Inotersen and Patisiran for Hereditary Transthyretin Amyloidosis

Public Meeting – Afternoon Session
September 13, 2018
Welcome and Introduction

Why are we here this afternoon?

The prospect of new treatments designed for slowing/stabilising hATTR offers significant hope to patients and their families. This is especially so given the context of the disease being hereditary, the negative impact it has on patients and carers’ quality of life, and there being no other licensed alternatives available with which to treat the disease.

~ Amyloidosis Research Consortium

Working for a private company that is self-insured does not give me unlimited access to funds. We will play this out to whatever our insurance carrier can provide and see what is left. If my portion becomes an amount that starts eroding my ability to care for my family, I will have no choice but to discontinue and eventually enter palliative care. My life insurance along with other provisions I have made will hopefully carry them to the end of their natural life.

~ Amyloidosis Patient
Welcome and Introduction

Why are we here this afternoon?

• Increasing health care costs affecting individuals, state and federal budgets

• New treatments for ultra-rare conditions often raise questions about long-term safety and efficacy, appropriate use, and affordability

• Patients can have difficulty accessing drugs
  – High out-of-pocket costs
  – Limited access to treatment centers and experts

• Need for objective evaluation and public discussion of the evidence on effectiveness and value
Welcome and Introduction

How was the ICER report on inotersen and patisiran developed?

- Scoping with guidance from patient groups and advocates, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis, with expertise from Boston Medical Center
- University of California, Davis cost-effectiveness modeling
- Public comment and revision
- Expert reviewers for the evidence report:
  - Merrill D. Benson, MD, Indiana University School of Medicine
  - John L. Berk, MD, Boston Medical Center
  - Rita Faria, MSc, University of York
  - Sarah Richard, Amyloidosis Research Consortium
  - Frederick L. Ruberg, MD, Boston Medical Center

- How is the evidence report structured to support CEPAC voting and policy discussion?
Goal: Sustainable Access to High-Value Care for All Patients

Long-Term Value for Money
- Comparative Clinical Effectiveness
- Incremental cost-effectiveness
- Other Benefits or Disadvantages
- Contextual Considerations

Short-Term Affordability
- Potential Budget Impact
Afternoon Agenda

12:45 pm: Welcome and Opening Remarks

1:00 pm: Presentation of the Evidence and Economic Modeling
  • Karen E. Lasser, MD, MPH, Boston Medical Center
  • Jeffrey S. Hoch, PhD, University of California, Davis

2:00 pm: Public Comments

2:45 pm: MW CEPAC Vote on Clinical Effectiveness and Value

3:45 pm: Policy Roundtable Discussion

4:45 pm: Reflections from Experts and MW CEPAC Panel

5:00 pm: Meeting Adjourned
Evidence Review

Karen E. Lasser, MD, MPH
Professor of Medicine
Boston Medical Center
**Key review team members:**
Kristin Mickle, MPH
Aqsa Mugal

**Disclosures:**
We have no conflicts of interest relevant to this report.
Hereditary transthyretin amyloidosis (hATTR)

• One of 130 gene mutations that causes protein made in liver to mis-fold and deposit
• Proteins disrupt the function of major organs
• Age of onset/clinical presentation varies
• Cardiac-predominant illness: most predictive of early death
• Neuropathy-predominant illness: most physically disabling, rare worldwide and in US
Therapies for hATTR

• Until recently, no therapy approved in US
• Remove source of transthyretin (TTR) protein
  • Liver transplant
• Stabilize TTR
  • Off-label use of diflunisal
• “Knock down” TTR levels by interfering with RNA
  • Inotersen-SQ- FDA approval expected 10/2018
  • Patisiran-IV+ steroid-FDA approved 8/2018
What we heard from patients

• Severe disabling illness that profoundly impacts all aspects of quality of life
• Affects multiple members and generations of families
• Difficult for patients to travel to centers of excellence to receive treatment
• New treatments for hATTR offer much-needed hope to patients and their families
• Affordability of new therapies is a major concern
Scope of the Review
• To evaluate the clinical effectiveness of inotersen and patisiran, respectively, for hATTR
• Comparator: Best supportive care

