.25, 0.66)</td>
</tr>
<tr>
<td>Geographical region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>125/0.99</td>
<td>127/3.00</td>
<td>0.33 (0.23, 0.48)</td>
</tr>
<tr>
<td>North America</td>
<td>111/0.84</td>
<td>111/2.15</td>
<td>0.39 (0.26, 0.59)</td>
</tr>
<tr>
<td>South America</td>
<td>87/0.92</td>
<td>87/1.49</td>
<td>0.62 (0.39, 0.98)</td>
</tr>
<tr>
<td>Central/Eastern Europe</td>
<td>38/1.14</td>
<td>39/1.22</td>
<td>0.93 (0.46, 1.88)</td>
</tr>
<tr>
<td>Western Europe plus Australia</td>
<td>86/1.11</td>
<td>85/2.68</td>
<td>0.41 (0.26, 0.65)</td>
</tr>
<tr>
<td>Rest of world</td>
<td>81/0.59</td>
<td>82/1.29</td>
<td>0.46 (0.27, 0.77)</td>
</tr>
<tr>
<td>ICS dose at study entry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>131/0.85</td>
<td>132/1.33</td>
<td>0.64 (0.43, 0.95)</td>
</tr>
<tr>
<td>High</td>
<td>397/0.95</td>
<td>398/2.38</td>
<td>0.40 (0.32, 0.49)</td>
</tr>
<tr>
<td>OCS at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>49/2.12</td>
<td>51/2.94</td>
<td>0.72 (0.41, 1.26)</td>
</tr>
<tr>
<td>Absent</td>
<td>479/0.82</td>
<td>480/2.00</td>
<td>0.41 (0.33, 0.50)</td>
</tr>
<tr>
<td>Age at asthma diagnosis*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child (&lt;18 years old)</td>
<td>197/0.90</td>
<td>202/1.73</td>
<td>0.52 (0.38, 0.71)</td>
</tr>
<tr>
<td>Adult (≥18 years old)</td>
<td>331/0.94</td>
<td>329/2.34</td>
<td>0.40 (0.32, 0.51)</td>
</tr>
</tbody>
</table>

![Graph showing rate ratios and confidence intervals](image-url)
Tezepelumab for Severe Asthma: Effectiveness and Value

R. Brett McQueen, PhD
Assistant Professor
University of Colorado Anschutz Medical Campus
Key Review Team Members

- **Brett McQueen, PhD**, Assistant Professor, University of Colorado Anschutz Medical Campus
- **Eric Gutierrez, MPH**, Statistical Analyst, University of Colorado Anschutz Medical Campus
- **Jon Campbell, PhD**, ICER
- **Noemi Fluetsch, MSc, MPH**, ICER

**Disclosures:**

Financial support provided to the University of Colorado from the Institute for Clinical and Economic Review (ICER).

University of Colorado researchers have no conflicts to disclose defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers.
Objective

• Assess the lifetime cost-effectiveness of tezepelumab plus standard of care (SoC) [e.g., inhaled corticosteroid therapy and at least one additional controller medication] versus SoC alone in patients with severe asthma
Methods in Brief
Methods Overview

- **Time Horizon**: Patient lifetime
- **Setting**: United States
- **Perspective**: Health care sector (direct medical care and drug costs); modified societal
- **Cycle Length**: 2 weeks
- **Discount Rate**: 3% per year (costs and outcomes)
- **Outcomes**: Total and incremental: costs, life years, quality-adjusted life years (QALY), equal value of life years (evLY), percent responder
### Model Cohort Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) Age in Years</td>
<td>52 (12)</td>
</tr>
<tr>
<td>Percent Female</td>
<td>66%</td>
</tr>
<tr>
<td>Mean (SD) Weight in kg</td>
<td>78 (18)</td>
</tr>
<tr>
<td>Proportion of Patients with Chronic Oral Corticosteroid Use (SoC)</td>
<td>9.6%</td>
</tr>
<tr>
<td>Source</td>
<td>NAVIGATOR and PATHWAY (Menzies-Gow, 2021 and Corren, 2017)</td>
</tr>
</tbody>
</table>

kg: kilogram, SD: standard deviation, SoC: standard of care
## Treatment Regimens

