BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES		**ORIGINAL EFFECTIVE DATE:**	**4/07/11**
SECTION: DRUGS		**LAST REVIEW DATE:**	**8/02/18**
		LAST CRITERIA REVISION DATE:	**8/02/18**
		ARCHIVE DATE:	

GILENYA™ (fingolimod) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

GILENYA™ (fingolimod) oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Gilenya (fingolimod) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 10 years of age or older

  2. A confirmed diagnosis of **ONE** of the following:
     - Relapsing-remitting multiple sclerosis (RRMS)
     - Secondary progressive multiple sclerosis (SPMS)
     - Progressive-relapsing multiple sclerosis (PRMS)
     - A first clinical episode that has magnetic resonance imaging (MRI) features that are consistent with multiple sclerosis

  3. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Complete blood count (CBC) within the last 6 months
     - Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin within the last 6 months
     - Electrocardiogram (ECG)
     - Ophthalmologic examination
     - Evidence of varicella zoster virus (VZV) immunity by either a healthcare provider-confirmed history of chickenpox, documented full course of VZV vaccination, OR testing for antibodies to VZV; any needed vaccination to be completed 1 month before initiation

  4. There are **NO** contraindications:
     - Contraindications include:
       - Myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure within the last 6 months
       - History or presence of Mobitz Type II second-degree or third-degree atrioventricular (AV) block or sick sinus syndrome, unless individual has a functioning pacemaker
       - Baseline QTc interval $\geq$ 500 msec
       - Treatment with Class IA or Class III anti-arrhythmic drugs
       - History of a hypersensitivity reaction to fingolimod or any of the excipients in Gilenya

  5. Will not be used in patients with an active infection

  6. Will not be used with live vaccines during therapy

  7. Woman patient of child bearing potential should use effective contraception during therapy

  8. Will not be used concurrently with other oral multiple sclerosis medications (e.g., Tecfidera, Aubagio, etc., except for Ampyra, which is intended to improve walking speed rather than disease progression) or injectable therapies for multiple sclerosis (e.g., interferon beta-1a or 1b, glatiramer, Lemtrada, Ocrevus, Tysabri, or mitoxantrone)

GILENYA™ (fingolimod) oral capsule (cont.)

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Gilenya (fingolimod) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition responded while on therapy
    - Response is defined as:
        - **THREE** of the following:
            - Mild/minimal to no functional neurologic (pyramidal, cerebellar, brainstem, sensory) disabilities
            - Ambulatory without need for assistance
            - Reduction in number of exacerbations or relapses of MS
            - Prolonged time to exacerbation or relapses of MS
            - Reduction in hospitalizations for MS

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect such as:
        - Severe, uncontrolled infection, Progressive Multifocal Leukoencephalopathy, Posterior Reversible Encephalopathy Syndrome, macular edema or uveitis

4. Will not be used concurrently with other oral multiple sclerosis medications (e.g., Tecfidera, Gilenya, etc., except for Ampyra, which is intended to improve walking speed rather than disease progression) or injectable therapies for multiple sclerosis (e.g., interferon beta-1a or 1b, glatiramer, Lemtrada, Ocrevus, Tysabri, or mitoxantrone)

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Gilenya™ is a sphingosine 1-phosphate receptor modulator indicated for 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. Gilenya is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator, and binds with high affinity to sphingosine 1-phosphate receptors 1, 3, 4, and 5. Fingolimod-phosphate blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which Gilenya exerts therapeutic effects in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

GILENYA™ (fingolimod) oral capsule (cont.)

MS is a chronic autoimmune disorder of the central nervous system (CNS) in which white blood cells (WBCs) attack and damage the myelin sheath of nerve cells in the CNS. This damage disrupts transmission of nerve impulses. Damage occurs in areas of the brain, spinal cord, and optic nerves. Over time, the damage ultimately leads to progressive physical and cognitive disabilities. The clinical course of MS is highly variable. There are four recognized clinical forms: relapsing remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and progressive relapsing (PRMS). RRMS is the most common form of the disease.

Because MS can affect any area of the brain, optic nerve, or spinal cord, MS can cause almost any neurologic symptom. Patients often present as young adults with 2 or more clinically distinct episodes of CNS dysfunction with at least partial resolution. Episodes involve numbness, weakness, or incoordination affecting an arm, a leg, or both. Additional symptoms include pain, vertigo, cognitive deficits (such as impaired memory, attention, or judgment), fatigue, speech deficits (such as dysarthria or less commonly aphasia), and bowel, bladder, and sexual dysfunction.