<table>
<thead>
<tr>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Neurologic impairment</td>
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<tr>
<td>Quality of life</td>
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<tr>
<td>Cardiac outcomes</td>
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<tr>
<td>Disease progression</td>
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<td>Functional impairment</td>
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<tr>
<td>Harms</td>
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<tr>
<td>Mortality</td>
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</table>
Body of Evidence

- Two trials of inotersen
  - 1 Phase III RCT with open label extension (OLE), 1 single-arm, open-label trial
- Two trials of patisiran
  - 1 Phase III RCT, 1 Phase II trial, and OLE
## Overview of Randomized Trials

<table>
<thead>
<tr>
<th>Key Trials</th>
<th>Treatment Groups</th>
<th>Patient Characteristics</th>
<th>Primary Outcome</th>
</tr>
</thead>
</table>
| **NEURO-TTR**  
Phase III  
Parallel-arm RCT  
15 months | Placebo  
Inotersen | N=173  
Mean age: 59  
92% white  
48% US  
67% FAP stage 1 | Modified Neuropathy Impairment Score+7  
(Ionis)-347 points  
Norfolk Quality of Life–Diabetic Neuropathy questionnaire |
| **APOLLO**  
Phase III  
Parallel-arm RCT  
18 months | Placebo  
Patisiran | N=225  
Median age: 62  
76% white  
20% US  
46% FAP stage 1 | Modified Neuropathy Impairment Score+7-304 points |
Primary clinical outcomes

• Modified Neuropathy Impairment Score+7
  • Composite score: motor strength, reflexes, sensation, nerve conduction, autonomic function
  • Higher score = worse neurologic function

• Norfolk Quality of Life–Diabetic Neuropathy questionnaire
  • Higher score = poorer quality of life
Secondary and exploratory outcomes

- Modified BMI
  - Used to measure wasting associated with progression of neuropathy and disability
- Disease progression
  - Familial Amyloid Polyneuropathy (FAP) stage
    - Three-stage measure from 1 (ambulate without assistance) to 3 (wheelchair or bedridden)
  - Polyneuropathy disability score (PND)
    - Five-stage measure from 0 (no impairment) to 4 (wheelchair or bedridden)
- Cardiac
  - N-terminal pro-BNP
  - Echocardiographic measures
Results: Inotersen
Co-primary outcome: change in mNIS+7

Figure 4 Least Squares mean Change from Baseline in mNIS+7. Adapted from Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis by Benson et al, 2018. Retrieved from https://www.nejm.org/doi/10.1056/NEJMoa1716793
Co-primary outcome: change in QOL

Figure 2 Least Squares mean Change from Baseline in Norfolk QOL-DN Score Adapted from Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis by Benson et al, 2018. Retrieved from https://www.nejm.org/doi/10.1056/NEJMoa1716793
Secondary Outcomes—Inotersen

• Polyneuropathy disability score
  • No difference between inotersen and placebo

• Cardiac
  • No improvement in echocardiographic measures

• Modified BMI
  • No significant differences in mBMI vs. placebo
## Harms, n (%) - Inotersen

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=60)</th>
<th>Inotersen (n=112)</th>
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<tbody>
<tr>
<td>Any AE leading to DC</td>
<td>1 (2)</td>
<td>16 (14)</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>13 (22)</td>
<td>36 (32)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>0</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1 (2)</td>
<td>15 (13)</td>
</tr>
<tr>
<td>Anti-inotersen antibodies</td>
<td>NR</td>
<td>34 (30)</td>
</tr>
</tbody>
</table>
Results: Patisiran
Primary outcome: change in mNIS+7

Figure 3 Least Squares Mean Change in mNIS+7. Adapted from Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis by Adams, et al 2018, retrieved from https://www.nejm.org/doi/10.1056/NEJMoa1716153
Secondary outcome: change in QOL

Figure 4 Least-Square Mean Change in Norfolk QOL-DN Score. Adapted from Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis by Adams, et al 2018, retrieved from https://www.nejm.org/doi/10.1056/NEJMoa1716153
Secondary Outcomes - Patisiran

• Modified BMI
  • Improved vs. placebo
• Familial Amyloid Polyneuropathy stage
  • Stable or improved vs. placebo
• Polyneuropathy Disability Score
  • Stable or improved vs. placebo
• Cardiac
  • NT-proBNP decreased vs. placebo; unclear clinical significance
  • Post-hoc analyses
## Harms, n (%) - Patisiran

