ICER SNAPSHOT

Reviewed by: Spinal Muscular Atrophy (SMA) UK

SMA UK 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 2025 Final Evidence Report on treatments for spinal muscular atrophy.

The information included is up to date as of August 2025. New information about these treatments may become available, but is not captured here.

Let's Take a Look

What is Spinal Muscular Atrophy?

Patient Community Insights

Treatments: Benefits and Risks

Treatments: What's A Fair Price?

Policy Recommendations

Impact of Patient Engagement



What is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a genetic disease that causes progressive nerve damage, affecting a person's ability to breathe, swallow, and move (sit, walk, or move limbs), and if left untreated, can result in early death. At the time of this ICER review, there are **three treatments that have dramatically improved outcomes for people with SMA**:

- **Spinraza®** (injection into space around spinal cord every 4 months)
- **Evrysdi®** (liquid or tablet form every day)
- **Zolgensma®** (a one-time gene therapy)

DID YOU KNOW?

These life-saving therapies have completely changed the course of this disease, as most infants with the severe form of SMA are now surviving, and many will be able to walk as they get older.

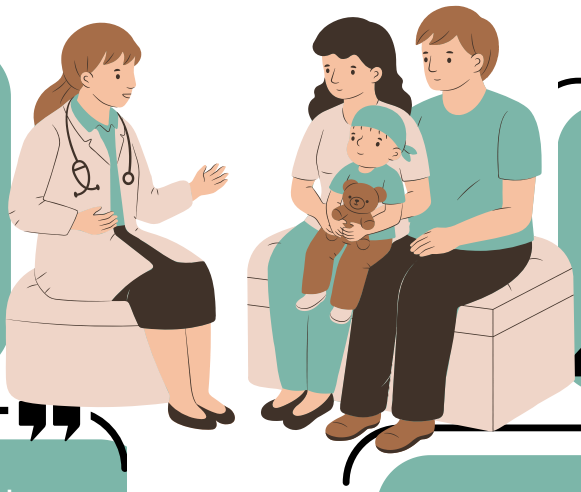
There are approximately 10,000 Americans living with SMA. Thanks to better screening, people with SMA are getting diagnosed and receiving treatment earlier. This has resulted in more children living with preserved muscle function and motor abilities, as well as living longer.

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Patient Community Insights

What ICER Learned from the Community

> It's really important to patients that **treatments improve or maintain muscle strength and function**, as it supports greater independence in daily life.



> **Stopping the disease from getting worse,** even while experiencing symptoms, is also important.

> Even small improvements on scales used to measure muscle function may translate to **meaningful improvements in quality of life** from a patient perspective.

> Several important areas of improvement following treatment, such as **ability to breathe and having more energy**, are not well studied in clinical trials.

Treatments of Focus

LIFE-SAVING

SPINRAZA®

Spinraza® was approved by the FDA on December 23, 2016.

Spinraza (nusinersen), made by Biogen, is injected into the spine and helps the body produce SMN protein, which helps muscles maintain and gain function.

EVRYSDI®

Evrysdi® was approved by the FDA on August 7, 2020.

Evrysdi (risdiplam), made by Roche, is administered as an oral liquid or tablet and works similarly to Spinraza in increasing SMN protein.

ZOLGENSMA®

Zolgensma® was approved by the FDA on May 24, 2019.

Zolgensma (onasemnogene abeparvovec), made by Novartis, is a gene therapy that delivers a functional copy of the SMN1 gene, which produces SMN protein.

STRENGTH-IMPROVING

APITEGROMAB

Apitegromab is currently under FDA review.

Apitegromab, made by Scholar Rock, works differently from the first three therapies. Instead of altering SMN protein, it blocks a protein called myostatin that limits muscle growth. By blocking this protein, apitegromab allows the muscles in the body to continue growing to counteract the muscle weakness from the SMA disease.

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ICER's Key Research Questions & Findings

1 How well does apitegromab work as an add-on therapy to Spinraza or Evrysdi?

P/I

The SAPPHIRE trial showed that in kids (ages 2 to 12) with Type 2 or 3 SMA already on Spinraza® or Evrysdi®, adding apitegromab gave a **small improvement in motor skills after one year** compared to kids receiving placebo. However, there were **more serious side effects for the group receiving apitegromab**, so the overall benefit of the drug is uncertain and considered **"promising but inconclusive"**.

2 How well do Spinraza® and Evrysdi® work as an add-on therapy to patients previously treated with Zolgensma®?

P/I

The RESPOND trial showed that **adding Spinraza®** after Zolgensma® led to **increase in motor function**. No new harms were found but the **repeated spinal injections** can be difficult, painful, and have rare but serious risks. Because of this uncertainty, we rate the add-on of Spinraza® as **"promising but inconclusive"**.

