Ensifentrine for Chronic Obstructive Pulmonary Disease: Effectiveness and Value

Public Meeting — June 14, 2024

Meeting materials available at: https://icer.org/assessment/copd-2024/
Patient Experts

Valerie Chang, Executive Director, Hawaii COPD Coalition

- Hawaii COPD Coalition receives annual sponsorships from a BCBS insurer and exhibit fees from pharmaceutical companies for the annual COPD Education Day. The COPD Foundation receives greater than 25% of funding from health care companies.

Phyliss DiLorenzo, Patient Expert, COPD Foundation Board Member

- No personal conflicts to disclose. The COPD Foundation receives greater than 25% of funding from health care companies.
Clinical Experts

Dr. Stephanie Christenson, MD, MAS, Associate Professor, Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine, UCSF

- Dr. Christenson reports grant support from the NIH, American Lung Association, COPD Foundation, and Department of Defense; consulting and advisory board fees from AstraZeneca, Sanofi, Regeneron, GSK, Verona Pharma, Glenmark Pharmaceuticals, Axon Advisors, Apogee Therapeutics, Amgen, Devpro Pharma, Kymera Therapeutics, and Genentech; Non-branded speaking fees from AstraZeneca, GSK, Sanofi, Regeneron, Amgen, Medscape, Horizon CME; writing fees from UpToDate.

Dr. Juan Rojas, MD, MS, Director of Clinical Informatics & Data Science, Division of Translational & Precision Medicine, and Assistant Professor, Department of Internal Medicine, Division of Pulmonary, Critical Care, & Sleep Medicine, Rush University

- No conflicts to disclose.
"I tire out a lot easier than I used to. I find that when I plan my day, I try to plan it for the mornings because I know by afternoon I’m done. I used to have a very active lifestyle, I used to walk everywhere. I can’t do that anymore. I’ve made many modifications around my home—I have chairs everywhere for support, so I can move around without a walker. I want to get a ramp to the front door, mainly for carrying oxygen tanks in and out of the house. Speaking of oxygen—that is another thing I need to factor in when planning for my day. COPD rules my life.”

Person with COPD
(https://www.lung.org/blog/living-with-copd)
Why Are We Here Today?

• What happens the day these treatments receive FDA approval?

• Questions about:
  • What are the risks and benefits?
  • How do new treatments fit into the evolving landscape?
  • What are reasonable prices and costs to patients, the health system, and the government?
  • What lessons are being learned to guide our actions in the future?
The Impact on Rising Health Care Costs for Everyone

100 Million People in America Are Saddled With Health Care Debt

By Noam N. Levey
JUNE 16, 2022

Why Delaware is eyeing a 27% premium hike on state employees' health insurance

Amanda Fries
Delaware News Journal
Published 4:35 a.m. ET Feb. 1, 2024 | Updated 9:29 p.m. ET Feb. 6, 2024
Organizational Overview

• Midwest CEPAC

• Institute for Clinical and Economic Review (ICER)
Funding 2024

- Nonprofit Foundations: 68%
- Health Plans and Provider Group Contributions: 14%
- Manufacturer Contributions: 8%
- ICER Analytics Subscribers: 9%
- Philanthropy/Other: 1%

ICER Policy Summit and non-report activities only

*ICER received significant funding from Arnold Ventures, California Health Care Foundation, & The Commonwealth Fund. Source: https://icer.org/who-we-are/independentfunding/sources-of-funding/
How Was the ICER Report Developed?

- Scoping with guidance from patients, clinical experts, manufacturers, and other stakeholders
- ICER evidence analysis in collaboration with University of California San Francisco, and cost-effectiveness modeling in collaboration with Tufts Medical Center
- Public comment and revision
- Expert reviewers:
  - Igor Barjaktarevic, MD, PhD, David Geffen School of Medicine at UCLA
  - David Mannino, MD, COPD Foundation
  - Martine Hoogendoorn-Lips, PhD, Erasmus University Rotterdam
- How is the evidence report structured to support Midwest 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 (CT)