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Dose</th>
<th>Approval Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab</td>
<td>210 mg subcutaneous injection every 4 weeks</td>
<td>Decision in early 2022</td>
</tr>
</tbody>
</table>

mg: milligram
*Exacerbation defined by different subcategories:

1. Mild exacerbation defined by asthma related event that requires an oral steroid burst (but not emergency room or hospitalization) and decrement to quality of life

2. Moderate exacerbation defined by asthma related event that requires admittance to the emergency department (but not a hospitalization) and decrement to quality of life

3. Severe exacerbation defined by asthma related event that requires a hospitalization, decrement to quality of life, and increased risk of mortality
Key Assumptions

• Utility for the non-exacerbation health state based on mapped relationship between the AQLQ and the EQ-5D
  - Utility allowed to be different for tezepelumab plus SoC vs. SoC alone due to potential improvements in day-to-day symptoms

• Increased mortality for severe exacerbations
  - Additional risks of death given oral steroid burst do not impact mortality over and above the severe asthma-related mortality rate

• Chronic OCS and impact on costs and disutility incorporated for doses greater than 5 mg per day

• No switching between biologics
## Key Model Inputs: SoC Clinical Inputs

<table>
<thead>
<tr>
<th>Key Input</th>
<th>Input Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized Exacerbation Rate, end of study (95% CI)</td>
<td>1.82 (1.58, 2.08)</td>
<td>Averaged across placebo arm of NAVIGATOR and PATHWAY trials</td>
</tr>
<tr>
<td>Proportion of Exacerbations Resulting in Steroid Burst (without ED visit or hospitalization)</td>
<td>76.8%</td>
<td>Soong et al. 2020 Figure 1</td>
</tr>
<tr>
<td>Proportion of Exacerbations Resulting in ED visit (without hospitalization)</td>
<td>9.1%</td>
<td>Soong et al. 2020 Figure 1</td>
</tr>
<tr>
<td>Proportion of Exacerbations Resulting in Hospitalization</td>
<td>14.1%</td>
<td>Soong et al. 2020 Figure 1</td>
</tr>
<tr>
<td>Severe Asthma Exacerbation Risk of Death</td>
<td>0.0068</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
</tbody>
</table>

CI: confidence interval, ED: emergency department
# Key Model Inputs: Tezepelumab plus SoC Clinical Inputs

<table>
<thead>
<tr>
<th>Key Input</th>
<th>Input Value for Tezepelumab plus SoC vs. SoC alone RR (95% CI)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab Rate Ratio for Exacerbations Resulting in Steroid Burst (without ED visit or hospitalization)</td>
<td>0.41 (0.33, 0.53)</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
<tr>
<td>Tezepelumab Rate Ratio for Exacerbations Resulting in ED Visit (without hospitalization)</td>
<td>0.20 (0.10, 0.41)</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
<tr>
<td>Tezepelumab Rate Ratio for Exacerbations Resulting in Hospitalization</td>
<td>0.20 (0.10, 0.41)</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
</tbody>
</table>

CI: confidence interval, ED: emergency department, RR: rate ratio, SoC: standard of care
## Key Model Inputs: Costs

<table>
<thead>
<tr>
<th>Key Input</th>
<th>Mean Input Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual Price for Therapy (Tezepelumab plus SoC)</td>
<td>$27,859 + annual SoC costs</td>
<td>Placeholder based on net pricing of dupilumab</td>
</tr>
<tr>
<td>Annual Cost for SoC</td>
<td>$6,494</td>
<td>Whittington et al. 2018</td>
</tr>
<tr>
<td>Exacerbation-Related Steroid Burst</td>
<td>$1,604</td>
<td>Suruki et al. 2017</td>
</tr>
<tr>
<td>Exacerbation-Related ED Visit</td>
<td>$2,161</td>
<td>Suruki et al. 2017</td>
</tr>
<tr>
<td>Exacerbation-Related Hospitalization</td>
<td>$9,442</td>
<td>Suruki et al. 2017</td>
</tr>
<tr>
<td>Annual Cost of Long-Term Oral Corticosteroid Use with Adverse Events</td>
<td>$8,326</td>
<td>Lefebvre et al. 2017</td>
</tr>
</tbody>
</table>