C++

Findings from two studies found that patients treated with Evrysdi® (following treatment with Zolgensma®) had improvements in motor function, swallowing, and respiratory function. Evrysdi® is easy to administer and **does not appear to have any serious harms**. Thus, we rate the drug as as add-on after gene therapy, as having **moderate certainty of a small to substantial benefit**.

3 When compared to each other, which treatment - Spinraza®, Evrysdi®, or Zolgensma® - works best as a first-line therapy?

I

All three treatments showed strong benefits (improved survival, improved motor function) in SMA patients, especially when given early to children before they have symptoms. However, there were **no clinical trials directly comparing Spinraza®, Evrysdi®, and Zolgensma® to each other**. Given the lack of comparative data, we conclude that there is **insufficient ("I")** data to answer this research question.

ICER's report findings are NOT recommendations that support the use Spinraza®, Evrysdi®, Zolgensma®, or apitegromab. Patients and families should always talk with their doctors to make shared decisions about treatment for SMA.

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Safety of Treatments

For the life-saving treatments:

- The most common side effects for **Spinraza®** are related to the lumbar puncture, such as fever, vomiting, and back pain. This treatment requires regular monitoring.
- Patients treated with **Evrysdi®** may experience side effects such as fever, diarrhea, rash, mouth ulcers, joint pain, and urinary tract infections.
- **Zolgensma®** may cause side effects during the infusion, such as rash, hives, vomiting, trouble breathing, and changes in heart rate or blood pressure. This gene therapy can also cause liver failure and even death. Patients also need close monitoring for low platelet counts, blood vessel damage, and heart injury.

For apitegromab, the strength-improving treatment:

- Patients in the **apitegromab** group experienced several severe events like pneumonia and dehydration that were not seen in placebo.

What We Still Don't Know



For apitegromab:

- **What is the optimal dose?** The 10mg/kg dose showed better outcomes than placebo, but the 20mg/kg did not.
- **What are the long-term benefits and harms?** The clinical trial was only one year long.
- **How well does it work in patients with other SMA subtypes, like Type 1 or 4, and in patients younger than 2 years old?**

For patients already treated with Zolgensma® and then receiving either Spinraza® or Evrysdi®:

- **Are changes in patient outcomes due to the gene therapy (Zolgensma®) not working or something else?** Children with SMA may naturally gain or lose function as they grow, and without randomized controlled trials, it is difficult to say what is causing these changes.
- **What is the actual benefit of additional treatment?** The clinical trials are small (less than 200 patients), and most are non-peer reviewed, making it difficult to compare benefits and risks.
- **What are the long-term results of Spinraza® as an add-on treatment?** The RESPOND trial is not yet complete and we are awaiting more detailed results from a longer follow-up.

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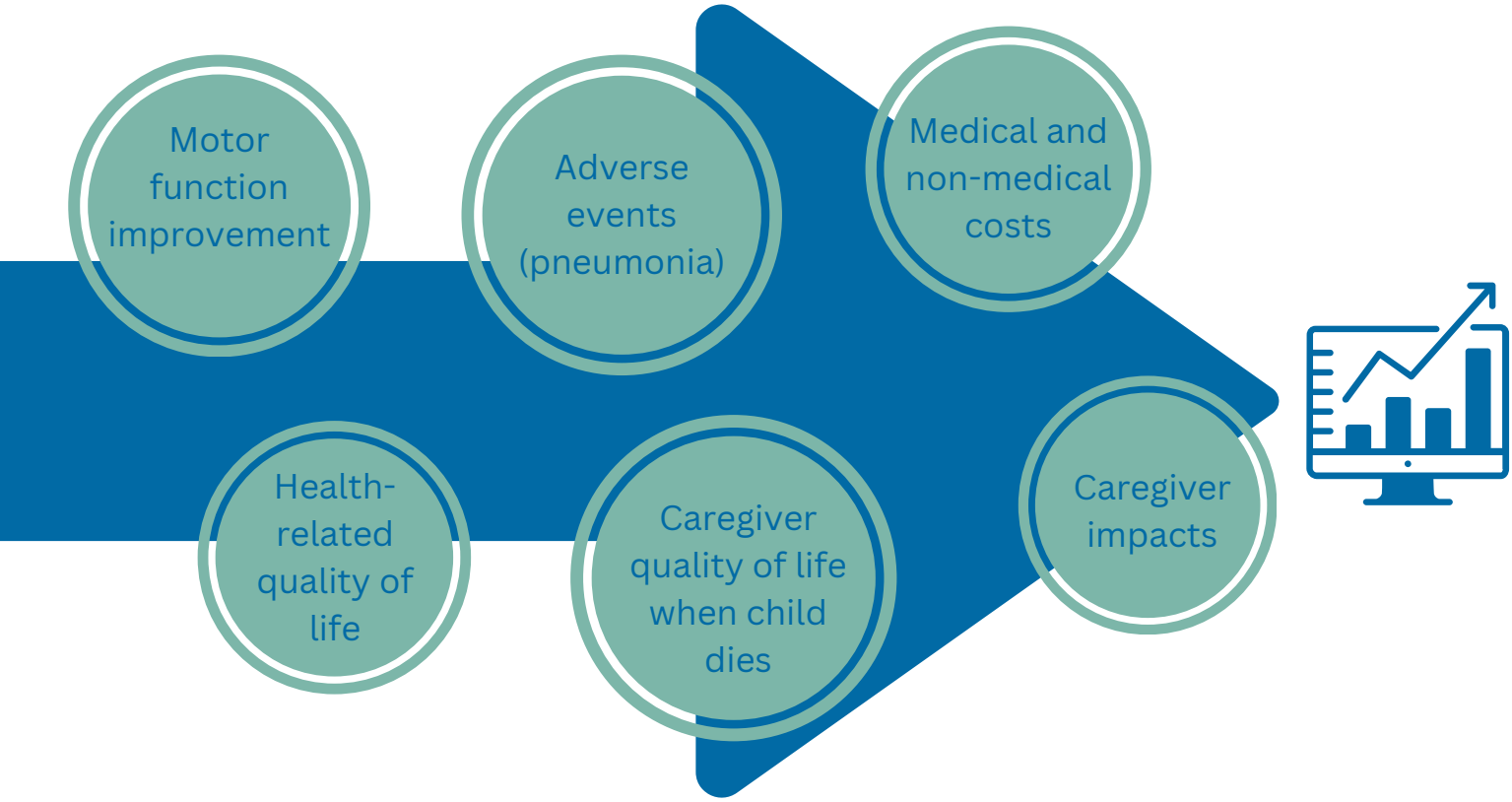
How Did ICER Calculate a Fair Price?

