Introduction

Multiple sclerosis is a disease that occurs when the body’s immune system reacts to and damages nerve cells. Damage occurs to nerves and their connections in the brain and spinal cord. Multiple sclerosis is also called MS. People with MS can have a variety of symptoms including vision problems, numbness and tingling, muscle weakness and other problems. Some people have only a few symptoms, and others may be severely disabled from the disease. There are several types of MS as well. This policy discusses the drugs used to treat MS and which of those drugs need to be pre-approved by the health plan.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs providers about when a service may be covered.

Policy Coverage Criteria

We will review specific intravenous (IV) and injectable drugs for medical necessity for all ages.
For those age 13 and older, we also will review the site of service for medical necessity. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home.

**Drugs subject to site of service review addressed in this policy are:**

- Ocrevus® (ocrelizumab)

<table>
<thead>
<tr>
<th>Site of Service Administration</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically necessary sites of service</td>
<td>IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost effective site:</td>
</tr>
<tr>
<td>• Physician’s office</td>
<td>• These are the preferred <strong>medically necessary</strong> sites of service for specified drugs.</td>
</tr>
<tr>
<td>• Infusion center</td>
<td></td>
</tr>
<tr>
<td>• Home infusion</td>
<td></td>
</tr>
<tr>
<td>Hospital-based outpatient setting</td>
<td>IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site.</td>
</tr>
<tr>
<td>• Outpatient hospital IV infusion department</td>
<td>This site is considered medically necessary for the first 90 days for the following:</td>
</tr>
<tr>
<td>• Hospital-based outpatient clinical level of care</td>
<td>• The initial course of infusion of a pharmacologic or biologic agent</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>• Re-initiation of an agent after 6 months or longer following discontinuation of therapy*</td>
</tr>
</tbody>
</table>

*Note:* This does not include when standard dosing between infusions is 6 months or longer

This site is considered medically necessary when there is no outpatient infusion center within 50 miles of the patient’s home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions of this drug.
Site of Service Administration | Medical Necessity
---|---
| This site is considered medically necessary only when the patient has a clinical condition which puts him or her at increased risk of complications for infusions, including any ONE of the following:
- Known cardiac condition (eg, symptomatic cardiac arrhythmia) or pulmonary condition (eg, significant respiratory disease, serious obstructive airway disease, %FVC ≤ 40%) that may increase the risk of an adverse reaction
- Unstable renal function which decreases the ability to respond to fluids
- Difficult or unstable vascular access
- Acute mental status changes or cognitive conditions that impact the safety of infusion therapy
- A known history of severe adverse drug reactions and/or anaphylaxis to prior treatment with a related or similar drug

**Hospital-based outpatient setting**
- Outpatient hospital IV infusion department
- Hospital-based outpatient clinical level of care

These sites are considered not medically necessary for infusion and injectable therapy services of various medical and biologic agents when the site-of-service criteria in this policy are not met.

**Note:** This policy does not address intravenous (IV) and injectable therapy services for patient’s receiving inpatient services.

