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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 19, 2019
Subject:	Mayzent	**Page:**	1 of 6

Last Review Date: June 16, 2022

Mayzent

Description

Mayzent (siponimod)

Preferred product: Mayzent

Background
Mayzent (siponimod) is a sphingosine-1-phosphate-receptor (S1P) modulator that binds with high affinity to S1P receptors 1 and 5. Mayzent 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 (MS) is unknown but may involve reduction of lymphocyte migration into the central nervous system (1).

Regulatory Status
FDA-approved indication: Mayzent is a sphingosine-1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Before therapy with Mayzent is initiated, a recent (i.e., within 6 months or after discontinuation of prior therapy) complete blood count (CBC) should be reviewed (1).

Mayzent causes a dose-dependent reduction in peripheral lymphocyte count to 20-30% of baseline values because of reversible sequestration of lymphocytes in lymphoid tissues. As a result, Mayzent may therefore increase the risk of infections (1).

Mayzent is contraindicated: (1)

- In patients with a CYP2C9*3/*3 genotype.

- In patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure.
- In patients who have a presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker.

After the initial titration is complete, if Mayzent treatment is interrupted for 4 or more consecutive daily doses, reinitiated treatment with Day 1 of the titration regimen (1).

If patients are taking antineoplastic, immunosuppressive or immune modulating therapies, or if there is a history of prior use of these drugs, possible additive immunosuppressive effects should be considered before starting treatment with Mayzent (1).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated. The use of live attenuated vaccines should be avoided while patients are taking Mayzent and for 4 weeks after stopping treatment (1-2).

The safety and effectiveness of Mayzent in pediatric patients less than 18 years of age have not been established (1).

Related policies
Acthar Gel, Ampyra, Aubagio, Gilenya, Kesimpta, Lemtrada, Mavenclad, MS Injectables, Ocrevus, Ponvory, Tecfidera, Tysabri, Zeposia

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Mayzent may be considered **medically necessary** in patients 18 years of age or older with Multiple Sclerosis (MS) and if the conditions indicated below are met.

Mayzent may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Relapsing forms of Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

AND ALL of the following:

1. Prescriber has reviewed baseline liver function tests (LFTs), complete blood count (CBC) including lymphocyte count, and electrocardiogram (ECG)
2. Prescriber agrees to monitor for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement for the first dose, as medically indicated
3. The CYP2C9 genotype has been confirmed prior to starting treatment **AND** patient does **NOT** have CYP2C9*3/*3 genotype
4. Prescriber will not exceed FDA labeled dose of 2 mg/day
   a. Genotypes CYP2C9 *1/*3 and *2/*3 **only**: Prescriber will not exceed FDA labeled dose of 1 mg/day
5. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure
6. **NO** history or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker
7. **NO** significant QTc prolongation (QTc greater than 500 msec)
8. **NO** severe untreated sleep apnea
9. Patients with a history of uveitis and/or diabetes **ONLY**: will have an ophthalmic evaluation of the fundus, including the macula, prior to initiation of therapy
10. **NO** concurrent use with other MS disease modifying agents
11. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Relapsing forms of Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

AND ALL of the following:

1. Prescriber will not exceed FDA labeled dose of 2 mg/day
   a. Genotypes CYP2C9 *1/*3 and *2/*3 **only**: Prescriber will not exceed FDA labeled dose of 1 mg/day
2. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure.
3. **NO** history or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker
4. **NO** significant QTc prolongation (QTc greater than 500 msec)
5. **NO** severe untreated sleep apnea
6. **NO** concurrent use with other MS disease modifying agents
7. **NOT** given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
Mayzent (siponimod) is a sphingosine-1-phosphate-receptor (S1P) modulator that binds with high affinity to S1P receptors 1 and 5. Mayzent 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 (MS) is unknown but may involve reduction of lymphocyte migration into the central nervous system. The safety and effectiveness of Mayzent in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Mayzent while maintaining optimal therapeutic outcomes.

References
1. Mayzent [package insert, East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2022.
2. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. Neurological Bulletin. 2010;2(1):17-21.

Policy History

Date	Action
April 2019	Addition to PA
June 2019	Annual review
July 2019	Added requirement that prescriber must not exceed FDA labeled dosing. Removed quantity limits due to titrations
September 2019	Annual review. Revised initiation requirement that the CYP2C9 genotype has to be confirmed before starting therapy and removed continuation requirement of no CYP2C9*3/*3 per SME. Changed diagnosis to relapsing forms of MS per SME. Updated regulatory status per SME
February 2020	Revised requirement to “Prescriber agrees to monitor for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement for the first dose, as medically indicated” per FEP
March 2020	Annual review
September 2020	Annual review. Addition of requirements per SME: obtain lymphocyte count prior to initiation of therapy; no significant QTc prolongation; no severe untreated sleep apnea; ophthalmic evaluation prior to therapy for patients with a history of uveitis and/or diabetes
December 2020	Annual review and reference update
June 2021	Annual review and reference update

June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.