Cigna National Preferred Formulary Coverage Policy

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Prior Authorization
Multiple Sclerosis – Gilenya® (fingolimod capsules)

Table of Contents
NPF Coverage Policy ............................... 1
Background ........................................ 2
References ........................................... 3
Last Revision Details ............................... 3

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

NPF Coverage Policy

Cigna covers fingolimod (Gilenya®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

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

FDA Indication(s)

1. Multiple Sclerosis. Approve for 1 year if the individual meets all of the following criteria (A and B):
   A) Individual has a relapsing form of multiple sclerosis; AND
      Note: Examples of relapsing forms of multiple sclerosis (MS) include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease.
   B) Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.

Conditions Not Covered
Fingolimod (Gilenya®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **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), Rebi® (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), Bafiertam® (monomethyl fumarate delayed-release capsules), Vumerity® (dioximel fumarate delayed-release capsules), Zeposia® (ozanimod capsules), Ocrevus® (ocrelizumab injection for intravenous use), Tysabri® (natalizumab injection for intravenous infusion), Lemtrada® (alemtuzumab injection for intravenous use), and Kesimpta® (ofatumumab injection for subcutaneous use). These agents are not indicated for use in combination. Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.

2. **Non-Relapsing Forms of Multiple Sclerosis.**
   **Note:** An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis. In the INFORMS trial Gilenya did not slow disease progression in individuals with primary progressive multiple sclerosis.

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**Background**

**Overview**
Gilenya, a sphingosine 1-phosphate receptor modulator, is indicated for the treatment of individuals with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in individuals 10 years of age and older.

**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. The condition is marked by inflammation and demyelination, as well as degenerative alterations. Individuals usually experience relapses and remissions in their neurological symptoms. For most individuals, the onset of MS symptoms occurs when individuals 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 individuals have a relapsing pattern at onset. However, this transitions over time in individuals 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 individuals 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 individuals 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, as well as in 2017. The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS. 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 designsations can be further characterized considering whether individuals 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.

**Guidelines**
In September 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS. Many options from various disease classes, involving different mechanisms of action and modes of administration, have shown benefits in individuals with MS. The American Academy of
Neurology has practice guidelines regarding disease-modifying therapies for adults with MS. The guidelines cites Gilenya as one of the agents to consider for individuals with MS who have highly active disease.

Safety
The initiation of Gilenya leads to decreases in heart rate. 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 individuals. The first dose of Gilenya should be given in a setting with resources to appropriately manage symptomatic bradycardia. Observe individuals for 6 hours after the first Gilenya dose for signs and symptoms of bradycardia. Individuals 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. There are several contraindications for use which mainly include individuals with background cardiovascular disease. 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 individuals who were given Gilenya in the postmarketing setting.

References

Last Revision Details
| Selected Revision | Multiple Sclerosis: Examples of relapsing forms of MS were added in a Note. Conditions Not Recommended for Approval: Regarding Use with Other Disease-Modifying Agents for MS, Kesimpta was added to the list of examples provided in the Note. | 09/09/2020 |

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