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00 AM</td>
<td>Meeting Convened and Opening Remarks</td>
</tr>
<tr>
<td>10:20 AM</td>
<td>Presentation of the Clinical Evidence</td>
</tr>
<tr>
<td>11:00 AM</td>
<td>Presentation of the Economic Model</td>
</tr>
<tr>
<td>11:40 AM</td>
<td>Public Comments and Discussion</td>
</tr>
<tr>
<td>12:00 PM</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>12:50 PM</td>
<td>MW CEPAC Deliberation and Vote</td>
</tr>
<tr>
<td>1:50 PM</td>
<td>Break</td>
</tr>
<tr>
<td>2:00 PM</td>
<td>Policy Roundtable Discussion</td>
</tr>
<tr>
<td>3:30 PM</td>
<td>Reflections from Midwest CEPAC</td>
</tr>
<tr>
<td>4:00 PM</td>
<td>Meeting Adjourned</td>
</tr>
</tbody>
</table>
Presentation of the Clinical Evidence

Grace Lin, MD, MAS

Medical Director for Health Technology Assessment, ICER

Associate Professor of Medicine and Health Policy, UCSF
Key Collaborators

• Abigail Wright, PhD, MSc, Research Scientist, ICER

• Avery McKenna, BS, Associate Research Lead, ICER

• Finn Raymond, BS, Research Assistant, ICER

Disclosures: Financial support provided to the Grace Lin from the Institute for Clinical and Economic Review (ICER)

Grace Lin, Abigail Wright, Avery McKenna, and Finn Raymond 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.
Background: COPD

COPD is a group of lung diseases that is characterized by progressive and persistent airflow obstruction in the lungs.

COPD affects 16 million people in the U.S. and is the 6th leading cause of death.

Smoking is the leading cause of COPD in the US. Other factors such as secondhand smoke exposure, occupational exposure, and chronic asthma can play a role.

COPD leads to 1 million ED visits and 50,000 hospitalizations, resulting in a cost of $50 million per year.
COPD Symptoms

- Diagnosis of COPD is based on lung function (e.g., FEV₁/FVC <0.7).

- Symptoms include persistent shortness of breath, fatigue, wheezing, chest tightness, sputum production, and cough.

- Exacerbations are also an important marker of disease.
COPD Diagnosis and Classification

COPD classification is based on:

• **Severity of airflow obstruction**

• **Annual exacerbation history**

• **Symptoms**
### Discussions with People with COPD

#### Impact on Daily Life
- Daily tasks are challenging, e.g., making the bed
- Needing to plan around symptoms - "pacing yourself"
- Travel can be difficult if oxygen tanks or wheelchairs are required

#### Treatment is Complex
- Needing to manage multiple inhalers/nebulizers, difficulty with proper inhaler technique
- Side effects (dry mouth, nausea, thrush, cough, diarrhea)
- Nebulized treatment can be time-consuming and less portable

#### Burden on Unpaid Caregivers
- Monitoring adherence
- Burden of physical and emotional support as disease progresses

#### Considerations for Future Treatments
- Disease-modifying treatments needed
- Decrease mucus production and need for supplemental oxygen
About **half of COPD patients reporting near daily symptoms**, and the majority reporting that symptoms have a moderate-to-great impact on everyday life.
Ensifentrine

**PDE3 Inhibition**

Airway Smooth Muscle

↑ Bronchial relaxation

**PDE4 Inhibition**

Inflammatory Cells

↑ Cell activation, migration, proliferation, & survival

Bronchial Epithelial Cells

↑ CFTR activation

↑ Ciliary function

Bronchodilation

Anti-inflammatory effects

Mucociliary clearance

*Figure adapted from Donohue et al. 2023*

CFTR: cystic fibrosis transmembrane, PDE: phosphodiesterase
Scope of Review

• Adults with moderate to severe COPD

• Comparative clinical effectiveness of ensifentrine as an add-on therapy to current maintenance therapy, including:
  • LABAs
  • LAMAs
  • ICS
  • Combination of the above

• Comparator: Current maintenance therapy
## Outcomes

### Annualized Moderate or Severe Exacerbation Rate

- **Moderate**
  - Worsening of symptoms (e.g., dyspnea, sputum volume, cough, wheezing) for > 2 days and requiring systemic corticosteroids and/or antibiotics
- **Severe**
  - Required worsening of symptoms and inpatient hospitalization

