

PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis – Mayzent® (siponimod tablets – Novartis)

TAC APPROVAL DATE: 07/17/2019

OVERVIEW

Mayzent, a sphingosine 1-phosphate receptor modulator, is 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.^{1,2}

Disease Overview

MS is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system (CNS) that impacts almost 1,000,000 people in the US.² The condition is marked by inflammation and demyelination, as well as degenerative alterations. Patients usually experience relapses and remissions in their neurological symptoms. For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults. The MS disease course is heterogeneous but has some patterns. Approximately 85% to 90% of patients have a relapsing pattern at onset. However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS). Around 10% to 15% of patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity. Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age) and the distribution is equivalent among the two genders. Advances in the understanding of the MS disease process, as well as in MRI technology, spurred updated disease course descriptions in 2013,³ as well as in 2017.⁴ The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.²⁻⁴ Clinically isolated syndrome is now more recognized among the course descriptions of MS. It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be MS but has yet to fulfill diagnostic criteria. It is notable that the other MS designations can be further characterized considering whether patients have active disease (or not active), as well as if disease is worsening or stable. Disability in MS is commonly graded on the deterioration of mobility per the Expanded Disability Status Scale (EDSS) an ordinal scale that ranges from 0 to 10, with higher scores indicating greater disability.

Safety

The initiation of Mayzent leads to decreases in heart rate.¹ First-dose 6-hour monitoring is recommended in certain patients with preexisting cardiac conditions. Additional monitoring beyond 6 hours may also be required. After the initial titration is complete, if Mayzent therapy is interrupted for four or more consecutive daily doses, reinstate treatment with Day 1 of the titration regimen and also complete first-dose monitoring for patients for whom it is recommended. The most common adverse events (AEs) with Gilenya include headache, hypertension, and transaminase elevations. Mayzent has Warnings/Precautions regarding infections, macular edema, bradyarrhythmias and atrioventricular conduction delays, respiratory effects, liver injury, increased blood pressure, and posterior reversible encephalopathy syndrome. It takes approximately 10 months to eliminate Mayzent from the body, therefore, women of childbearing potential should use effective contraception to avoid pregnancy during and for up to 10 days after cessation of Mayzent therapy.

Guidelines

In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.² Many options from various disease classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Mayzent. All approvals are provided for the duration cited below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Mayzent is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Multiple Sclerosis.** Approve for 1 year if the patient meets the following criteria (A and B):
 - A) The patient has a relapsing form of multiple sclerosis; AND
 - B) The agent is prescribed by or in consultation with neurologist or a physician who specializes in the treatment of multiple sclerosis.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Mayzent has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Non-Relapsing Forms of Multiple Sclerosis (MS).** Note: An example of a non-relapsing form of MS is primary progressive MS. The efficacy of Mayzent has not been established in patients with MS with non-relapsing forms of the disease.¹
2. **Current Use with Other Disease-Modifying Agents Used for Multiple Sclerosis.** Note: Examples of disease-modifying agents used for multiple sclerosis include Avonex[®] (interferon beta 1a injection [intramuscular]), Betaseron[®]/Extavia[®] (interferon beta-1b injection), Rebif[®] (interferon beta-1a injection [subcutaneous]), Copaxone[®]/Glatopa[®] (glatiramer acetate injection), Plegridy[®] (peginterferon beta-1a injection), Aubagio[®] (teriflunomide tablets), Gilenya[®] (fingolimod tablets), Mavenclad[®] (cladribine tablets), Tecfidera[®] (dimethyl fumarate delayed-release capsules), Ocrevus[®] (ocrelizumab injection for intravenous use), Tysabri[®] (natalizumab injection for intravenous infusion), and Lemtrada[®] (alemtuzumab injection for intravenous use).² These agents are not indicated for use in combination. Additional data are required to determine if use of disease-modifying MS agents in combination is safe provides added efficacy.
3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Mayzent™ tablets [prescribing information]. East Hanover, NJ: Novartis; March 2019.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated June 2019. Available at: http://ms-coalition.org/wp-content/uploads/2019/06/MS_CDMTPaper_062019.pdf. Accessed on July 7, 2019.
3. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
4. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New policy	--	03/27/2019
Early annual revision	<p>The following criteria changes were made.</p> <ol style="list-style-type: none"> 1. Multiple Sclerosis: The criterion that requires that the patient has a relapsing form of MS was revised to remove the phrase that stated “to include relapsing remitting MS or active secondary progressive MS”. 2. Conditions Not Recommended for Approval: For patients with Non-Relapsing Forms of MS, the example of primary progressive MS is now listed as a note. Regarding Use with Other Disease-Modifying Agents for MS, the examples were listed as a note with Mavenclad added. 	07/17/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.