Mayzent

**Description**

Mayzent (siponimod)

**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, Lemtrada, Mavenclad, MS Injectables, Ocrevus, Tecfidera, Tysabri

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), and electrocardiogram (ECG)
2. Member must be observed for 6 hours after the first dose for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement
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 concurrent use with other MS disease modifying agents
8. 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 concurrent use with other MS disease modifying agents
5. 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

Policy History

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td>April 2019</td>
<td>Addition to PA</td>
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<tr>
<td>June 2019</td>
<td>Annual review</td>
</tr>
<tr>
<td>July 2019</td>
<td>Added requirement that prescriber must not exceed FDA labeled dosing. Removed quantity limits due to titrations</td>
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<tr>
<td>September 2019</td>
<td>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</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.