Transthyretin Amyloid Cardiomyopathy 2024

ICER SNAPSHOT

Reviewed by: Amyloidosis Support Groups

Amyloidosis Support Groups is not responsible for the final contents of ICER's Report or Snapshot, nor should their review be assumed to support any part of ICER's findings.

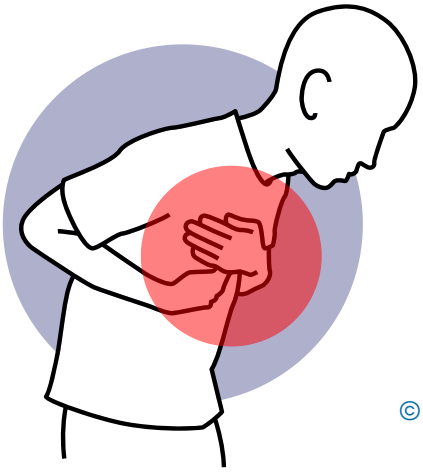
The ICER Snapshot is a summary designed to help patients and the broader community learn about the key results and recommendations from ICER's 2024 Final Evidence Report on Treatments for Transthyretin Amyloid Cardiomyopathy.

The information included is up to date as of October 2024. New information about these therapies may become available, but is not captured here.

Let's Take a Look

What is Transthyretin Amyloid Cardiomyopathy?

Transthyretin Amyloid Cardiomyopathy (ATTR-CM) is a heart condition where amyloid deposits (abnormal clumps of protein) pile up in the heart, causing it to become stiff and weak. This makes it harder for the heart to pump blood properly and can cause shortness of breath, heart failure, and early death. ATTR-CM can also affect a person's nervous system and kidneys.



Patients typically develop ATTR-CM when they are older ("wild-type"), but can inherit genes that make it more likely to develop symptoms earlier ("variant"). While ATTR-CM is considered a rare disease, recent improvements in diagnostic tools and increased awareness among healthcare professionals have led to more frequent diagnoses.

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Impact on Patients and Families

What ICER Learned from the Community

Patients commonly experience multiple symptoms of ATTR-CM at once and **require multiple specialists** to help treat and manage their disease.

Even with current treatments, patient quality of life is worsened by symptoms like **fatigue, neuropathy, and mobility limitations.**

Patients with hereditary (able to pass on from parents to children) forms of ATTR-CM worry about the **risk to family members**.

Early diagnosis and access to effective new treatment options are important as patients often face **misdiagnosis or delays** in diagnosis.

Patients in rural areas face **long travel times** and difficulty accessing amyloidosis treatment centers.

The **high costs of current medications** like Vyndaqel® force patients to seek financial assistance programs that may be hard to qualify for or have limited funding.

ATTR-CM Clinical Context

NYHA Functional Class

The New York Heart Association (NYHA) functional class is a way to categorize the severity of congestive heart failure in patients based on their symptoms.

NYHA Class I — No symptoms

NYHA Class II — Mild symptoms, slight limitation on physical activity

NYHA Class III — Moderate limitations on physical activity, symptoms only relieved at rest

NYHA Class IV — Severe limitations, symptoms present even at rest

Helpful Clinical Terms

Cardiovascular:
Relating to the heart and blood vessels

Congestive:
The build up of fluid that results when the heart fails to pump properly

Neuropathy:
A nerve-related problem that causes pain, numbness, and tingling in the hands and feet, issues related to digestion, and dizziness upon standing

Protein:
An important structure of the cell that helps the body function properly

RNA:
Stands for ribonucleic acid; an important part of the cell that helps make proteins

Transthyretin Amyloid Cardiomyopathy 2024

ICER's Review of Transthyretin (TTR) Stabilizers

Tafamidis (Vyndaqel® and Vyndamax®) and Acoramidis (Attruby™)

Vyndaqel® (made by Pfizer) and Attruby™ (made by BridgeBio) are treatments in the class of transthyretin (TTR) stabilizers which help keep TTR, a specific protein in the body, to fold correctly. By stabilizing the TTR, these treatments prevent the build up of amyloid deposits (abnormal clumps of protein) in the heart. TTR stabilizers are taken orally (by mouth) every day.

Vyndaqel® was FDA-approved in 2019 and Attruby™ was FDA-approved in 2024.

What Did Clinical Trials Show?

