BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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VUMERITY™ (diroximel fumarate) oral delayed-release 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.**

VUMERITY™ (diroximel fumarate) oral delayed-release capsule

Criteria:

- **Criteria for initial therapy:** Vumerity (diroximel fumarate) delayed-release capsule is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

  4. Individual has failure, contraindication or intolerance to **ALL** the following preferred step therapy agents: [**Note**: each of the following requires precertification]
     - Tecfidera (dimethyl fumarate)
     - Gilenya (fingolimod)
     - Aubagio (teriflunomide)

  5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Complete blood count, including lymphocyte count
     - Serum aminotransferase, alkaline phosphatase, and total bilirubin

  6. There are **NO** contraindications
     - Contraindications include:
       - Hypersensitivity (eg, anaphylaxis, angioedema) to diroximel fumarate, Tecfidera (dimethyl fumarate), or to any component of the formulation
       - Concomitant use of Tecfidera (dimethyl fumarate)

  7. Will not be used concurrently with other oral multiple sclerosis medications (e.g., Aubagio, 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)

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Vumerity (diroximel fumarate) delayed-release capsules is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

  2. Individual's condition responded while on therapy

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- 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

3. Individual has been adherent with the medication

4. 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:
     - Anaphylaxis or angioedema
     - Progressive multifocal leukoencephalopathy
     - Lymphopenia
     - Persistent lymphocyte count < 0.5 x 10^9/L
     - Liver injury

5. Will not be used concurrently with other oral multiple sclerosis medications (e.g., Aubagio, 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)

6. Will not be used in an individual that does not tolerate maintenance dose of 462 mg twice daily

Renewal duration: 12 months

Description:

Vumerity (diroximel fumarate) delayed-release capsule is indicated for the treatment of relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease, in adults.

The mechanism by which diroximel fumarate exerts its therapeutic effect in MS is unknown. MMF, the active metabolite of diroximel fumarate, has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway *in vitro* and *in vivo* in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. MMF has been identified as a nicotinic acid receptor agonist *in vitro*.

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Diroximel fumarate undergoes rapid pre-systemic hydrolysis by esterases and is converted to its active metabolite, monomethyl fumarate (MMF). Another agent for MS, Tecfidera (dimethyl fumarate) also undergoes metabolism to MMF.

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.

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 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.

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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.

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:

Vumerity (diroximel fumarate) delayed-release capsules product information accessed 11-07-19 at DailyMed