About Mayzent® (siponimod)
Media factsheet

Mayzent® (siponimod) is approved by the US Food and Drug Administration (FDA) for the treatment of relapsing forms of multiple sclerosis (RMS), to include clinically isolated syndrome (CIS*), relapsing remitting disease, and active secondary progressive disease, in adults. It is the only oral drug specifically approved by the FDA for active secondary progressive MS (SPMS) based on proven efficacy in the typical SPMS patient population[1], which is reflected in its label. Mayzent addresses a critical unmet need for RRMS patients in transition and those with active SPMS who have transitioned. Patients starting Mayzent treatment do not require a first dose observation, unless they have certain pre-existing cardiac conditions.

EXPAND study and results[1]

EXPAND is a randomized, double-blind, placebo-controlled Phase III study, comparing the efficacy and safety of Mayzent versus placebo in people with SPMS with varying levels of disability, Expanded Disability Status Scale (EDSS) scores of 3.0–6.5. It is the largest randomized, controlled study in SPMS to date, including 1,651 people with a diagnosis of SPMS from 31 countries. 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, had a median EDSS score of 6.0, with more than 50% of patients with an EDSS score of 6.0 or more who relied on a walking aid.

Full EXPAND data show that compared to placebo, Mayzent:

- Reduced the risk of three-month confirmed disability progression (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)
- Showed a significant benefit on cognitive processing speed (CPS), the key cognitive function impacted by MS, which frequently deteriorates in people with the disease[2]
- 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 binds with high affinity to S1P1 and S1P5 receptors. Mayzent blocks the capacity of lymphocytes from egressing the lymph nodes and as a consequence, from entering the central nervous system (CNS) of patients with MS, leading to its anti-inflammatory effects[1]. Mayzent also enters the CNS and directly binds to the S1P5 and S1P1 sub-receptors on specific cells (oligodendrocytes and astrocytes)[2] to promote re-myelination and prevent inflammation. The mechanism by which Mayzent exerts therapeutic effects in MS is unknown, but may involve the reduction of lymphocyte migration into the CNS.

**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 system[3].*

References

1. Kappos L, Cree B, Fox R, et al. Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomized, phase 3 study. Lancet. Published online March, 2018. http://dx.doi.org/10.1016/S0140-6736(18)30475–6.
2. Tavares A, et al. Brain distribution of MS565, an imaging analogue of Mayzent (BAF312), in non-human primates. Neurology. 2014;82(10):suppl. P1.168.
3. National MS Society. Clinically Isolated Syndrome (CIS). https://www.nationalmssociety.org/Symptoms-Diagnosis/Clinically-Isolated-Syndrome-(CIS). Accessed May 2019.