### Quality of Life Measures

- Transition Dyspnea Index (TDI), Evaluating-Respiratory Symptoms (E-RS), St. George's Respiratory Questionnaire (SGRQ), EuroQol-5-Domain Questionnaire (EQ-5D-5L)

### Lung Function Measures

- Change in FEV$_1$ from baseline

### Other Outcomes

- Time to first exacerbation and daily average rescue medication
Clinical Evidence
# Key Clinical Trials

## Two Phase III RCTs (ENHANCE-1 and ENHANCE-2)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>N</th>
<th>Population</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENHANCE-1</td>
<td>Phase III randomized, double-blind, placebo-controlled trial</td>
<td>763</td>
<td>Adults with moderate (56%) to severe (44%) COPD</td>
<td>24 weeks (with a 48-week safety subset)</td>
</tr>
<tr>
<td>ENHANCE-2</td>
<td></td>
<td>790</td>
<td>COPD</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>
Background Therapy

**Permitted**
- Rescue medication:
  - Albuterol/salbutamol
- **Maintenance use:**
  - LAMA or LABA therapy
  - ICS taken with LAMA or LABA

**Prohibited**
- LAMA/LABA combinations
- Oral, systemic or parenteral steroid therapies
- High dose of ICS
- Antibiotics for respiratory tract infection
- Beta-2 agonists (<4 hours)
- Theophylline, leukotriene, and PDE4 inhibitors (48 hrs prior)
ENHANCE Trials

Baseline Characteristics

- Mean age of 65 years
- 92% White
- 53% male
- 62% on background therapy
  - 31% on LAMA, 1% on LAMA+ICS, 12%
  - on LABA, 18% on LABA+ICS
- 24% of participants had an exacerbation
  ≤15 months prior to screening

Trial Withdrawal

- Trial withdrawal was high
  - ENHANCE-1 at week 48: 14.8%
  - ENHANCE-2 at week 24: 23.1%
- Of those who withdrew:
  - 37-45% withdrew consent
  - 13-15% had COVID-19

Pooled baseline characteristics from the ENHANCE-1 and -2 trials.
Ensifentrine Decreases Moderate or Severe COPD Exacerbations

Exacerbation Rate Versus Placebo

ENHANCE-1

ENHANCE-2

Summary RR: 0.60 (0.41, 0.79)

Favors ensifentrine
Ensifentrine Increases Time to First Exacerbation

**Time to First Exacerbation**
**Versus Placebo**

ENHANCE-1

ENHANCE-2

**Summary**
HR: 0.60 (0.41, 0.78)

Favors ensifentrine

HR: Hazard Ratio
Effect on Quality of Life was Inconsistent

• Mean changes vs placebo did not exceed MCID for two of three quality of life measures (E-RS, SGRQ).

• However, a greater proportion of patients in ensifentrine group reached or exceeded MCID for E-RS, SGRQ.

• Mean change in TDI exceeded MCID in ENHANCE-1.

• Statistically significant improvement in EQ-5D in ENHANCE-2.
Other Outcomes

• Ensifentrine groups had a significant improvement in FEV$_1$ at 12 weeks in ENHANCE-1 and 2.

• Ensifentrine decreases use of rescue medication at 24 weeks (pooled data from ENHANCE-1 and 2).
## Harms

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Adverse Events</td>
<td>Similar reporting between ensifentrine and placebo arms (~6-7%).</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>Comparable reporting of TEAEs leading to discontinuation between arms (~6-10%). Similar trend was seen when COVID-19 cases were removed.</td>
</tr>
<tr>
<td>Gastrointestinal Harms</td>
<td>Reported by 5.2% in both arms, 0.4% were causally related to ensifentrine.</td>
</tr>
<tr>
<td>Other Harms</td>
<td>Low percentage of pneumonia, UTIs, hypertension, and cardiac disorder.</td>
</tr>
</tbody>
</table>
Controversies and Uncertainties

Demographic Differences to Real-world Patients
- Younger and had fewer exacerbations
- Background therapy did not reflect current standard of practice
  - 35-40% on no background therapy at baseline
  - No dual or triple therapy

Impact on Quality of Life
- Smaller changes in ENHANCE-2 since placebo group had relatively larger changes from baseline
- Two of the three QOL measures did not exceed MCID