Using economic modeling, we calculated the **cost-effectiveness of apitegromab based on motor function improvement** following treatment. See below for what types of information ICER considered to calculate a fair price range for this treatment.

Population

Patients with non-ambulatory (not able to walk/move) SMA Type 2 or 3, being treated with apitegromab + Spinraza®/Evrysdi® or only Spinraza®/Evrysdi®

Factors Included in ICER's Economic Analysis



Fair Price for Apitegromab

$4,600 - $30,200 per year

A fair price is how much a treatment should cost based on how well it works for patients. Our economic analysis concluded that a fair price range for apitegromab is between $4,600 and $30,200 per year.

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Key Policy Recommendations

The Policy Roundtable at the ICER public meeting included two SMA patient advocacy representatives who are also caregivers to children living with SMA. Their contributions informed several policy recommendations for pricing, access, guidelines, and future research in SMA. A few key recommendations are summarized below.

1 Patient groups should continue to provide updated information on the changing patterns and the needs of members of the patient community.

CureSMA's annual State of SMA report was invaluable in the development of ICER's assessment. Given how quickly the characteristics of patients have changed since the availability of effective SMA treatments and newborn screening, it is critical for all stakeholders to be aware of ongoing updates about these changes in patient profiles and needs.

2 Patient groups should collaborate with clinical specialty societies to exercise their joint power to advocate for drug prices that do not exceed a fair value for added clinical benefit.

Patients often have significant out-of-pocket costs for drugs like apitegromab that must be infused (administered into your vein). **Patient groups and related organizations have an opportunity and responsibility to advocate for fair insurance access linked to fair prices for drugs**. Drug prices that align with analyses of added benefit will often be lower than those initially set by drug makers, and lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equal access to therapies that provide the most patient benefit.



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3 Patient groups should help raise international awareness about the value of newborn screening.



Newborn screening and immediate treatment have transformed the lives of patients living with SMA in the United States. Unfortunately, newborn screening is not universally available in other countries.

4 All stakeholders have a responsibility to make sure that effective treatments for patients with SMA and muscle weakness are introduced in ways that will help reduce health inequities.

Muscle weakness remains a significant unmet healthcare need in patients with SMA even with the current treatment options. This is true for patients who were not diagnosed with newborn screening and so received treatment months to years after birth. Health equity concerns include the availability of specialists in SMA management, the costs of treatment, and the challenges faced by patients with limited mobility in traveling for care.

Impact of Patient Engagement

Patient representatives emphasized that **clinical trial outcomes fail to capture subtle but meaningful improvements in function**. We updated our report to capture some of these meaningful improvements including **increased lung capacity and bite strength**,

Through patient engagement, we learned about the **variability of SMA symptoms** within each SMA type, leading us to revise the classification of SMA in our report to **better reflect SMA as a spectrum**.

Patient representatives emphasized the **importance of universal newborn screening, which remains unavailable outside the US**. We highlighted this need in our policy recommendations to support **earlier treatment initiation and better patient outcomes**.

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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