Vyndaqel® in the ATTR-ACT Trial

- Studied in 441 adults patients with ATTR-CM
- Compared Vyndaqel® (80 mg or 20 mg dose) to placebo
- Patient outcomes studied for 30 months

FEWER deaths

DECREASED Cardiovascular-related hospitalizations

Attruby™ in the ATTRibute-CM Trial

- Studied in 632 adults patients with ATTR-CM
- Compared Attruby™ to placebo
- Patient outcomes studied for 30 months

DECREASED Cardiovascular-related hospitalizations

These represent some, but not all outcomes that were measured in the clinical trials.

WHAT DOES THAT MEAN?

Placebo: An inactive treatment intended to hide whether a patient received the studied drug

Cardiovascular-related hospitalization: Unplanned admission to hospital for at least 24 hours to treat conditions like heart failure, abnormal heart beats, heart attack, and stroke (loss of blood flow to the brain)

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Transthyretin Amyloid Cardiomyopathy 2024

ICER's Review of An RNA Silencer

Vutrisiran (Amvuttra®)

Amvuttra® (made by Alnylam) is an RNA silencer. It blocks the genetic instructions (messenger RNA) that tell cells to make the protein TTR. By "silencing" the RNA and reducing TTR production, it aims to slow or stop the progression of ATTR-CM. Amvuttra® is injected under the skin once every 3 months.

Amvuttra® is still under FDA review for ATTR-CM.

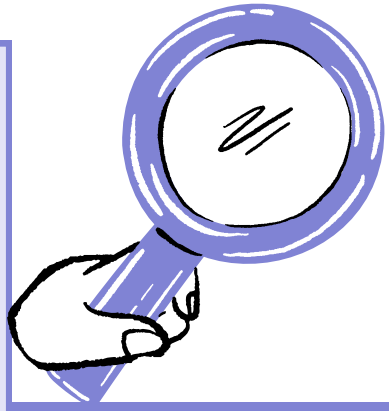
What Did Clinical Trials Show?

Amvuttra® in HELIOS-B Trial

- Studied in 655 adults patients with ATTR-CM
- Compared Amvuttra® to placebo
- Patient outcomes studied for 33-36 months

FEWER deaths

DECREASED Cardiovascular-related hospitalizations



These represent some, but not all outcomes that were measured in the clinical trials.

ICER's report findings are NOT recommendations that support the use of Vyndaqel®, Attruby™, or Amvuttra®. Individuals and families should always talk with their doctors to make shared decisions about treatment for ATTR-CM.

What We Still Don't Know

- How the three treatments compare to one another
- How well Vyndaqel® works in patients who are diagnosed in earlier stages of ATTR-CM
- Whether adding a TTR stabilizer to Amvuttra improves outcomes compared with Amvuttra® alone

Safety of Vyndaqel®, Attruby™, & Amvuttra®

All three therapies are tolerable and safe. Patients taking Amvuttra® are recommended to take vitamin A supplements.

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Transthyretin Amyloid Cardiomyopathy 2024

How Did ICER Calculate a Fair Price?

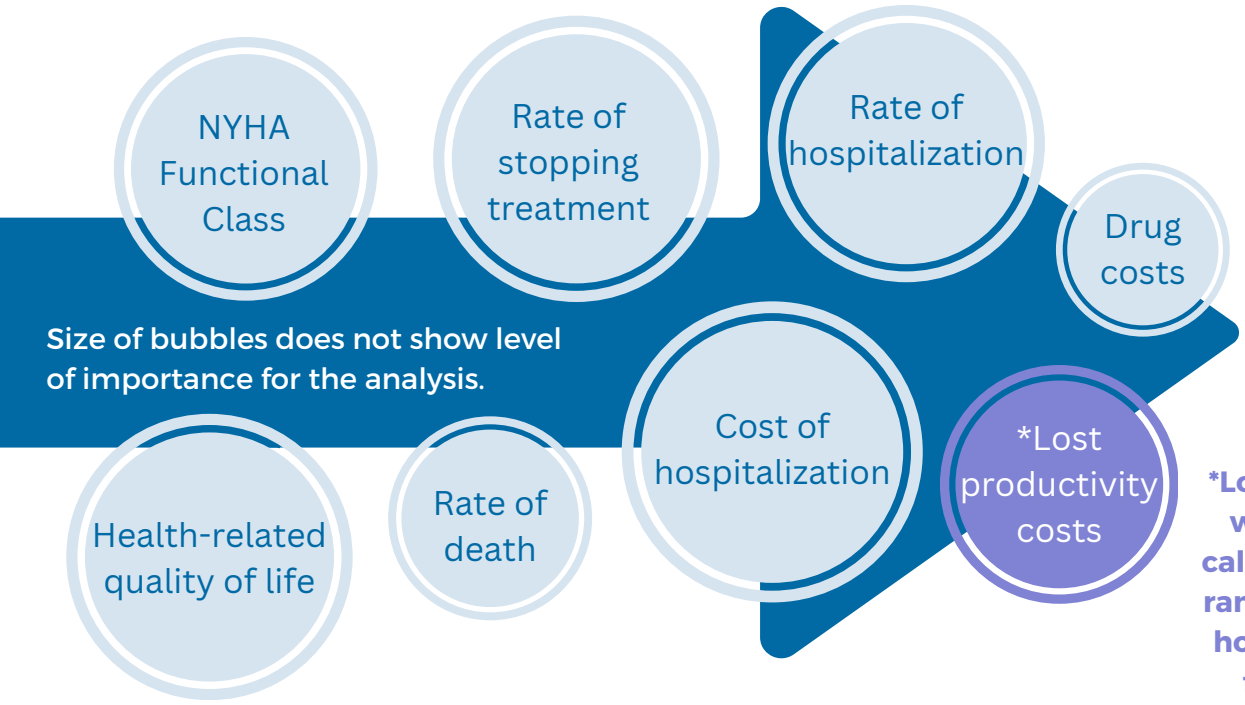
A fair price is how much a treatment should cost based on how well it works for patients. Using economic modeling, we calculated the cost effectiveness of TTR stabilizers (assuming Vyndaqel® and Attruby™ had the same clinical benefit) compared to current standard of care based on progression of ATTR-CM functional class. See below for what types of information ICER considered to calculate a fair price range for these treatments.