ED: emergency department, SD: standard deviation, SoC: standard of care
## Key Model Inputs: Utilities

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tezepelumab plus SoC</th>
<th>SoC (Placebo Arm)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Patient-Reported Outcome Measure</td>
<td>AQLQ</td>
<td>AQLQ</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
<tr>
<td>Asthma Patient-Reported Outcome Mean Change Difference vs. SoC (95% CI)</td>
<td>0.34 (0.17, 0.49)</td>
<td>Reference</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
<tr>
<td>Non-Exacerbation Mean Health State Utility for Biologic plus SoC vs. SoC Alone (95% CI)</td>
<td>0.788 (0.774, 0.801)</td>
<td>0.75</td>
<td>Pooled PATHWAY and NAVIGATOR trials</td>
</tr>
<tr>
<td>Steroid Burst</td>
<td>-0.1 (2-week duration)</td>
<td></td>
<td>Lloyd et al. 2007</td>
</tr>
<tr>
<td>ED Visit</td>
<td>-0.15 (2-week duration)</td>
<td></td>
<td>Lloyd et al. 2007 and assumption</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>-0.20 (2-week duration)</td>
<td></td>
<td>Lloyd et al. 2007</td>
</tr>
<tr>
<td>Chronic Oral Corticosteroid Use</td>
<td>-0.023 (annualized for a lifetime duration)</td>
<td></td>
<td>Norman et al. 2013</td>
</tr>
</tbody>
</table>

AQLQ: Asthma Quality of Life Questionnaire, CI: confidence interval, ED: emergency department, SoC: standard of care
Results
## Base-Case Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intervention Cost</th>
<th>Other Non-intervention Costs</th>
<th>Total Cost</th>
<th>QALYs</th>
<th>LYs</th>
<th>evLYs</th>
<th>% Responder†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab plus SoC*</td>
<td>$657,000</td>
<td>$40,000</td>
<td>$697,000</td>
<td>15.00</td>
<td>19.11</td>
<td>15.02</td>
<td>82%</td>
</tr>
<tr>
<td>SoC Alone</td>
<td>$122,000</td>
<td>$106,000</td>
<td>$228,000</td>
<td>13.91</td>
<td>18.80</td>
<td>13.91</td>
<td>70%</td>
</tr>
</tbody>
</table>

evLYs: equal value of life years, LYs: life years, QALYs: quality-adjusted life years, SoC: standard of care

*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
## Base-Case Incremental Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY Gained</th>
<th>Cost per evLY Gained</th>
<th>Cost per Responder†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab plus SoC*</td>
<td>SoC alone</td>
<td>$430,000</td>
<td>$422,000</td>
<td>$4.7 million</td>
</tr>
</tbody>
</table>

evLY: equal value of life year, QALY: quality-adjusted life year, SoC: standard of care

*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
One Way Sensitivity Analyses

Tezepelumab price is a placeholder based on net pricing of dupilumab; grey shade indicates lower input’s impact on the cost-per-QALY estimate whereas black shade indicates higher input’s impact.