Short trial follow-up and high withdrawal rate
- Primary outcomes at 12 and 24 weeks
- Around 40% withdrawal rate, likely affected by pandemic
Benefits Beyond Health and Special Ethical Priorities

Key Points

• Has potential to fill gaps in COPD care
  • May be particularly valuable in patients with suboptimal disease control, continue to experience symptoms, or have side effects on therapy
• Impact on ability to achieve long-term goals
  • Ensifentrine not thought to be disease-modifying nor have a large effect on patient/caregiver ability to achieve long-term goals
• Impact on access limited
  • Delivered via nebulizer, likely will not have an impact on access
The symptom burden associated with COPD is significant.

Quality of life measures do not capture the full spectrum of impact of COPD.
Summary

• Ensifentrine improved measures of lung function, including average FEV$_1$, at 12 weeks.

• Ensifentrine also decreased annualized rate of moderate to severe exacerbations by 40% at 24 weeks, maintained until 48 weeks.

• Evidence of the impact on quality of life was mixed.

• Adverse events and discontinuation rates were similar among those who received ensifentrine and placebo.
## ICER Evidence Ratings

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Evidence Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine added on to maintenance therapy</td>
<td>Maintenance therapy alone</td>
<td>B+</td>
</tr>
</tbody>
</table>
Questions?
Presentation of the Economic Evidence

Melanie D. Whittington, PhD, MS

Center for the Evaluation of Value and Risk in Health

Tufts Medical Center
Key Review Team Members

• Melanie Whittington, PhD, Senior Fellow, CEVR, Tufts Medical Center

• Marina Richardson, PhD, Associate Director, HTA Methods and Health Economics, ICER

Disclosures:

Financial support was provided from the Institute for Clinical and Economic Review.

No conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.
Objective

To evaluate the lifetime cost-effectiveness of ensifentrine added on to current maintenance therapy compared to current maintenance therapy alone for the treatment of COPD in patients with moderate to severe COPD at baseline.
# Unmet Need

<table>
<thead>
<tr>
<th>Condition</th>
<th>Absolute evLY Shortfall</th>
<th>Proportional evLY Shortfall</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>8.1</td>
<td>54%</td>
</tr>
</tbody>
</table>

**Other Example Conditions**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Absolute evLY Shortfall</th>
<th>Proportional evLY Shortfall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Sclerosis</td>
<td>18.9</td>
<td>52%</td>
</tr>
<tr>
<td>PTSD</td>
<td>7.4</td>
<td>21%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2.6</td>
<td>19%</td>
</tr>
</tbody>
</table>

COPD: chronic obstructive pulmonary disease; evLY: equal value of life years gained; PTSD: post-traumatic stress disorder
Methods in Brief
## Methods Overview

<table>
<thead>
<tr>
<th>Model</th>
<th>Markov</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td>United States</td>
</tr>
<tr>
<td>Perspective</td>
<td>Health Care Sector and Modified Societal</td>
</tr>
<tr>
<td>Time Horizon</td>
<td>Lifetime</td>
</tr>
<tr>
<td>Discount Rate</td>
<td>3% per year (costs and outcomes)</td>
</tr>
<tr>
<td>Cycle Length</td>
<td>One year</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Costs, Quality-adjusted life years (QALYs); Equal value life years (evLYs); Life years; Exacerbations</td>
</tr>
</tbody>
</table>

evLYs: equal value life years, QALYs: quality-adjusted life years
Model Schematic

- Moderate COPD
- Severe COPD
- Very Severe COPD

From all living health states

Death
Exacerbations as Events

• **Moderate Exacerbation**
  • An exacerbation that results in a prescription of a corticosteroid and/or an antibiotic but did not result in a hospitalization.

• **Severe Exacerbation**
  • An exacerbation that results in a hospitalization for COPD.
## Cohort Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67</td>
</tr>
<tr>
<td>Female, %</td>
<td>56.4%</td>
</tr>
<tr>
<td>Current Smokers, %</td>
<td>41.2%</td>
</tr>
<tr>
<td>Moderate COPD* at Baseline, %</td>
<td>78.1%</td>
</tr>
<tr>
<td>Severe COPD† at Baseline, %</td>
<td>21.9%</td>
</tr>
</tbody>
</table>

COPD: chronic obstructive pulmonary disease

*Defined as an FEV₁ of 50%-79%

†Defined as an FEV₁ of 30% to 49%
Key Assumptions

Ensifentrine’s effect on lung function did not translate to health state changes.