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=77)</th>
<th>Patisiran (n=148)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE leading to DC</td>
<td>11 (14)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>31 (40)</td>
<td>54 (36)</td>
</tr>
<tr>
<td>Death</td>
<td>6 (8)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>17 (22)</td>
<td>44 (30)</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>7 (9)</td>
<td>28 (19)</td>
</tr>
</tbody>
</table>
Harms-Patisiran

Low-moderate risk long-term harm from concomitant steroid administration

• Depends on patient characteristics
• Based on analogous steroid use in other therapeutic areas
Controversies & Uncertainties

• Unknown clinical significance for magnitude of changes

• Not yet possible to determine which patients are likely to respond to treatment

• Studies not powered on cardiac outcomes
  • Limited generalizability to US

• Loss to follow-up in inotersen arm higher

• Long-term safety unknown
  • Patisiran is the first RNAi therapeutic approved by the US FDA
## ICER Evidence Ratings

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>ICER Evidence Rating</th>
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<tbody>
<tr>
<td>Inotersen vs. Placebo</td>
<td>Comparable or better (C+)</td>
</tr>
<tr>
<td>Patisiran vs. Placebo</td>
<td>Incremental or better (B+)</td>
</tr>
</tbody>
</table>
Potential Other Benefits and Contextual Considerations

• Patisiran is first US medication approved to treat hATTR, inotersen may follow

• Injectable formulation of inotersen

• New treatments may positively impact caregiver and family burden

• Hope for affected families

• Potential to increase screening and diagnosis
Public Comments Summary

• Initial evidence rating of P/I for inotersen was too low
• Some outcomes that matter most to patients not captured in trials
• Tafamidis: an important new treatment on the horizon
• Important questions that remain: when to initiate therapy, how long to continue
Conclusions

• New therapies appear to halt progression or improve neuropathy symptoms and quality of life in hATTR

• Uncertainty regarding specific safety issues and long-term safety overall

• Studies with primary cardiac endpoints are needed

• Affordability is a major concern for patients and their families
Long-Term Cost-Effectiveness

Jeffrey Hoch, PhD
Professor and Chief, Division of Health Policy and Management
Associate Director, Center for Healthcare Policy and Management
Department of Public Health Sciences
University of California, Davis
Key Team Members

Lauren Cipriano, PhD, Western University, London, Ontario, Canada
Elise Evers, University of York, York, United Kingdom
Yi Zhang, PhD, University of California, Davis
Kristin Mickle, MPH, Institute for Clinical and Economic Review
Daniel A. Ollendorf, PhD, Institute for Clinical and Economic Review
Rick Chapman, PhD, Institute for Clinical and Economic Review

Disclosures:
Financial support was provided to the University of California, Davis from the Institute for Clinical and Economic Review.
University 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

• To estimate the incremental cost effectiveness of inotersen and patisiran in comparison to best supportive care* for hereditary transthyretin amyloidosis from a health care sector (and modified societal) perspective over a lifetime.

*Best supportive care is defined for inotersen as in the NEURO-TTR trial and for patisiran as in the APOLLO trial.
Methods Overview

• **Model:** Markov model
• **Setting:** United States
• **Perspective:** Health care sector (and modified societal) perspectives
• **Time horizon:** Lifetime
• **Discount rate:** 3% per year (costs and outcomes)
• **Cycle Length:** 1 month
• **Primary outcome:** Cost per quality-adjusted life year (QALY) gained
  • **Secondary outcome:** Cost per life year (LY) gained
## Base-Case Population (Inotersen)

<table>
<thead>
<tr>
<th>Cohort Characteristic (Baseline)</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>59 years</td>
</tr>
<tr>
<td>Female</td>
<td>31%</td>
</tr>
<tr>
<td>FAP Stage 1</td>
<td>67%</td>
</tr>
<tr>
<td>FAP Stage 2</td>
<td>33%</td>
</tr>
<tr>
<td>Severe Cardiac Involvement (NT-proBNP &gt; 3,000)</td>
<td>14.2%</td>
</tr>
</tbody>
</table>