**Relapsing Multiple Sclerosis (RMS)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **Anti-CD52**
- Lemtrada® (alemtuzumab) IV | Lemtrada® (alemtuzumab) may be considered medically necessary for the treatment of relapsing forms of multiple sclerosis when the following conditions are met:
- Lemtrada® (alemtuzumab) is not used concurrently with other MS disease modifying drugs AND |
### Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• The patient has had an inadequate response to two or more disease modifying drugs indicated for the treatment of multiple sclerosis (any two of the following: B-interferon(s), dimethyl fumarate, fingolimod, glatiramer, natalizumab, ocrelizumab, siponimod or teriflunomide)</td>
</tr>
<tr>
<td><strong>β-interferons</strong></td>
<td><strong>Interferon-β 1a or interferon-β 1b may be considered medically necessary as a first-line treat of relapsing forms of multiple sclerosis, when the following conditions are met:</strong>&lt;br&gt;• The patient must have an expanded disability status score (EDSS) of less than 6 AND&lt;br&gt;• β-interferons are not used concurrently with other MS disease modifying drugs</td>
</tr>
<tr>
<td>• Avonex®, Rebif®, Plegridy® (Interferon-β 1a) IM/SC&lt;br&gt;• Betaseron®, Extavia® (Interferon-β 1b) SC</td>
<td></td>
</tr>
<tr>
<td><strong>Copolymers</strong></td>
<td><strong>Glatiramer or Glatopa® (glatiramer) may be considered medically necessary as a first-line agent for the treatment of relapsing forms of multiple sclerosis when the following conditions are met:</strong>&lt;br&gt;• The patient must have an expanded disability status score (EDSS) of less than 6 AND&lt;br&gt;• Glatiramer or Glatopa® (glatiramer) are not used concurrently with other MS disease modifying drugs</td>
</tr>
<tr>
<td>• Glatiramer SC; generic&lt;br&gt;• Glatopa® (glatiramer) SC; generic&lt;br&gt;• Copaxone® (glatiramer) SC; brand</td>
<td><strong>Copaxone® (glatiramer) may be considered medically necessary for the treatment of relapsing forms of multiple sclerosis when the following criteria are met:</strong>&lt;br&gt;• The patient must have an expanded disability status score (EDSS) of less than 6 AND&lt;br&gt;• Copaxone® is not used concurrently with other MS disease modifying drugs AND&lt;br&gt;• There has been documented inadequate response to or intolerance of generic glatiramer or Glatopa® (glatiramer) of the same strength.</td>
</tr>
</tbody>
</table>
# Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **Dihydroorotate Dehydrogenase Inhibitor**  | Aubagio® (teriflunomide) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when the following conditions are met:  
- The patient must have an expanded disability status score (EDSS) of less than 6  
- Aubagio® (teriflunomide) is not used concurrently with other MS disease modifying drugs |
| • Aubagio® (teriflunomide) Oral | |
| **Nrf2 Pathway Activator**  | Tecfidera® (dimethyl fumarate) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease when the following conditions are met:  
- The patient must have an expanded disability status score (EDSS) of less than 6  
- Tecfidera® (dimethyl fumarate) is not used concurrently with other MS disease modifying drugs  
- Dose is ≤ 480 mg per day (240 mg twice a day) |
| • Tecfidera® (dimethyl fumarate) Oral | |
| **Nrf2 Pathway Activator**  | Vumerity™ (diroximel fumarate) may be considered medically necessary in the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease when the following conditions are met:  
- The patient must have an expanded disability status score (EDSS) of less than 6  
- The patient has tried Tecfidera® (dimethyl fumarate) first for 3 months and had an inadequate response or intolerance to Tecfidera®  
- AND |
| • Vumerity™ (diroximel fumarate) Oral | |
# Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| • Vumerity™ (diroximel fumarate) is not used concurrently with other MS disease modifying drugs AND  
  • Dose is ≤ 924 mg per day (462mg twice a day) |                                                                                  |
| **Sphingosine 1-Phosphate Receptor Modulator** | **Gilenya® (fingolimod) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when the following conditions are met:**  
  • The patient must have an expanded disability status score (EDSS) of less than 6 AND  
  • Gilenya® (fingolimod) is not used concurrently with other MS disease modifying drugs AND  
  • Dose is ≤ 0.5 mg per day                                      |
| **α4 Integrin Inhibitors** | **Tysabri® (natalizumab) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when the following conditions are met:**  
  • The patient must have an expanded disability status score (EDSS) of less than 6 AND  
  • Tysabri® (natalizumab) is not used concurrently with other MS disease modifying drugs |
| • Tysabri® (natalizumab) IV |                                                                                  |
| **Note:** Due to safety concerns, access to Tysabri® requires enrollment in the TOUCH registry maintained by the manufacturer (see https://www.touchprogram.com/TPP/). |                                                                                  |
| • Ocrevus® (ocrelizumab) IV | **Ocrevus® (ocrelizumab) is subject to review for site of service administration.**  
  **Ocrevus® (ocrelizumab) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when the following conditions are met:**  
  • The patient must have an expanded disability status score (EDSS) of less than 6 AND |
## Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Ocrevus® (ocrelizumab) is not used concurrently with other MS disease modifying drugs</td>
</tr>
<tr>
<td>Purine Antimetabolite</td>
<td><strong>Mavenclad</strong>® (cladribine) may be considered medically necessary in the treatment of relapsing forms of multiple sclerosis, including relapsing-remitting disease, and active secondary progressive disease when the following conditions are met:</td>
</tr>
<tr>
<td>• Mavenclad® (cladribine) Oral</td>
<td>• The patient must have an expanded disability status score (EDSS) of less than 6</td>
</tr>
<tr>
<td></td>
<td>• Mavenclad® (cladribine) is not used concurrently with other MS disease modifying drugs</td>
</tr>
<tr>
<td></td>
<td>• The patient has had an inadequate response to one or more disease modifying drugs indicated for the treatment of multiple sclerosis (any one of the following: B-interferon(s), dimethyl fumarate, fingolimod, glatiramer, natalizumab, ocrelizumab, siponimod or teriflunomide)</td>
</tr>
<tr>
<td>Sphingosine 1-Phosphate Receptor Modulator</td>
<td><strong>Mayzent® (siponimod) may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease when the following conditions are met:</strong></td>
</tr>
<tr>
<td>• Mayzent® (siponimod) Oral</td>
<td>• The patient must have an expanded disability status score (EDSS) of less than 7</td>
</tr>
<tr>
<td></td>
<td>• Mayzent® (siponimod) is not used concurrently with other MS disease modifying drugs</td>
</tr>
<tr>
<td></td>
<td><strong>AND</strong></td>
</tr>
<tr>
<td></td>
<td>• Mavenclad® (cladribine) is limited to 2 treatment courses</td>
</tr>
</tbody>
</table>
### Relapsing Multiple Sclerosis (RMS)

