Pharmacy Policy Bulletin: J-0912 Mayzent (siponimod) – Commercial and Healthcare Reform	
Number: J-0912	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0912-011	**Original Date:** 05/01/2019
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Mayzent (siponimod)
FDA-Approved Indication(s):	• Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease, in adults.

Background:	• Mayzent (siponimod) is an oral sphingosine 1-phosphate (S1P) receptor modulator. It binds to S1P receptors 1 and 5 and blocks the capacity of lymphocytes to leave lymph nodes, effectively reducing the number of lymphocytes in the blood stream. It is unknown how it exerts therapeutic effect in MS;it may involve reduction of lymphocyte migration in the central nervous system (CNS). • Mayzent carries warnings for infections, macular edema, bradyarrhythmia and atrioventricular (AV) conduction delays, respiratory effects, liver injury, cutaneous malignancies, increased blood pressure, and fetal risk. • Mayzent is contraindicated in patients with a CYP2C9*3/*3 genotype. Determination of CYP2C9 genotype must be determined before initiating treatment and dosage adjustments must be made as needed. • Mayzent is also contraindicated in patients with presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker, and patients who, in the last 6 months, experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or class III/IV heart failure. • Assessments are required prior to initiating Mayzent, including a complete blood count, liver function tests, electrocardiogram, ophthalmic evaluation, and tests for antibodies to varicella zoster virus. Additionally, periodic skin examinations are recommended, and pulmonary function should be assessed if clinically indicated. Blood pressure should be monitored during treatment. • First-dose monitoring is recommended for patients with sinus bradycardia, first- or second-degree [Mobitz type I] AV block, or a history of myocardial infarction or heart failure.

	• Clinically isolated syndrome is the first episode of neurological symptoms caused by inflammation and demyelination in the central nervous system. Relapsing-remitting MS (RRMS) is characterized by clearly defined attacks of new or increasing neurologic symptoms. The attacks are followed by periods of partial or complete recovery (remissions). Secondary progressive disease follows an initial relapsing remitting course, with disability gradually increasing over time.
	• Prescribing Considerations:
	  ○ Mayzent should be prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.
	  ○ Avoid live attenuated vaccines during and for up to 4 weeks after treatment.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Mayzent may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of MS (ICD-10: G35), classified as one (1) of the following relapsing forms **(1., 2., or 3.):**

1. Clinically isolated syndrome

2. Relapsing-remitting disease

3. Active secondary progressive disease.

C. The member meets both of the following **(1. and 2.)**:

1. The member has been tested for CYP2C9 variants to determine CYP2C9 genotype.

2. The member does not have a CYP2C9*3/*3 genotype.

II. Reauthorization

When a benefit, reauthorization of Mayzent may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced a therapeutic response defined as one (1) of the following **(1., 2., or 3.):**

1. Disease stability

2. Disease improvement

3. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Combination use of Mayzent with other disease modifying MS agents (for example,. Aubagio, Gilenya, interferons, Copaxone, Tysabri, etc.) will not be authorized.

II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 24 month authorization may be granted.

Automatic Approval Criteria

- None.

References:

1. Mayzent [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2024.
2. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline: Disease-modifying therapies for adults with multiple sclerosis. *Neurol*. 2018 April 24;90(17):1-228.
3. National Multiple Sclerosis Society. Types of MS. Available at: https://www.nationalmssociety.org/What-is-MS/Types-of-MS. Accessed April 30, 2025.

Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.

The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.