*All from NEURO-TTR, except the 14.2% assumption based on the relative frequency of general cardiac sub-populations in the NEURO-TTR (inotersen) and the APOLLO trials (patisiran)*
# Base-Case Population (Patisiran)

<table>
<thead>
<tr>
<th>Cohort Characteristic (Baseline)</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>62 years</td>
</tr>
<tr>
<td>Female</td>
<td>26%</td>
</tr>
<tr>
<td>FAP Stage 1</td>
<td>46%</td>
</tr>
<tr>
<td>FAP Stage 2</td>
<td>54%</td>
</tr>
<tr>
<td>Severe Cardiac Involvement (NT-proBNP &gt; 3,000)</td>
<td>12%</td>
</tr>
</tbody>
</table>

*All from the APOLLO trial*
Polyneuropathy

FAP Stage 1

FAP Stage 2

FAP Stage 3

1) Improvement possible
2) Death (from all states)
3) Severe Cardiac Involvement

Polyneuropathy with Severe Cardiac Involvement

FAP 1 with NT-proBNP > 3,000

FAP 2 with NT-proBNP > 3,000

FAP 3 with NT-proBNP > 3,000
Key Assumptions

• Patients do not undergo liver transplantation.
  • Infrequent use; unclear impact

• Some quality of life utility benefit for new treatments within the same FAP stage
  • Difference in Norfolk QoL does not match large % with “no change” in FAP Stage progression

• Patients stay on treatment until drug discontinuation.
  • Assumed numbers match that seen in the respective trials.
Key Parameters: Cost Inputs

• Drug cost: $345,000 per year (net expected price)
• Plus annual costs of
  • Inotersen:
    • Training visit for first injection ($74)
  • Patisiran:
    • 4.3% markup ($14,835)
    • Infusion administration ($3,965)
    • Pre-infusion drugs ($50)
• Office visits, ED visits, hospitalization costs from Medicare fee schedule
• Stage-specific annual costs of caregiving
  • including disease-related acute events and treatment costs
## Key Parameters: Health Utilities

<table>
<thead>
<tr>
<th>Health State</th>
<th>Utility Value if NT-proBNP ≤ 3,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAP Stage 1</td>
<td>0.710</td>
</tr>
<tr>
<td>FAP Stage 2</td>
<td>0.570</td>
</tr>
<tr>
<td>FAP Stage 3</td>
<td>0.170</td>
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</table>

Patients with:
- Severe cardiac involvement incur an additional 10% loss of utility;
- New treatment incur 0.05 to 0.14 more utility (depending on stage and drug)
Key Parameters: Mortality

- 3 different death rates incorporated:
  - “Natural” age-specific death rate (matches trials’ Female/Male ratio)
    - US Life tables
  - “FAP stage” death rate
    - Swiecicki et al. (2015)
  - “Severe cardiac involvement” death rate
    - Slama et al. (2018)


INOTERSEN Results
# Inotersen Results: Total Cost and QALYs

<table>
<thead>
<tr>
<th>Health Care Sector Perspective</th>
<th>3% Discount Rate</th>
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<tbody>
<tr>
<td></td>
<td>Total Costs</td>
</tr>
<tr>
<td>Inotersen</td>
<td>$1,510,000</td>
</tr>
<tr>
<td>Best Supportive Care</td>
<td>$330,000</td>
</tr>
</tbody>
</table>
Inotersen Results (Continued, 3% Discount Rate)

<table>
<thead>
<tr>
<th>How much more?</th>
<th>Inotersen vs. Best Supportive Care</th>
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<tbody>
<tr>
<td><strong>Incremental Costs</strong></td>
<td></td>
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<tr>
<td>Health Care Sector Perspective</td>
<td>$1,180,000</td>
</tr>
<tr>
<td><strong>Incremental Outcomes</strong></td>
<td></td>
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<tr>
<td>QALYs</td>
<td>0.68 QALYs</td>
</tr>
<tr>
<td><strong>Incremental Cost-Effectiveness Ratio (QALYs)</strong></td>
<td></td>
</tr>
<tr>
<td>Health Care Sector Perspective</td>
<td>$1,730,000 per QALY</td>
</tr>
</tbody>
</table>
One-Way Sensitivity Analyses: Inotersen, Health Care Sector Perspective