ED: emergency department, QALY: quality-adjusted life year, SoC: standard of care

- Key drivers of cost-effectiveness estimates include utility for non-exacerbation state for tezepelumab plus Soc and SoC alone, severe asthma exacerbation risk of death, annualized exacerbation rate for SoC alone, and exacerbation rate ratio for tezepelumab plus SoC
### Probabilistic Sensitivity Analysis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost-Effective at $50,000 per QALY Gained</th>
<th>Cost-Effective at $100,000 per QALY Gained</th>
<th>Cost-Effective at $150,000 per QALY Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab plus SoC*</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Drug</td>
<td>Cost Effective at $50,000 per evLY Gained</td>
<td>Cost Effective at $100,000 per evLY Gained</td>
<td>Cost Effective at $150,000 per evLY Gained</td>
</tr>
<tr>
<td>Tezepelumab plus SoC*</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Notes:**
- evLY: equal value of life year
- QALY: quality-adjusted life year
- SoC: standard of care
- *Price is a placeholder based on net pricing of dupilumab
Scenario Analyses: Modified Societal Perspective

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY Gained</th>
<th>Cost per evLY Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezepelumab plus SoC</td>
<td>SoC alone</td>
<td>$424,000</td>
<td>$416,000</td>
</tr>
</tbody>
</table>

evLY: equal value of life year, QALY: quality-adjusted life year, SoC: standard of care
Limitations

• Placeholder price for tezepelumab

• Lack of evidence on long-term response and discontinuation; assumed full adherence and constant treatment benefits over lifetime

• No difference in direct mortality observed in trials. Future evidence on indirect mortality needed
Comments Received

- Mortality risks from exacerbations occurring directly from and outside of hospital settings
- Request for comparisons to 2018 review
- Changes to clinical and utility inputs for omalizumab and dupilumab, respectively
Conclusions

• Tezepelumab plus SoC provide clinical benefit in terms of gains in QALYs, LYs, and evLYs over SoC alone

• If price is similar to other asthma biologics it would not meet commonly cited cost-effectiveness thresholds
Questions?
Manufacturer Public
Comment and Discussion
Andrew Lindsley, MD, PhD, Asset Lead, Medical Director, Amgen

Conflicts of Interest:

- Dr. Lindsley is a full-time employee of Amgen.
Kyle Hvidsten, MPH, Head, Health Economics & Value Assessment, Sanofi

Conflicts of Interest:

- Kyle Hvidsten is a full-time employee of Sanofi.
Public Comment and Discussion
Kenneth Mendez, President & CEO, Asthma and Allergy Foundation of America

Conflicts of Interest:

• AAFA receives funding from pharmaceutical manufacturers, PhRMA, and PCMA.

• Kenneth has equity interests in Abbott Labs and AbbVie in excess of $10,000.
Conflicts of Interest:

- No financial conflicts to disclose.
Brenda Young, Patient Expert, Allergy and Asthma Network Volunteer

Conflicts of Interest:

• No financial conflicts to disclose.
Lunch

Meeting will resume at 12:45pm
Voting Questions
1. For adults and adolescents with severe asthma, is the evidence adequate to demonstrate that the net health benefit of tezepelumab added to standard-of-care therapy without biologics, is superior to that provided by standard-of-care therapy alone?

A. Yes

B. No
2. For adults and adolescents with severe eosinophilic asthma, is the evidence adequate to distinguish the net health benefit provided by tezepelumab from that provided by dupilumab?

A. Yes

B. No
2a. If the answer to question 2 is yes, which therapy has the greater net health benefit?

A. Tezepelumab

B. Dupilumab
3. For adults and adolescents with severe allergic asthma, is the evidence adequate to distinguish the net health benefit provided by tezepelumab from that provided by omalizumab?

A. Yes
B. No
3a. If the answer to question 3 is yes, which therapy has the greater net health benefit?

A. Tezepelumab
B. Omalizumab
4. For adults with steroid-dependent asthma, is the evidence adequate to distinguish the net health benefit provided by tezepelumab from that provided by dupilumab?

