# ICER SNAPSHOT

Reviewed by: Multiple Sclerosis Coalition

The MS Coalition 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 tolebrutinib for multiple sclerosis.

**The information included is up to date as of July 2025. New information about this therapy may become available, but is not captured here.**

## Let's Take a Look

What is Multiple Sclerosis?
Impact on Patients and Families
Treatment: Benefits and Risks
Treatment: What's A Fair Price?
Policy Recommendations & Impact of Engagement



## What is Multiple Sclerosis?

Multiple sclerosis (MS) is a long-term condition that causes damage to the central nervous system (brain and spinal cord), affecting nearly a million people in the United States (US). Symptoms of MS include weakness, fatigue, vision changes, memory and concentration problems, pain, and physical, emotional, and cognitive impairment. MS is a costly disease, with an estimated annual economic burden in the US being over $85 billion.



Relapsing-remitting MS (RRMS) is the most common form of MS and is characterized by episodes of new MS symptoms that last greater than 24 hours and may persist for several weeks or more; the majority of people with RRMS eventually transition to secondary progressive MS (SPMS). SPMS can be active (with or without clinical relapse) or inactive (without clinical relapse). Active forms of SPMS without clinical relapse and all inactive SPMS are considered "non-relapsing", and there are currently no approved treatments for this patient population at the time of this report.

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# Impact on Patients and Families

## What ICER Learned from the Community

Maintaining **independence** is a goal for people living with SPMS, which is why early diagnosis, and treatment plans that include disease modifying therapies (DMTs) are important. People often develop symptoms years before getting a diagnosis.

Current DMT's are effective at stopping relapses (the appearance of new or returning symptoms) from happening, but some people will take **additional medications** to treat other symptoms like: **fatigue, pain or tingling, and cognitive function.**

Many people living with SPMS feel frustrated because there is not always easy access to different specialists, and there is a **lack of coordination and communication between the specialists** for their care.

**Caregivers' level of responsibility depends on the patients' level of disability (emotional, cognitive, and/or physical challenges).** This requires caregivers to plan their days to care for a loved one, and can sometimes lead to full-time caregiving.

# Treatment of Focus & Clinical Context

### TOLEBRUTINIB

Tolebrutinib, made by Sanofi, is an oral medication for the treatment of non-relapsing SPMS and possibly other forms of MS.

### HOW IT WORKS

Tolebrutinib blocks the activation of Bruton's Tyrosine Kinase (BTK) enzyme to potentially reduce brain inflammation and nerve damage.

**Tolebrutinib is under FDA review as of July 2025.**

### HELPFUL CLINICAL TERMS

**Confirmed disability progression:** A confirmed and permanent increase in physical disability as measured by the EDSS (see definition below) clinical tool

**Cognitive function:** Brain's ability to think, learn, remember, and solve problems

**DMTs:** Disease modifying therapy; treatments that could change (for the better) how MS develops over time

**EDSS**: Expanded Disability Status Scale, a clinical tool that measures disability with MS and progression over time

**Liver enzyme elevation:** An enzyme is a special kind of protein that speeds up chemical reactions in the body; an increase in liver enzymes indicate liver damage or inflammation

**Neurologic:** Related to the nervous system, impacting your bodily functions, movement, senses, and cognitive function

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

**Relapse:** A new or worsening neurologic symptom that lasts at least 24-48 hours and stabilizes and resolves gradually, though not always completely

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# What Did Clinical Trials Show?

| | |
|---|---|
| **TRIAL NAME** | **HERCULES PHASE III** |
| **PARTICIPANTS** | **Studied in 1,131 adults with a confirmed diagnosis of SPMS with no clinical relapses in the past two years AND documented evidence of disability progression in the last 12 months** |
| **TREATMENT GROUPS** | **Tolebrutinib** vs. **Placebo** |

## RESULTS

Main outcome for patients receiving tolebrutinib vs. placebo:

**REDUCED disability progression**

Results were inconsistent for secondary outcomes such as hand function, lower limb function/ mobility, and brain volume loss.