Parameters of interest
- Drug cost (10% to 110%)
- HR for progression on drug (0.2 to 1.0)
- Transition from NT-proBNP > 3000
- Discount rate (0% to 10%)
- Initial NT-proBNP > 3000 (0% / 25%)
- Age (55 to 70)
- HR for NT-proBNP > 3000 (4x -/+)
- Stage 3 utility (30% -/+)

Base case incremental cost-effectiveness ratio: $1,730,000 per QALY gained
PATISIRAN Results
Patisiran Results: Total Cost and QALYs

<table>
<thead>
<tr>
<th>Health Care Sector Perspective</th>
<th>3% Discount Rate</th>
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<tbody>
<tr>
<td></td>
<td>Total Costs</td>
</tr>
<tr>
<td>Patisiran</td>
<td>$3,170,000</td>
</tr>
<tr>
<td>Best Supportive Care</td>
<td>$310,000</td>
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Patisiran Results (Continued, 3% Discount Rate)

<table>
<thead>
<tr>
<th>How much more?</th>
<th>Patisiran vs. BSC</th>
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<tr>
<td><strong>Incremental Costs</strong></td>
<td></td>
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<tr>
<td>Health Care Sector Perspective</td>
<td>$2,860,000</td>
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<tr>
<td><strong>Incremental Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>QALYs</td>
<td>3.43 QALYs</td>
</tr>
<tr>
<td><strong>Incremental Cost-Effectiveness Ratio (QALYs)</strong></td>
<td></td>
</tr>
<tr>
<td>Health Care Sector Perspective</td>
<td>$835,000 per QALY</td>
</tr>
</tbody>
</table>
One-Way Sensitivity Analyses: Patisiran, Health Care Sector

Parameters of interest
- Drug cost (10% to 110%)
- HR for progression on drug (0.2 to 0.75)
- Discount rate (0% to 10%)
- Transition from NT-proBNP > 3000
- Age (55 to 70)
- Initial NT-proBNP > 3000 (0% / 25%)
- Stage 3 utility (30% -/+)
- HR for NT-proBNP > 3000 (4x -/+)

Base case incremental cost-effectiveness ratio: $835,000 per QALY gained.
Scenario Analyses for Both Treatments

• Different utilities
  • Prior UK model’s utilities (↑)
  • Worst utilities reported in the literature (↑)
  • No utility bonus within FAP Stage (↑)

• Different health care costs
  • Double costs (↑)
  • Half costs (↓)
Cost-Effectiveness Acceptability Curves (CEACs) for Inotersen and Patisiran

Results from probabilistic sensitivity analysis
Limitations

• Lack of relevant cost-effectiveness data; modeling points out where the uncertainty matters
• Lack of long-run clinical evidence on discontinuation, benefits, and risks from using new treatments; role for more evidence
• Differences in trials make direct comparison not feasible
Public Comments

• Allow for “benefit” in quality of life even within FAP Stage (plateau)

• Consider liver transplant

• Explore impact on caregivers

• Keep analysis of the new treatments separate
Conclusions from the Cost-Effectiveness Analysis

• The estimated cost-effectiveness of inotersen is not near commonly used cost-effectiveness thresholds.

• The estimated cost-effectiveness of patisiran is not near commonly used cost-effectiveness thresholds.

• For treatments for ultra-rare diseases, policymakers often consider other benefits and contextual considerations that may lead to funding at higher cost-effectiveness thresholds.
Supplemental Slides
Other Results

![Graph showing ICER vs. Annual Drug Price for Patisiran and Inotersen. The graph plots annual drug prices on the x-axis ranging from $0 to $500,000, and ICER on the y-axis ranging from $0 to $2,500,000. Two lines are shown: one for Patisiran and one for Inotersen, each representing a linear increase in ICER with increasing drug price.]

- Patisiran
- Inotersen
Public Comment and Discussion
Conflict of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies.

- Amyloidosis Support Groups is a 501c3 non-profit charity comprised of volunteers.