**Drug**

<table>
<thead>
<tr>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| • Documented test confirms the patient does NOT have CYP2C9*3/*3 genotype  
**AND**  
• Dose is ≤ 2 mg per day |

**Note:** Mayzent® (siponimod) is contraindicated in patients with CYP2C9*3/*3 genotype because of substantially elevated plasma levels of drug.

### Primary Progressive Multiple Sclerosis (PPMS)

**Drug**

<table>
<thead>
<tr>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| CD20-directed cytolytic antibody  
• Ocrevus® (ocrelizumab) IV |

**Ocrevus® (ocrelizumab) is subject to review for site of service administration.**

**Ocrevus® (ocrelizumab) may be considered medically necessary as a first-line agent in the treatment of primary progressive multiple sclerosis.**

### Investigational

**Drug**

<table>
<thead>
<tr>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>As listed</td>
</tr>
</tbody>
</table>

**All other uses of the medications listed in this policy are considered investigational.**

### Length of Approval

**Approval**

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial authorization</td>
</tr>
</tbody>
</table>

**Drugs listed in policy may be approved up to 12 months.**

**Re-authorization criteria**

**Future re-authorization of drugs listed in policy, except Mavenclad® (cladribine), may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the patient continues to show a positive clinical response to therapy.**

**Future re-authorization of Mavenclad® (cladribine) following the administration of two treatment courses is considered investigational.**
**Documentation Requirements**

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

**Coding**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0202</td>
<td>Injection, alemtuzumab, 1 mg</td>
</tr>
<tr>
<td>J1595</td>
<td>Injection, glatiramer acetate, 20 mg (used to report Glatopa® and Copaxone®)</td>
</tr>
<tr>
<td>J1826</td>
<td>Injection, interferon beta-1a, 30 mcg</td>
</tr>
<tr>
<td>J1830</td>
<td>Injection interferon beta-1b, 0.25 mg</td>
</tr>
<tr>
<td>J2323</td>
<td>Injection, natalizumab (Tysabri®), 1mg</td>
</tr>
<tr>
<td>J2350</td>
<td>Injection, ocrelizumab (Ocrevus®), 1 mg</td>
</tr>
<tr>
<td>Q3027</td>
<td>Injection, interferon beta-1a (Avonex®), 1 mcg for intramuscular use</td>
</tr>
</tbody>
</table>

**Related Information**

**Consideration of Age**

The age described in this policy for Site of Service reviews for medical necessity is 13 years of age or older. The age criterion is based on the following: Pediatric patients are not small adults. Pediatric patients differ physiologically, developmentally, cognitively, and emotionally from adult patients, and vary by age groups from infancy to teen. Children often require smaller doses than adults, lower infusion rates, appropriately sized equipment, the right venipuncture site determined by therapy and age, and behavioral management during administration of care. Specialty infusion training is therefore necessary for pediatric IV insertions and therapy. Due to
Evidence Review

It is currently thought that multiple sclerosis (MS) is the result of a combination of factors including immune response, genetics, infection, and environmental issues. MS is characterized by the destruction of the myelin sheath that surrounds axons of the central nervous system (CNS) and eventual axonal damage. This is believed to be an autoimmune attack against myelin and the myelin-producing oligodendrocytes. There is an associated inflammatory response involving B-cells, T-cells, macrophages, antibodies, and complement. The myelin sheath is replaced by sclerotic plaques. The damage to the myelin sheath can delay or halt nerve impulses. Axonal damage leads to loss of nerve impulses.

