BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.60.08

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	June 7, 2012
Subject:	Gilenya	**Page:**	1 of 7

Last Review Date: June 16, 2022

Gilenya

Description

Gilenya (fingolimod)

Preferred product: Gilenya

Background
Gilenya (fingolimod) is a sphingosine-1-phosphate-receptor (S1PR) modulator that binds to receptors in the body that block progression of lymphocytes (white blood cells) into the blood and may reduce the movement of lymphocytes into the central nervous system. Although the exact mechanism of action in Multiple Sclerosis (MS) is unknown, it is thought that through this inhibition, lymphocytes are unable to destroy the myelin sheath which leads to lesions that are characteristic of MS and reducing the severity of MS (1).

Gilenya is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability (1).

Regulatory Status
FDA approved indication: Gilenya 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 patients 10 years of age and older (1).

Patients with some pre-existing conditions (e.g., ischemic heart disease, history of myocardial infarction, congestive heart failure, history of cardiac arrest, cerebrovascular disease, history of

symptomatic bradycardia, history of recurrent syncope, severe untreated sleep apnea, AV block, sino-atrial heart block) may poorly tolerate the Gilenya-induced bradycardia, or experience serious rhythm disturbances after the first dose of Gilenya. Prior to treatment with Gilenya, patients should have a cardiac evaluation by a physician appropriately trained to conduct such evaluation, and, if treated with Gilenya after the first dose patients should be monitored for 6 hours for signs and symptoms of bradycardia with hourly pulse and blood pressure measurement and overnight with continuous ECG in a medical facility (1).

Gilenya is contraindicated in patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, baseline QT interval ≥500 ms, or Class III/IV heart failure (1).

Gilenya is contraindicated in patients with Mobitz Type II 2nd degree or 3rd degree AV block, a prolonged QTc interval or at risk for QT prolongation, or concomitant use of Class Ia or Class III anti-arrhythmic drugs (1).

If Gilenya therapy is discontinued for more than 14 days, after the first month of treatment, the effects on heart rate and AV conduction may recur on reintroduction of Gilenya treatment and the same precautions (first dose monitoring) as for initial dosing should apply. Within the first 2 weeks of treatment, first dose procedures are recommended after interruption of one day or more, during week 3 and 4 of treatment first dose procedures are recommended after treatment interruption of more than 7 days (1).

Before initiating treatment with Gilenya, a recent CBC should be available due to Gilenya increasing the risk of infection. Macular edema occurred in 0.4% of patients receiving Gilenya therefore an ophthalmologic evaluation should be performed at baseline and 3 to 4 months after initiation of treatment; patients with diabetes with a history of uveitis are at increased risk. Elevations of liver enzymes may occur in patients and a recent transaminase and bilirubin level should be done before initiation of Gilenya therapy. Gilenya may cause a decrease in pulmonary function tests and spirometry and diffusion lung capacity for carbon monoxide should be obtained with clinically indicated. Gilenya should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (1).

Gilenya has not been administered concomitantly with antineoplastic, immunosuppressive or immune modulating therapies used for treatment of MS. Concomitant use of Gilenya with any of these therapies would be expected to increase the risk of immunosuppression (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 (2).

Gilenya has been approved in the US with a Risk Evaluation and Mitigation Strategy (REMS) to inform patients and healthcare providers on the safe use and serious risks of Gilenya in treating relapsing forms of MS. The approved REMS includes a medication guide for patients, and a letter and safety information guide for healthcare providers (1).

Safety and effectiveness in pediatric patients with MS below the age of 10 have not been established (1).

Related policies
Acthar Gel, Ampyra, Aubagio, Kesimpta, Lemtrada, Mavenclad, Mayzent, 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.

Gilenya may be considered **medically necessary** in patients 10 years of age or older that have a documented diagnosis of a relapsing form of Multiple Sclerosis (MS) and if the conditions indicated below are met.

Gilenya may be considered **investigational** in patients less than 10 years of age and for all other indications.

Prior-Approval Requirements

Age 10 years of age or older

Diagnosis

Patient must have the following:

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

AND ALL of the following:

1. Member must be observed for 6 hours after the first dose for signs and symptoms of bradycardia with hourly pulse and blood pressure measurements and an ECG prior to dosing and at the end of the observation period
2. Prescriber has reviewed baseline complete blood count (CBC) including lymphocyte count
3. **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
4. **NO** history or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker
5. **NO** significant QTc prolongation (QTc greater than or equal to 500 msec)
6. 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
7. **NO** concurrent use with other MS disease modifying agents
8. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Age 10 years of age or older

Diagnosis

Patient must have the following:

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

AND ALL of the following:

1. **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.
2. **NO** history or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker
3. **NO** significant QTc prolongation (QTc greater than or equal to 500 msec)

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

Quantity

Strength	Quantity Limit
0.25 mg capsule*	90 capsules per 90 days
0.5 mg capsule	

*This strength is included in this policy but is not available in the market as of yet

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Gilenya (fingolimod) is indicated in the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability. The first dose of Gilenya should be administered in a setting in which resources to appropriately observe and manage symptomatic bradycardia are available. Gilenya is contraindicated in patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure or Class III/IV heart failure. Gilenya is also contraindicated in patients with Mobitz Type II 2nd degree or 3rd degree AV block. Safety and effectiveness in pediatric patients with MS below the age of 10 have not been established (1).

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

References

1. Gilenya [package insert, East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2019.
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 2012	New PA policy
March 2013	Annual editorial review and reference update Addition to criteria that the patient must not have a history or presence of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome; unless patient has a pacemaker. Added no concurrent therapy with Class Ia or Class III anti-arrhythmic drugs.
September 2013	Annual editorial review and reference update
December 2014	Annual editorial review and reference update. Removal of “not being treated with Class Ia and Class III anti-arrhythmics” and examples from criteria of other MS disease modifying agents
February 2015	Change in PA Allowance from 84 caps per 84 days to accommodate new packaging of 30 count
March 2015	Annual editorial review and reference update
September 2016	Annual editorial review. Reference update. Policy code changed from 5.07.08 to 5.60.08
December 2016	Annual editorial review and reference update Addition of not given concurrently with live vaccines
March 2017	Annual review
June 2017	Annual review
June 2018	Decrease in age to 10 years of age and older. Addition of 0.25 mg strength
September 2018	Annual review
September 2019	Annual review and reference update
December 2019	Revised relapsing MS indication to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
March 2020	Annual review and reference update
April 2020	Added statement that Gilenya is a preferred product
June 2020	Annual review

September 2020	Annual review. Addition of requirements per SME: obtain CBC and lymphocyte count prior to initiation of therapy, no significant QTc prolongation; ophthalmic evaluation prior to therapy for patients with a history of uveitis and/or diabetes
December 2020	Annual review
June 2021	Annual review
June 2022	Annual editorial review and reference update

Keywords

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