Ensifentrine’s effect on improved quality of life was downstream of its effect on exacerbations.

Adverse event-related discontinuation occurred at week 12 and only impacted the percent receiving the treatment cost.
## Exacerbations, Current Maintenance Therapy Alone

<table>
<thead>
<tr>
<th>Health State</th>
<th>Exacerbations§ per Year</th>
<th>Severe Exacerbations per Year#</th>
<th>Moderate Exacerbations per Year¤</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate COPD*</td>
<td>1.17 (0.93, 1.44)</td>
<td>0.16</td>
<td>1.01</td>
</tr>
<tr>
<td>Severe COPD†</td>
<td>1.61 (1.49, 1.74)</td>
<td>0.22</td>
<td>1.39</td>
</tr>
<tr>
<td>Very Severe COPD‡</td>
<td>2.10 (1.46, 2.86)</td>
<td>0.29</td>
<td>1.81</td>
</tr>
</tbody>
</table>

* Defined as an FEV₁ of 50%-79%, GOLD 2  
† Defined as an FEV₁ of 30% to 49%, GOLD 3  
‡ Defined as an FEV₁ of less than 30%, GOLD 4  
§ Either a moderate or severe exacerbation.  
# A severe exacerbation is defined as an exacerbation leading to a hospitalization for COPD.  
¤ A moderate exacerbation is defined as an exacerbation leading to a prescription of systemic corticosteroids and/or antibiotics.
## Exacerbations, Ensifentrine

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Exacerbation Rate Ratio (95% Confidence Interval)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine</td>
<td>0.60 (0.41, 0.79)</td>
<td>From ICER’s meta-analysis of ENHANCE-1 and ENHANCE-2 at week 24</td>
</tr>
</tbody>
</table>
### Mortality

<table>
<thead>
<tr>
<th>Non-Exacerbation Mortality</th>
<th>Standardized Mortality Ratio</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate COPD*</td>
<td>1.6</td>
<td>For COPD not due to exacerbations; Applied to age- and sex-adjusted all-cause mortality</td>
</tr>
<tr>
<td>Severe COPD†</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>Very Severe COPD‡</td>
<td>1.9</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exacerbation Mortality</th>
<th>Case-Fatality Rate</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Exacerbation§</td>
<td>15.6%</td>
<td>Applied per severe exacerbation</td>
</tr>
</tbody>
</table>

* Defined as an FEV₁ of 50%-79%, GOLD 2
† Defined as an FEV₁ of 30% to 49%, GOLD 3
‡ Defined as an FEV₁ of less than 30%, GOLD 4
§ A severe exacerbation is defined as an exacerbation leading to a hospitalization for COPD.
# Treatment Costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Annual Estimate</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine</td>
<td>$18,000</td>
<td>Placeholder price based on IPD Analytics</td>
</tr>
<tr>
<td>Current Maintenance Therapy</td>
<td>$3,453</td>
<td>Basket of drugs within LAMA only, LABA+ICS, and LABA+LAMA+ICS regimens</td>
</tr>
</tbody>
</table>
Results
## Lifetime Model Outcomes – Cost Outcomes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Intervention Cost*</th>
<th>Non-Intervention Cost</th>
<th>Total Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine + Current Maintenance Therapy</td>
<td>$144,300</td>
<td>$280,600</td>
<td>$424,900</td>
</tr>
<tr>
<td>Current Maintenance Therapy Alone</td>
<td>$0</td>
<td>$283,600</td>
<td>$283,600</td>
</tr>
</tbody>
</table>