*We did not have enough information to include Amvuttra® in the model.

Population

Adult patients with earlier stage (NYHA Class I, II, and III) ATTR-CM

Factors Included in ICER's Economic Analysis



***Lost productivity costs were not included in calculating the fair price range. See full report for how these inputs were factored into other economic results.**

Fair Price Range for TTR Stabilizers

$13,600 - $39,000 per year

Based on the known price of Vyndaqel® ($268,000 per year), our economic analysis concluded that the fair-price range for the two TTR stabilizers is between $13,600 to $39,000 per year.

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Key Policy Recommendations

The Policy Roundtable at the ICER public meeting informed several policy recommendations for pricing, access, and future research in ATTR-CM. A few key recommendations are summarized below.

1 Improve efforts for early and accurate diagnosis and access to ATTR-CM care.

Federal and state policy makers should remove barriers to the use of telemedicine, including across state lines, so that individuals with ATTR-CM can access centers of excellence, regardless of geographic location. Clinical specialty societies should establish cutoffs for diagnosis informed by gender and/or body size to reduce potential for misdiagnosis of ATTR-CM among women and smaller patients.

2 Manufacturers should set prices that will foster affordability and access for all patients by aligning prices with how well their treatments work for patients.

Progress in therapeutics for ATTR-CM has been remarkable. Despite that progress, patients have limited access to Vyndaqel® since the price is much higher than a cost-effective price. As new options become available soon, there needs to be more attention to the harmful effect of high prices on patient access.

3 When setting prices for existing and new therapies for ATTR-CM, manufacturers should not assume that ATTR-CM is a rare disease.

The number of new cases of ATTR-CM is unclear and diagnosis is often incorrect or delayed. The price of therapies should account for the possibility that the total number of cases of ATTR-CM may be more than the FDA's 200,000 limit to be considered a rare disease.

4 Researchers and funding agencies should focus future research to understand how well Vyndaqel®, Attruby™, and Amvuttra® work compared to each other in similar populations.

Payers could consider coverage of dual therapy with a stabilizer medication and Amvuttra®, but concerns about the evidence and the obvious cost implications are likely to lead most payers to withhold coverage until further evidence is generated.

Impact of Patient Engagement

Amyloidosis Research Consortium (ARC) provided us with **data to support** the average time for a correct diagnosis of ATTR-CM (6 years) which informed our policy recommendation **to improve accurate and timely diagnosis.**

Amyloidosis Support Groups (ASG) emphasized FDA-approved **dosage and indication for Vyndaqel®** which informed public meeting **discussion related to affordability.**

Testimony from individuals living with ATTR-CM helped shape ICER's recommendation for policy makers to **ensure access to an adequate network of specialists** for the care of ATTR-CM.

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit organization that does research on how well new treatments work and what a fair price should be. Patients and families should always talk with their doctor to make shared decisions about the best treatment option for them.

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