About Mayzent® (siponimod)
Media factsheet

In the European Union (EU), Mayzent® (siponimod) is indicated for the treatment of adult patients with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapsing or imaging features of inflammatory activity. Mayzent addresses an unmet need for European SPMS patients with active disease who previously did not have an oral treatment that has been shown to be effective in delaying progression in this patient population based on evidence from a study in a broad SPMS population.

Additionally, Mayzent is approved in the US for the treatment of relapsing forms of MS, to include clinically isolated syndrome (CIS*), relapsing remitting disease and active secondary progressive disease. In November 2019, Novartis received approval from the Australian Therapeutic Goods Administration for Mayzent for adult patients with SPMS.

The approvals in the US, Australia, and EU are based on the Phase III EXPAND trial, the largest controlled clinical study of a broad range of SPMS patients, showing Mayzent significantly reduced the risk of disease progression, including impact on physical disability and cognitive decline[1].

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, 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. EXPAND included a subgroup of patients with active disease (n=779), defined as patients with relapses in the two years prior to the study and/or presence of Gd-enhancing T1 lesions at baseline. The baseline characteristics were similar except for signs of activity compared to the overall population.

Full EXPAND data show that compared to placebo, Mayzent:

- Significantly reduced the risk of three-month confirmed disability progression (CDP) by 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%
- Had a meaningful benefit on cognition and demonstrated clinically relevant effects on cognitive processing speed[2]
- More patients were free from gadolinium-enhancing lesions (89%) and from new or enlarging T2 lesions (57%)

In the subgroup of Mayzent-treated patients with active disease, results showed:

- The risk of three-month and six-month CDP was significantly reduced by 31% compared to placebo and by 37% compared to placebo, respectively[3]
- Significant favorable outcomes in other relevant measures of MS disease activity, including ARR (confirmed relapses), MRI disease activity and brain volume loss (brain shrinkage)[3]

Mayzent demonstrated a safety profile that was overall consistent with the known effects of S1P receptor modulation.

How does Mayzent work?

Mayzent is a sphingosine 1-phosphate receptor modulator that selectively binds to S1P1 and S1P5 receptors. In relation to the S1P1 receptor, it prevents the lymphocytes from egressing the lymph nodes and as a consequence, from entering the central nervous system (CNS) of patients with MS[1]. This leads to the anti-inflammatory effects of Mayzent[4]. Mayzent also enters

the CNS[5,6,7] and binds to the S1P5 sub-receptor on specific cells in the CNS, including astrocytes and oligodendrocytes and has shown pro-remyelinating and neuroprotective effects in preclinical models of MS[8,9,10].

*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[11].

References

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