The pathological hallmark of MS is the cerebral or spinal plaque seen on magnetic resonance imaging (MRI). Plaques are discrete regions of demyelination with relative preservation of axons. The neurologic history and physical examination help establish the diagnosis of MS. Diagnostic criteria are symptoms and signs disseminated in time and space (i.e., more than one episode involving more than one area of the CNS). These criteria have been largely replaced by the McDonald criteria, developed in 2001 by the International Panel on the Diagnosis of Multiple Sclerosis. The McDonald criteria retain many features of the original criteria and are intended for use in both clinical practice and clinical trial settings. Diagnoses of “definite MS,” “possible MS,” or, if there is a better explanation for the clinical presentation, “not MS” are determined by findings on clinical exam, MRI, cerebrospinal fluid, and visual evoked potentials. The term “clinically isolated syndrome” (CIS) describes patients who have suffered a first clinical attack but do not meet diagnostic criteria for definite MS. The most recent update in 2010 allows the diagnosis of MS in some patients with CIS.

Definitions:

Forms of Multiple Sclerosis (MS):

Relapsing remitting multiple sclerosis (RRMS)
This form of MS is characterized by acute relapses that are followed by some degree of recovery; patients do not develop worsening of disability between relapses.

Secondary progressive multiple sclerosis (SPMS)
This form of MS is defined as sustained progression of physical disability occurring separately from relapses, in patients who previously had RRMS. There may, or may not be intermittent relapses, remissions, or periods of temporary minor improvements. As long as the person continues to have relapses, the SPMS course is considered to be both progressive and relapsing.

Progressive relapsing multiple sclerosis (PRMS)
This form of MS is characterized by steadily worsening disease from the beginning, but with occasional relapses along the way. PRMS is considered to be both a progressive and a relapsing form of the disease because people experience steady disease progression and relapses.

GILENYA™ (fingolimod) oral capsule (cont.)

Primary progressive multiple sclerosis (PPMS)

This form of MS is defined as progression of disability from onset without superimposed relapses. This type of MS is characterized by a steady decline in function from the beginning without acute attacks. There are no distinct relapses or remissions. This is not a relapsing form of MS.

McDonald criteria:

Clinical Presentation	Additional Data Needed
* 2 or more attacks (relapses) * 2 or more objective clinical lesions	None; clinical evidence will suffice (additional evidence desirable but must be consistent with MS)
* 2 or more attacks * 1 objective clinical lesion	Dissemination in space, demonstrated by: * MRI * **or** a positive CSF and 2 or more MRI lesions consistent with MS * **or** further clinical attack involving different site
* 1 attack * 2 or more objective clinical lesions	Dissemination in time, demonstrated by: * MRI * **or** second clinical attack
* 1 attack * 1 objective clinical lesion (monosymptomatic presentation)	Dissemination in space demonstrated by: * MRI * **or** positive CSF and 2 or more MRI lesions consistent with MS **and** Dissemination in time demonstrated by: * MRI * **or** second clinical attack
Insidious neurological progression suggestive of MS (primary progressive MS)	One year of disease progression (retrospectively or prospectively determined) **and** Two of the following: a. Positive brain MRI (nine T2 lesions or four or more T2 lesions with positive VEP) b. Positive spinal cord MRI (two focal T2 lesions) c. Positive CSF

Resources:

Gilenya package insert revised by manufacturer on 05/2018 reviewed on 06-26-2018

Gilenya package insert revised by manufacturer on 02/2016 reviewed on 05-23-2016, 07-06-2017

Gilenya package insert revised by manufacturer on 05/2015 reviewed on 06-15-2015

Gilenya. Package Insert. Review on September 2010

National Multiple Sclerosis Society: http://www.nationalmssociety.org/about-multiple-sclerosis/relapsing-ms/index.aspx

Gilenya. Package Insert, T2012-108/T2012-109. Revised by manufacturer on 05-2012. Reviewed on 05/28/12

GILENYA™ (fingolimod) oral capsule (cont.)

Polman CH, Reingold SC, Banwell B, et al.: Annals of Neurology 2011;69:292-302: Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

Rio J, Cornabella M, Montalban X: Multiple sclerosis: Current treatment algorithms. Curr Opin Neurol 2011:24:230-237

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.