- Amyloidosis Support Groups is largely dependent on donations from the general public, but also receives donations and grants from pharmaceutical companies. In the last year, the group received financial assistance from Bridge Bio (Eidos), Pfizer, Alnylam, Ionis, Akcea, and Prothena. These funds help support the group’s annual meeting.
Charles Horwath
Patient Advocate

Conflict of interest:
• None declared.
Kristen Hsu
Executive Director, Clinical Research, Amyloidosis Research Consortium

**Conflict of interest:**

- A relationship that could reasonably be considered a financial conflict of interest.

- Over the past year, Amyloidosis Research Consortium (ARC) has received financial support for projects from the following companies: Ionis, Pfizer, Alnylam, Takeda, Janssen, and Prothena. ARC retains all influence, control, and autonomy over projects for which it’s received external support.
Dawn Myers
Patient Advocate

Conflict of interest:
• None declared.
Manufacturer Public Comment and Discussion
# Speakers

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Company</th>
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<tbody>
<tr>
<td>Sonalee Agarwal, PhD</td>
<td>Head, Value &amp; Evidence Strategy</td>
<td>Alnylam</td>
</tr>
<tr>
<td>Spencer Guthrie, MPH</td>
<td>Vice President, Global TTR Strategy</td>
<td>Akcea</td>
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Voting Questions

WIFI Network: Marriott Guests
Password: 0809
The Art Institute of Chicago holds the largest collection of ________ paintings outside the Louvre.

A. Realist
B. Surrealist
C. Impressionist
D. Abstract
Patient Population for all questions:

For each question, we are considering adults with hereditary transthyretin amyloidosis (hATTR).
1. Is the evidence adequate to demonstrate that the net health benefit of inotersen plus best supportive care is superior to that provided by best supportive care alone?

A. Yes
B. No
2. Is the evidence adequate to demonstrate that the net health benefit of patisiran plus best supportive care is superior to that provided by best supportive care alone?

A. Yes

B. No
3. Is the evidence adequate to distinguish the net health benefit between inotersen and patisiran when added to best supportive care?

A. Yes
B. No
4. When compared to best supportive care alone, does the addition of inotersen or patisiran offer one or more of the following “other benefits”?

A. Offers reduced complexity that will significantly improve patient outcomes.

B. Will reduce important health disparities across racial, ethnic, gender, socioeconomic, or regional categories.

C. Will significantly reduce caregiver or broader family burden.

D. Offers a novel mechanism of action or approach that will allow successful treatment of many patients who have failed other available treatments.

E. Will have a significant impact on improving patients’ ability to return to work and/or their overall productivity.

F. Will have a significant positive impact outside the family, including on schools and/or communities.

G. Will have a significant impact on the entire “infrastructure” of care, including effects on screening for affected patients, on the sensitization of clinicians, and on the dissemination of understanding about the condition, that may revolutionize how patients are cared for in many ways that extend beyond the treatment itself.

H. There are other important benefits or disadvantages that should have an important role in judgments of the value of this intervention: ______________
5. Are any of the following contextual considerations important in assessing inotersen’s or patisiran’s long-term value for money in patients?

A. Intended for the care of individuals with a condition of high severity.

B. Intended for the care of individuals with a high lifetime burden of illness.

C. First to offer any improvement for patients with this condition.

D. Compared to best supportive care, there is significant uncertainty about the long-term risk of serious side effects of this intervention.

E. Compared to best supportive care, there is significant uncertainty about the magnitude or durability of the long-term benefits.

F. There are additional contextual considerations that should have an important role in judgments of the value of this intervention:

__________________________.
6. For adults with hereditary transthyretin amyloidosis, given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of inotersen plus best supportive care compared with best supportive care alone?

A. High  
B. Intermediate  
C. Low
7. For adults with hereditary transthyretin amyloidosis, given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of patisiran plus best supportive care compared with best supportive care alone?

A. High
B. Intermediate
C. Low
# Policy Roundtable Participants

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>COI Declaration</th>
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<tbody>
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Expert and CEPAC Panel Reflections
Next Steps

• Meeting recording posted to ICER website next week
• Final Report published on/about October 4
  • Includes description of CEPAC votes, deliberation; policy roundtable discussion
• Materials available at
  https://icer-review.org/topic/amyloidosis/
Adjourn