## SAFETY

More patients in the tolebrutinib group (versus placebo) experienced **infections**, **liver enzyme elevations**, and **severe liver injury** due to liver toxicity. All cases of severe liver injury occurred within the first 90 days of treatment with tolebrutinib. Two patients died in the tolebrutinib group, with one death due to complications from liver transplant related to receiving tolebrutinib.

# What We Still Don't Know

- Tolebrutinib's impact on health-related **quality of life** and **cognitive function**
- Whether there are **differences** in how well tolebrutinib works between patients with **active (MRI relapses only) and non-active forms of SPMS**
- If **long-term data** will support the continued slowing of MS disease progression
- If tolebrutinib **improves disability**

# Clinical Conclusion

**P/I**

People with non-relapsing SPMS, especially inactive type, have few treatment choices. **Tolebrutinib showed promise** in slowing disease progression, **but results were inconsistent** for other patient-important outcomes. The drug carries a small but significant risk of severe liver injury. Compared with best supportive care, ICER rated the evidence for tolebrutinib as **promising but inconclusive (P/I)**.

**ICER's report findings are NOT recommendations that support the use of tolebrutinib. Patients and families should always talk with their doctors to make shared decisions about treatment for multiple sclerosis.**

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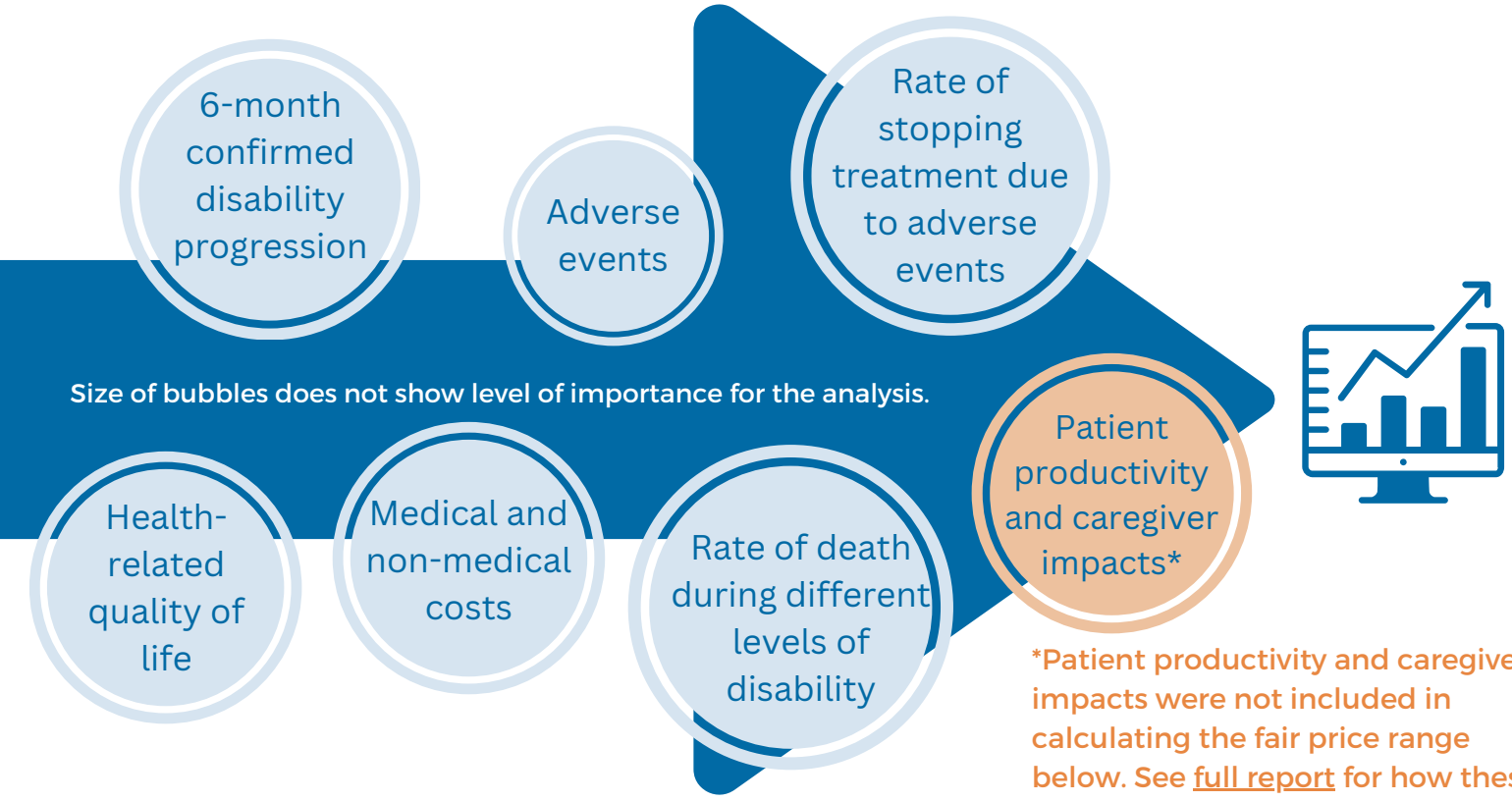
# How Did ICER Calculate a Fair Price?