A. Yes

B. No
4a. If the answer to question 4 is yes, which therapy has the greater net health benefit?

A. Tezepelumab

B. Dupilumab
Contextual Considerations and Potential Other Benefits or Disadvantages
5. When making judgments of overall long-term value for money, what is the relative priority that should be given to any new effective treatment for severe asthma, on the basis of the following contextual considerations:

Acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability

A. Very low priority
B. Low priority
C. Average priority
D. High priority
E. Very high priority
6. When making judgments of overall long-term value for money, what is the relative priority that should be given to any new effective treatment for severe asthma, on the basis of the following contextual considerations:

Magnitude of the lifetime impact on individual patients of the condition being treated

A. Very low priority
B. Low priority
C. Average priority
D. High priority
E. Very high priority
7. What are the relative effects of tezepelumab versus standard-of-care alone on the following outcomes that inform judgment of the overall long-term value for money of tezepelumab?

Patients’ ability to achieve major life goals related to education, work, or family life

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect
8. What are the relative effects of tezepelumab versus standard-of-care alone on the following outcomes that inform judgment of the overall long-term value for money of tezepelumab?

Caregivers’ quality of life and/or ability to achieve major life goals related to education, work, or family life

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect
9. What are the relative effects of tezepelumab versus standard-of-care alone on the following outcomes that inform judgment of the overall long-term value for money of tezepelumab?

Patients’ ability to manage and sustain treatment given the complexity of regimen

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect
10. What are the relative effects of tezepelumab versus standard-of-care alone on the following outcomes that inform judgment of the overall long-term value for money of tezepelumab?

**Society’s goal of reducing health inequities**

A. Major negative effect  
B. Minor negative effect  
C. No difference  
D. Minor positive effect  
E. Major positive effect
Long-term Value for Money
13. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with tezepelumab versus standard-of-care alone?

A. Low long-term value for money at current prices

B. Intermediate long-term value for money at current prices

C. High long-term value for money at current prices
Break

Meeting will resume at 3:30pm
Policy Roundtable
<table>
<thead>
<tr>
<th>Policy Roundtable Participant</th>
<th>Conflict of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mindy Bauer, PharmD, Associate Director, Clinical Pharmacy, IPD Analytics</td>
<td>Dr. Bauer is a full-time employee of IPD Analytics.</td>
</tr>
<tr>
<td>Melanie Carver, Chief Mission Officer, Asthma and Allergy Foundation of America</td>
<td>AAFA receives funding from Pharmaceutical manufacturers, PhRMA, and PCMA.</td>
</tr>
<tr>
<td>Kyle Hvidsten, MPH, Head, Health Economics &amp; Value Assessment, Sanofi</td>
<td>Kyle Hvidsten is a full-time employee of Sanofi.</td>
</tr>
<tr>
<td>Tony R. Vancauwelaert, MD, FAAFP, Executive Medical Director, Enterprise Medical Operations - Pharmacy, Health Care Services Corporation</td>
<td>Dr. Vancauwelaert is a full-time employee of Heath Care Services Corporation.</td>
</tr>
<tr>
<td>Michael E. Wechsler, MD, Professor of Medicine, Director of NJH Cohen Family Asthma Institute, National Jewish Health</td>
<td>Dr. Wechsler has received consulting fees and honoraria from the following health care companies: AstraZeneca, Amgen, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Regeneron, and Sanofi.</td>
</tr>
<tr>
<td>Tonya Winders, MBA, President &amp; Chief Executive Officer, Allergy &amp; Asthma Network</td>
<td>Tonya Winders serves as a speaker &amp; advisor to AstraZeneca, Amgen, GSK, Novartis, Sanofi, Regeneron &amp; ALK Abello. The Allergy &amp; Asthma Network receives funding from healthcare companies for unbranded disease awareness, education, advocacy &amp; research.</td>
</tr>
<tr>
<td>David Zimmer, BS, MBA, Vice President US Value and Access, Amgen</td>
<td>David Zimmer is a full-time employee of Amgen.</td>
</tr>
</tbody>
</table>
Next Steps

• Meeting recording posted to ICER website next week

• Final Report published on or around December 16
  • Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion

• Materials available at: https://icer.org/asthma-2021/#timeline
Adjourn