

PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis – Gilenya® (fingolimod capsules – Novartis)

DATE REVIEWED: 07/17/2019

OVERVIEW

Gilenya, a sphingosine 1-phosphate receptor modulator, is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) in patients 10 years of age and older.¹

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 Gilenya leads to decreases in heart rate.¹ After the first dose of Gilenya, the heart rate decreases are noted within an hour and generally are greatest at 6 hours, although the effects can be observed 24 hours after the first dose in some patients. The first dose of Gilenya should be given in a setting with resources to appropriately manage symptomatic bradycardia. Observe patients for 6 hours after the first Gilenya dose for signs and symptoms of bradycardia. Patients with prolonged QTc interval at baseline or during the observation period, or taking medications with known risks of torsades de pointes, should be observed overnight with continuous electrocardiographic (ECG) monitoring. When restarting Gilenya after discontinuation for more than 14 days after the first treatment month, perform first-dose monitoring. The most common adverse events (AEs) with Gilenya include headache, influenza, diarrhea, back pain, liver transaminase elevations, and cough. Gilenya is associated with serious toxicities such as decreased heart rate and/or atrioventricular condition after the first dose; an increased risk of infections; macular edema; pulmonary toxicity; and

elevated liver enzymes. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in patients who were given Gilenya in the postmarketing setting. Based on animal studies, Gilenya may cause fetal harm. It takes approximately 2 months to eliminate Gilenya from the body, therefore, women of childbearing potential should use effective contraception to avoid pregnancy during and for up to 2 months after cessation of Gilenya 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.² The American Academy of Neurology has practice guidelines regarding disease-modifying therapies for adults with MS.⁵ The guidelines cites Gilenya as one of the agents to consider for patients with MS who have highly active disease.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Gilenya. Because of the specialized skills required for evaluation and diagnosis of patients treated with Gilenya as well as the monitoring required for AEs and efficacy, approval requires Gilenya to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 1 year in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Gilenya is recommended in those who meet the following criteria.

FDA-Approved Indications

- 1. Multiple Sclerosis (MS).** Approve for 1 year if the patient meets all of 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 a neurologist or a physician who specializes in the treatment of MS.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Gilenya 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.** Note: An example of a non-relapsing form of multiple sclerosis (MS) is primary progressive MS. In the INFORMS trial Gilenya did not slow disease progression in patients with primary progressive MS.⁶

2. **Concurrent 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), Mavenclad[®] (cladribine tablets), Mayzent[®] (siponimod 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. Gilenya[®] capsules [prescribing information]. East Hanover, NJ: Novartis; January 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.
5. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:777-788.
6. Lublin F, Miller DH, Freedman MS, et al, on behalf of the INFORMS Study Investigators. Oral fingolimod in primary progressive multiple sclerosis (INFORMS): a phase 3, randomized, double-blind, placebo-controlled trial. *Lancet*. 2016;387:1075-1084.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Under the “Conditions Not Recommended for Approval” section, added Ocrevus to the list of disease-modifying agents used for MS in which concurrent use with Gilenya is not recommended.	08/02/2017
Selected revision	The title of this policy was changed to add that it applies to the new Care Value program. For MS, the approval duration was changed from 3 years to 1 year. Initial therapy criteria was altered to remove the criterion that allows exceptions if the patient is unable to administer injections due to dexterity issues or visual impairment. Also, the criterion was removed that required the patient to try one of the following agents before receipt of Gilenya: Avonex, Rebif, Betaseron, Extavia, Copaxone, Glatopa, or Plegridy. A trial of generic glatiramer is required in the accompanying <i>MS – PSM Policy</i> and <i>MS – Care Value Policy</i> . These changes resulted in the criteria for initial therapy and for patients currently receiving Gilenya or have received Gilenya in the past to be the same; therefore, these criteria sets were merged.	12/13/2017
Selected revision	Selected revision to add information from the Gilenya prescribing information which details its indication for use in children.	Not applicable
Annual revision	Zinbryta was removed from the market. Therefore, Zinbryta was deleted from the list of medications in which Gilenya should not be used with concomitantly.	08/15/2018
Annual revision	The wording of “for PSM” was removed from the document title. The following criteria changes were made. <ol style="list-style-type: none"> 1. Multiple Sclerosis: The examples of relapsing forms of MS were removed. 2. Conditions Not Recommended for Approval: For patients with Non-Relapsing Forms of MS, the example of primary progressive MS is now 	07/17/2019

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	listed as a note. Regarding Use with Other Disease-Modifying Agents for MS, the examples are now listed as a note with Mavenclad and Mayzent added.	
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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>; MS – Multiple sclerosis; PSM – Preferred Specialty Management.