*Based on placeholder price of $18,000 per year
### Lifetime Model Outcomes – Health Outcomes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total Exacerbations</th>
<th>Life Years</th>
<th>QALYs</th>
<th>evLYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine + Current Maintenance Therapy</td>
<td>8.03</td>
<td>8.43</td>
<td>6.25</td>
<td>6.34</td>
</tr>
<tr>
<td>Current Maintenance Therapy Alone</td>
<td>12.26</td>
<td>7.71</td>
<td>5.68</td>
<td>5.68</td>
</tr>
</tbody>
</table>

evLYs: equal value of life years, QALYs: quality-adjusted life years
### 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>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine + Current Maintenance Therapy</td>
<td>Current Maintenance Therapy Alone</td>
<td>$248,000</td>
<td>$214,000</td>
</tr>
</tbody>
</table>

*Based on placeholder price of $18,000 per year

evLY: equal value life year, QALY: quality-adjusted life year
## One Way Sensitivity Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine exacerbation rate ratio</td>
<td>$167,299</td>
<td>$472,003</td>
</tr>
<tr>
<td>Percent of exacerbations that are moderate</td>
<td>$171,698</td>
<td>$440,387</td>
</tr>
<tr>
<td>Case-fatality rate per severe exacerbation</td>
<td>$202,075</td>
<td>$326,179</td>
</tr>
<tr>
<td>Total exacerbations per year, moderate COPD</td>
<td>$225,582</td>
<td>$273,342</td>
</tr>
<tr>
<td>Total exacerbations per year, very severe COPD</td>
<td>$239,809</td>
<td>$256,869</td>
</tr>
<tr>
<td>Annual maintenance therapy cost</td>
<td>$243,541</td>
<td>$259,645</td>
</tr>
<tr>
<td>Total exacerbations per year, severe COPD</td>
<td>$241,936</td>
<td>$253,946</td>
</tr>
<tr>
<td>Cost per severe exacerbation</td>
<td>$242,397</td>
<td>$252,753</td>
</tr>
<tr>
<td>Utility of very severe COPD</td>
<td>$243,431</td>
<td>$252,533</td>
</tr>
<tr>
<td>Cost per moderate exacerbation</td>
<td>$244,655</td>
<td>$250,703</td>
</tr>
</tbody>
</table>
Probabilistic Sensitivity Analysis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost-Effective at $50,000 per evLY</th>
<th>Cost-Effective at $100,000 per evLY</th>
<th>Cost-Effective at $150,000 per evLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine*</td>
<td>0%</td>
<td>0%</td>
<td>12%</td>
</tr>
</tbody>
</table>

evLY: equal value life year
*Based on placeholder price of $18,000 per year
## Scenario Analyses

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Modified Societal Perspective* ($/evLY)</th>
<th>Exclusion of Unrelated Costs* ($/evLY)</th>
<th>Ensifentrine Effect on Quality of Life* ($/evLY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensifentrine</td>
<td>$230,000</td>
<td>$190,000</td>
<td>$175,000</td>
</tr>
</tbody>
</table>

evLY: equal value life year
*Based on placeholder price of $18,000 per year
## Health Benefit Price Benchmarks (HBPBs)

<table>
<thead>
<tr>
<th>Annual Prices Using...</th>
<th>Annual Price at $100,000 Threshold</th>
<th>Annual Price at $150,000 Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>QALYs Gained</td>
<td>$7,500</td>
<td>$11,000</td>
</tr>
<tr>
<td>evLYs Gained</td>
<td>$8,600</td>
<td>$12,700</td>
</tr>
</tbody>
</table>
Limitations

Top Limitations

- The evidence to inform the treatment basket for current maintenance therapy predated LABA/LAMA combination products.
- The modified societal perspective may not fully represent the impact of COPD on patients and caregivers.
Comments Received

• Use the GOLD ABE classification to define the health states.

• Allow for exacerbations to impact disease progression.

• Incorporate an effect of ensifentrine on day-to-day quality of life in the base case.
Conclusions

• Treatment with ensifentrine results in fewer exacerbations and in greater QALYs, evLYs, and life years.

• At a placeholder price of $18,000 per year, ensifentrine exceeds commonly used thresholds.