An estimated 250,000 to 400,000 cases exist in the United States. In 2000, the estimated prevalence was 191/100,000 Caucasians in the United States, with an incidence rate of 7.3/100,000 person-years at risk. Diagnosis usually occurs when patients are between 20 and 50 years of age. The disease is more prevalent: 1) further away from the equator; 2) in Caucasians; and 3) in women. Other risk factors include Epstein-Barr virus exposure, vitamin D deficiency, and smoking.

MS usually follows one of the following four disease courses, but individual presentation can vary quite widely.

1. Relapsing-remitting MS (RRMS): clearly defined acute attacks followed by periods of partial or full recovery. This is the most common course of the disease describing approximately 85% of MS patients.

2. Primary-progressive MS (PPMS): the disease steadily progresses although there may be occasional plateaus or remissions. The patient does not experience acute attacks. Approximately 10% of MS patients have PPMS.

3. Secondary-progressive MS (SPMS): often follows RRMS. Patient experiences acute attacks similar to RRMS, but with progressively less recovery after acute attacks and progressively worsening function between attacks. As with PPMS, there may be occasional plateaus or remissions.
Progressive-relapsing MS (PRMS): initially presents as PPMS with steady disease progression, but later experiences acute attacks with followed by partial recovery. This is only seen in approximately 5% of MS patients.

New Oral Agents for Multiple Sclerosis

Fingolimod is an oral modulator of sphingosine-1-phosphate receptor. After absorption, fingolimod is phosphorylated and fingolimod phosphate acts as agonist on the sphingosine-1-phosphate-1 receptors of the lymphocyte and thymocytes. This interaction results in the internalization of the receptor and thus without signaling the lymphocytes become sequestered within the lymph nodes. It is hypothesized that the resulting decrease in circulating lymphocytes then leads to fewer lymphocytes entering the CNS. Additionally, it is also hypothesized that when fingolimod crosses the BBB the resulting binding down modulates the S1P in neural cells and thus there is a reduction in the astrogliosis that can lead to neurodegeneration. Fingolimod has not been shown to inhibit the effector functions of T and B cells, humoral immunity, or virus-specific cytotoxic T cells.

The efficacy of fingolimod was demonstrated by two Phase III randomized placebo-controlled trials. Fingolimod was found to be significantly better than placebo at the strength of 0.5 mg at reducing the annualized relapse rate, MRI assessment measures, and disease progression measurements. The primary endpoint was reduction in annualized relapse rate over 24 months was 0.18 (0.15-0.22) for 0.5 mg fingolimod and 0.40 (0.34-0.47) for placebo with a p-value <0.001. This represents a 54% relative reduction in relapses as compared to placebo. Disease progression confirmed after 6 months had a probability of 12.5% for 0.5 mg fingolimod versus 19% for placebo.

Fingolimod was compared to IM interferon beta-1a in one clinical trial. Fingolimod proved superior in the primary endpoint of annualized relapse rate. The ARR for fingolimod 0.5 mg was 0.16 (0.12-0.21) versus 0.31 (0.22-0.41) for interferon beta-1a with a p-value <0.001. Additionally, fingolimod was superior in the secondary endpoint of T1 lesion amount. For fingolimod 0.5 mg the mean volume was 22.61±111.59 versus 50.68±198.16 for interferon beta-1a with a p-value of <0.001. However, fingolimod did not prove superior at prevention of disease progression as compared to interferon beta-1a.

Overall, fingolimod has a reasonable safety profile. There is a potential for bradycardia or AV block after administration of the first dose that may require monitoring. Additional concerns are potential increased susceptibility to infections, macular edema, and lymphopenia. The only
deaths that occurred during the clinical trial were in the 1.25mg fingolimod arm and suffered a herpes zoster and herpes simplex encephalopathy infections respectively.

Dimethyl fumarate, (Tecfidera) and diroximel fumarate (Vumerity) are oral agents indicated for the treatment of relapsing forms of MS (RMS). The exact mechanism whereby they exert therapeutic effects is unknown. However, dimethyl fumarate and its metabolite, monomethyl fumarate (MMF), activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, which is involved in cellular response to oxidative stress and implicated in regulation of myelin maintenance in the central nervous system. In vitro, MMF has also been identified as a nicotinic acid receptor agonist.

