

About secondary progressive multiple sclerosis (SPMS) and Mayzent® (siponimod)

Media factsheet

Understanding SPMS

Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss¹. MS, which affects approximately 2.3 million people worldwide², is often characterized in three forms: relapsing remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)³.

On average, up to 80% of patients with RRMS – the most common form of MS at diagnosis – will develop SPMS². SPMS is a devastating form of MS characterized by progressive and irreversible neurological disability⁴.

Most patients transition from RRMS over time, which can vary if a patient is on treatment or not⁵⁻⁷:

On treatment	Not on treatment
20% in 10 years	50% in 10 years
40% in 17 years	90% in 25 years

Symptoms of SPMS

Every patient who transitions from RRMS to SPMS will have a unique experience. Following an initial period of RRMS, symptoms gradually worsen over time, with or without evidence of disease activity (with relapses and/or evidence of new MRI activity), which can be difficult to notice⁴. Changes can include:

- Symptoms that are worsening, new or lingering between relapses^{8,9}
- A need for enhanced walking aids and wheelchairs¹⁰
- Physical activities such as walking the dog or visiting family become harder⁸
- Bladder dysfunction¹⁰
- Mental activities such as reading a book or concentrating become harder^{8,11}
- Relapsing less often⁸
- Decreasing number of active lesions on MRI scans¹²

Importance of early diagnosis

As a result of these physical and cognitive impairments, this stage of the disease can substantially impact the lives of patients and those around them². For this reason, early diagnosis and treatment are critical for patients to help slow the rate of disability progression and help patients preserve their independence for longer.

It is important for patients to learn how to identify and tackle progression. Caregivers play an integral role in the daily management of SPMS and initiation of treatment, as appropriate, and recognizing these changes in symptoms.

MS patients experiencing new or worsening symptoms should talk to their doctors about the changes they are noticing, as an early professional diagnosis of SPMS and initiation of treatment, as appropriate, may lead to better patient outcomes.

About Mayzent

Mayzent® (siponimod) is approved by the US Food and Drug Administration for the treatment relapsing forms of multiple sclerosis, to include SPMS with active disease, RRMS and clinically isolated syndrome (CIS)*, in adults. Mayzent is the first and only treatment specifically approved for patients with active SPMS in over 15 years¹³, addressing a critical unmet need for RRMS patients in transition and those with active SPMS who have transitioned. Mayzent is approved across the MS spectrum for CIS, RRMS and active SPMS, with most patients not requiring a first dose observation.

Approval was based on the Phase III EXPAND trial, the largest controlled clinical study of SPMS patients, including 1,651 people with a diagnosis of SPMS from 31 countries¹⁴.

EXPAND study and results¹⁴

EXPAND is a randomized, double-blind, placebo-controlled clinical study compared the efficacy and safety of Mayzent with placebo in people living with SPMS. Patients enrolled in EXPAND were representative of a typical SPMS population: at study initiation, patients had a mean age of 48 years, had been living with MS for approximately 16 years and more than 50% had a median Expanded Disability Status Scale (EDSS) score of 6.0 and relied on a walking aid.

Full EXPAND data show that compared to placebo, Mayzent:

- Reduced the risk of three-month CDP by a statistically significant 21% (p=0.013; primary endpoint; 33% reduction versus placebo in patients with relapse activity in the two years prior to screening, p=0.0100)
- Meaningfully delayed the risk of six-month CDP (26% versus placebo, p=0.0058) and reduced the annualized relapse rate (ARR) by 55%
- Showed significant favorable outcomes in other relevant measures of MS disease activity and progression, including cognition, MRI disease activity, and brain volume loss (brain shrinkage)
- More patients were free from gadolinium-enhancing lesions (89%) and from new or enlarging T2 lesions (57%)
- Mayzent demonstrated a safety profile that was overall consistent with the known effects of S1P receptor modulation

How does Mayzent work?

Mayzent is a next generation, selective sphingosine 1-phosphate receptor modulator. It selectively binds to S1P1 and S1P5 receptors. Mayzent prevents lymphocytes from egressing the lymph nodes and as a consequence, from entering the CNS of patients with MS, leading to its anti-inflammatory effects¹⁴. Mayzent also enters the CNS and directly binds to the S1P5 and S1P1 sub-receptors on specific cells (oligodendrocytes and astrocytes)¹⁵ to promote remyelination and prevent inflammation.

**Clinically isolated syndrome (CIS) is defined as a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination in the central nervous system¹⁶.*

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