Using economic modeling, we calculated the cost-effectiveness of tolebrutinib based on confirmed disability progression at 6 months following treatment. See below for what types of information ICER considered to calculate a fair price range for this treatment.

## Population

Adults ages 18 years and older in the United States with the non-relapsing form of SPMS

## Factors Included in ICER's Economic Analysis




*Patient productivity and caregiver impacts were not included in calculating the fair price range below. See full report for how these inputs were factored into other economic results.

# Fair Price for Tolebrutinib

**$3,250 - $5,900 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 tolebrutinib is between $3,250-$5,900 per year.

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# Key Policy Recommendations

The Policy Roundtable at the ICER public meeting included an MS patient advocacy representative and an individual living with SPMS. Their contributions informed several policy recommendations for pricing, access, guidelines, and future research in MS. A few key recommendations are summarized below.

**1** **Patient organizations should continue to work with manufacturers and researchers to provide patient input into study design, recruitment, and retention in clinical trials, to ensure studies reflect the needs of minority populations.**

There are many barriers to clinical trial participation for minority populations (Black and Hispanic populations), including a lack of trust in the medical community, a lack of awareness about trials, as well as logistical barriers such as transportation, time commitment, costs of participation, and language barriers.



**2** **Drug manufacturers should set prices that will promote affordability and good access for all patients by aligning prices with the value of their treatments and centering what outcomes are important to patients.**

While tolebrutinib is a new treatment for nrSPMS, and there is hope associated with the promise of tolebrutinib, there is also meaningful uncertainty about how effective and safe it is. Manufacturer pricing should also reflect these considerations by moderating its starting price.

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## 3 Clinical specialty societies should facilitate the education of general neurologists about SPMS diagnosis and treatment.

There is a shortage of MS specialists in the US. We recommend that clinical specialty societies should facilitate the education of general neurologists about SPMS diagnosis and treatment, including education in order to prompt earlier diagnoses of SPMS, standard of care treatment for SPMS, and the effectiveness and safety of new therapies such as tolebrutinib. It is important that patients can get timely access to treatment and diagnosis.

## 4 All stakeholders have a responsibility in ensuring that effective new treatment options for patients with non-relapsing SPMS (nrSPMS) are created to help reduce health inequities.

Many existing inequities in care for SPMS exist, including biases in the healthcare system that increase barriers for minority populations, and barriers to accessing treatment, like high costs and poor insurance coverage.

# Impact of Patient Engagement

The MS Coalition published **a survey about the MS Patient Experience**. We were able to incorporate the findings of the survey into our report and help inform our summary of the broader SPMS patient experience.

Patients highlighted experiences navigating the healthcare system; for instance, the **lack of MS specialists**, as well as the **frustration with having to coordinate their own care** when seeing multiple specialists. These insights are emphasized in our report.

Patient representatives at our public meeting emphasized that the **EDSS scale is insufficient in capturing many symptoms that affect daily life with SPMS**. This helped inform the policy recommendations for our final evidence report.

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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