• If ensifentrine is shown to improve the quality of life of patients not experiencing an exacerbation, cost-effectiveness improves.
Questions?
Manufacturer Public Comment and Discussion
Kavita Aggarwal, PharmD  
SVP Medical Affairs, Verona Pharma  

Conflicts of Interest:  

• Dr. Aggarwal is a full-time employee at Verona Pharma.
Public Comment and Discussion
Tonya Winders, MBA  
President and CEO, Global Allergy and Airways Patient Platform

Conflicts of Interest:

- Tonya has acted as a paid advisor for unbranded disease awareness, education and advocacy for AZ, Chiesi, GSK, Roche, MSD, and Sanofi Regeneron and has received <25% of overall funds from these health care companies.
Lunch

Meeting will resume at 12:50PM CT
Voting Questions
Patient Population for all questions: Adults with Moderate to Severe COPD on maintenance therapy. Maintenance therapy can be: LAMA, LABA, combination therapy or combination therapy with ICS.
Clinical Evidence
1. Is the current evidence adequate to demonstrate that the net health benefit of ensifentrine added to maintenance therapy is superior to that of maintenance therapy alone?
Benefits Beyond Health and Special Ethical Priorities
2. There is substantial unmet need despite currently available treatments.
3. This condition is of substantial relevance for people from a racial/ethnic group that have not been equitably served by the healthcare system.
To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements based on the relative effects of ensifentrine added to maintenance therapy versus maintenance therapy alone:
4. The treatment is likely to produce substantial improvement in caregivers’ quality of life and/or ability to pursue their own education, work, and family life.
5. The treatment offers a substantial opportunity to improve access to effective treatment by means of its mechanism of action or method of delivery.
Long-Term Value for Money
7. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering benefits beyond health and special ethical priorities:
What is the long-term value for money of ensifentrine added to maintenance therapy compared to maintenance therapy alone at assumed pricing?
Break

Meeting will resume at 2:00PM CT
<table>
<thead>
<tr>
<th>Participant</th>
<th>Conflict of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mindy Bauer, PharmD</strong>, Pharmacist, IPD Analytics</td>
<td>Mindy Bauer is a full-time employee at IPD Analytics.</td>
</tr>
<tr>
<td><strong>Valerie Chang, BA, JD</strong>, Executive Director, Hawaii COPD Coalition,</td>
<td>Hawaii COPD Coalition receives annual sponsorships from a BCBS insurer and exhibit fees from pharmaceutical companies for the annual COPD Education Day. The COPD Foundation also receives greater than 25% of funding from health care companies.</td>
</tr>
<tr>
<td><strong>Stephanie Christenson, MD, MAS</strong>, Associate Professor, Division of</td>
<td>Dr. Christenson reports grant support from the NIH, American Lung Association, COPD Foundation, and Department of Defense; consulting and advisory board fees from AstraZeneca, Sanofi, Regeneron, GSK, Verona Pharma, Glenmark Pharmaceuticals, Axon Advisors, Apogee Therapeutics, Amgen, Devpro Pharma, Kymera Therapeutics, and Genentech; Non-branded speaking fees from AstraZeneca, GSK, Sanofi, Regeneron, Amgen, Medscape, Horizon CME; writing fees from UpToDate.</td>
</tr>
<tr>
<td>Pulmonary, Critical Care, Allergy, and Sleep Medicine, UCSF</td>
<td></td>
</tr>
<tr>
<td><strong>Phyliss DiLorenzo</strong>, Patient Expert, COPD Foundation Board Member</td>
<td>No personal conflicts to disclose. The COPD Foundation receives greater than 25% of funding from health care companies.</td>
</tr>
<tr>
<td><strong>David Dohan, MD, MHCM</strong>, Medical Director for Pharmacy and Appeals,</td>
<td>Dr. Dohan is a full-time employee at Point34Health.</td>
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<tr>
<td>Point34Health</td>
<td></td>
</tr>
<tr>
<td><strong>Juan Rojas, MD, MS</strong>, Director of Clinical Informatics &amp; Data Science,</td>
<td>No conflicts to disclose.</td>
</tr>
<tr>
<td>Division of Translational &amp; Precision Medicine, and Assistant Professor,</td>
<td></td>
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<tr>
<td>Department of Internal Medicine, Division of Pulmonary, Critical Care,</td>
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<tr>
<td>&amp; Sleep Medicine, Rush University</td>
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Midwest CEPAC Council Reflections
Next Steps

• Meeting recording posted to ICER website next week

• Final Report published on or around July 16th, 2024
  • Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion

• Materials available at: https://icer.org/assessment/copd-2024/
Adjourn