

# Mayzent (siponimod)



**NEW PRODUCT SLIDESHOW**

**MPR**

# Introduction

- **Brand name:** Mayzent
- **Generic name:** Siponimod
- **Pharmacological class:** Sphingosine 1-phosphate receptor modulator
- **Strength and Formulation:** 0.25mg, 2mg; tablets
- **Manufacturer:** Novartis
- **How supplied:** Starter Pack (0.25mg)—12, Tabs (0.25mg)—28; (2mg)—30
- **Legal Classification:** Rx

# Mayzent



# Indication

- **Relapsing forms of multiple sclerosis (MS)**, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

# Dosage & Administration

- Determine CYP2C9 genotype before initiation
- **CYP2C9 genotypes (\*1/\*1, \*1/\*2, or \*2/\*2):** initially 0.25mg once daily on Day 1 and Day 2; 0.50mg once daily on Day 3; 0.75mg once daily on Day 4; then 1.25mg once daily on Day 5
- **Maintenance:** 2mg once daily starting on Day 6.

# Dosage & Administration

- **CYP2C9 genotypes (\*1/\*3 or \*2/\*3):** initially 0.25mg once daily on Day 1 and Day 2; 0.50mg once daily on Day 3; then 0.75mg once daily on Day 4
- **Maintenance:** 1mg once daily starting on Day 5
- First dose 6hr monitoring for bradycardia, other abnormalities: see full labeling
- Re-initiation of therapy after interruption for  $\geq 4$  days: start with Day 1 of titration regimen

# Considerations for Special Populations

- **Pregnancy:** No available data to inform drug-associated risk; advise females of reproductive potential to use effective contraception during and for 10 days after discontinuation
- **Nursing mothers:** Consider benefits of breastfeeding with potential adverse effects on child
- **Pediatric:** Not established
- **Elderly:** Insufficient number studied
- **CYP2C9 genotype:** test before initiating treatment

# Contraindications

- CYP2C9 \*3/\*3 genotype
- Recent (within the last 6 months) occurrence of: MI, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, Class III/IV heart failure
- History or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless paced

# Warnings/Precautions

- Risk of bradyarrhythmia, AV conduction delays: titration is required for treatment initiation
- **Obtain ECG** in all patients to determine if preexisting conduction abnormalities are present
- History of cardiac arrest, cerebrovascular disease, uncontrolled hypertension, severe untreated sleep apnea: not recommended; refer to cardiologist if treatment is considered

# Warnings/Precautions

- History of recurrent syncope or symptomatic bradycardia: do benefit/risk assessment; refer to cardiologist if treatment is considered
- Monitor BP during treatment
- Increased risk of infections (may be fatal)
- **Obtain recent CBC** before starting treatment
- Consider suspending therapy if serious infection develops
- Active infection: do not start until infection resolved

# Warnings/Precautions

- **Test for antibodies to varicella zoster virus**; if negative, consider immunization before starting siponimod
- Immunosuppressed
- Withhold and evaluate if signs/symptoms of progressive multifocal leukoencephalopathy (PML) is suspected
- Diabetes, history of uveitis: increased risk of macular edema
- Do ophthalmic exam at baseline, and if any change in vision during therapy

# Warnings/Precautions

- **Evaluate recent LFTs** (within 6 months) prior to initiation
- Monitor for hepatic dysfunction; discontinue if significant liver injury is confirmed
- History of severe liver disease
- Respiratory dysfunction; obtain spirometry when needed
- Monitor for severe increase in disability after treatment discontinuation

# Interactions

- Concomitant **QT prolonging drugs** (eg, quinidine, procainamide, amiodarone, sotalol): risk of torsades de pointes
- Concomitant  $\beta$ -blockers, digoxin, ivabradine, diltiazem, verapamil during initiation may be associated with severe bradycardia or heart block
- Avoid **live virus vaccines** 1 week before, during therapy, and for 4 weeks after discontinuing siponimod; may have suboptimal response

# Interactions

- Antineoplastic, immunosuppressant or immunomodulating therapies may increase risk of immunosuppression; use caution when switching from long-acting immunotherapies; caution for 3–4 weeks after discontinuing siponimod
- Initiation after treatment with alemtuzumab: not recommended
- Concomitant moderate CYP2C9 and moderate or strong CYP3A4 inhibitors: not recommended; caution with concomitant moderate CYP2C9 inhibitors

# Interactions

- Concomitant moderate CYP2C9 and strong CYP3A4 inducers: not recommended; caution with moderate CYP2C9 inducers
- For CYP2C9 \*1/\*3 and \*2/\*3 genotypes: concomitant moderate (eg, modafinil, efavirenz) or strong CYP3A4 inducers: not recommended

# Adverse Reactions

- Headache
- Hypertension
- Transaminase increased
- Falls
- Edema peripheral
- Nausea
- Dizziness
- Diarrhea
- Bradycardia
- Pain in extremity
- Macular edema
- Decreased pulmonary function
- **Rare:** posterior reversible encephalopathy syndrome (discontinue if suspected)

# Mechanism of Action

- Siponimod is a sphingosine-1-phosphate (S1P) receptor modulator
- It binds with high affinity to S1P receptors 1 and 5
- Siponimod blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood
- The mechanism by which siponimod exerts therapeutic effects in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system

# Clinical Studies

- The efficacy of Mayzent was demonstrated in a randomized, double-blind, parallel-group, placebo-controlled time-to-event study in patients with secondary progressive multiple sclerosis (SPMS) who had evidence of disability progression in the prior 2 years, no evidence of relapse in 3 months prior to study enrollment, and an Expanded Disability Status Scale (EDSS) score of 3.0-6.5 at study entry

# Clinical Studies

- Patients (N=1651) were randomized to receive either once daily Mayzent 2mg or placebo, beginning with a dose titration
- The primary endpoint of the study was the time to 3-month confirmed disability progression (CDP), defined as at least a 1-point increase from baseline in EDSS (0.5-point increase for patients with baseline EDSS of 5.5 or higher) sustained for 3 months
- Additional endpoints included annualized relapse rate (relapses/year) and MRI measures of inflammatory disease activity

# Clinical Studies

- Mayzent was superior to placebo in reducing the risk of confirmed disability progression, based on a time-to-event analysis (hazard ratio 0.79,  $P < .0134$ )
- Patients treated with Mayzent had a 55% relative reduction in annualized relapse rate, compared to patients on placebo ( $P < .0001$ )
- The absolute reduction in the annualized relapse rate was 0.089

# Clinical Studies

- Although Mayzent had a significant effect on disability progression compared to placebo in patients with active SPMS (e.g., SPMS patients with an MS relapse in the 2 years prior to the study), the effect in patients with non-active SPMS was not statistically significant
- For more clinical trial data, see full labeling

# New Product Monograph

- For more information view the product monograph available at:

<https://www.empr.com/drug/mayzent/>