Well designed and adequate evidence consistently supports the efficacy of dimethyl fumarate at approved dosing for reduction of relapse and improving neuroradiologic outcomes over 2 years in patients with relapsing-remitting MS. Whether the agent is “disease modifying” or delays disease progression is unclear because of the conflicting results for 12-week confirmed disability progression from the two registrational Phase III trials.

After two years therapy in the placebo-controlled Phase III trials, the most common adverse events were mostly mild to moderate flushing and GI events (nausea, vomiting, and abdominal pain). Incidence of these events was highest in the first month of use and then generally decreased thereafter. Discontinuation due to AEs was similar to that for placebo. Excepting for relapse of MS, SAEs were reported very infrequently. Mean lymphocyte counts decreased approximately 30% during the first year of treatment with dimethyl fumarate then levels plateaued. However, incidence of infections and serious infections were similar between patients receiving the drug and those receiving placebo. Elevations in aminotransferase levels were also observed. In the Phase IIb study, transaminase elevations were considered dose related.

Other Agents

Ocrelizumab (Ocrevus) is second-generation humanized (murine) anti-CD20 monoclonal antibody that targets CD20+ B-lymphocytes; hence, it is an immunosuppressant. Rituximab (Rituxan) is another similar chimeric (murine/human) anti-CD20 monoclonal antibody that is used off-label for the treatment of MS. In vitro studies suggest ocrelizumab has greater antibody-dependent cell-mediated cytotoxicity and less complement-dependent cytotoxicity compared to rituximab. Whether this is of clinical relevance remains to be established. Development of rituximab for MS was discontinued by the manufacturer given its imminent patent expiration and development of ocrelizumab ensued.
2018 Update

Annual Review: Literature review from 5/1/17 to 3/12/18. Zinbryta section removed due to withdrawal from market.

2019 Update

Reviewed prescribing information for all drugs listed in policy and no changes to indication and usage were identified. Added medical necessity criteria for Mavenclad® (cladribine) and Mayzent® (siponimod) for the treatment of relapsing forms of multiple sclerosis. Removed a separate Dosage and Quantity Limits table and inserted the applicable quantity limits from table into the medical necessity criteria.

References

12. Mavenclad® (cladribine) prescribing information. EMD Serono, Inc; Rockland, MA. April 2019.


History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/16</td>
<td>New policy, add to Prescription Drug section, approved June 14, 2016. This information was extracted from policy 5.01.550 and addresses medically necessary first and second line treatment options for multiple sclerosis.</td>
</tr>
<tr>
<td>11/01/16</td>
<td>Interim review, changes approved October 11, 2016. Inclusion of a new agent daclizumab (Zinbryta®), its criteria, and background. Also, included administration route for each of the agents listed in the “dosing” section.</td>
</tr>
<tr>
<td>01/01/17</td>
<td>Interim review, changes approved December 13, 2016. Types of the first-line drugs to be tried before Zinbryta can be approved have been added for clarity.</td>
</tr>
<tr>
<td>01/27/17</td>
<td>Coding update. HCPCS code J0202 added to policy; it was inadvertently left off when the policy was extracted from 5.01.550 on 06/14/16.</td>
</tr>
<tr>
<td>05/01/17</td>
<td>Annual review, changes approved April 11, 2017. Criteria for newly approved agent ocrelizumab have been added.</td>
</tr>
<tr>
<td>01/01/18</td>
<td>Coding update; added HCPCS code J2350 (new code effective 1/1/18)</td>
</tr>
<tr>
<td>11/01/18</td>
<td>Interim Review, approved October 9, 2018. Added criteria for ocrelizumab as first line therapy for RRMS and for Copaxone 40mg stepped through generic equivalent.</td>
</tr>
<tr>
<td>08/01/19</td>
<td>Annual Review, approved July 9, 2019. Added criteria for Mavenclad (cladribine) and Mayzent (siponimod) for the treatment of relapsing forms of multiple sclerosis. Removed HCPCS codes J3490 and J3590.</td>
</tr>
<tr>
<td>12/01/19</td>
<td>Interim Review, approved November 12, 2019, effective March 5, 2020. Added site of service review for Ocrevus (ocrelizumab) (for dates of service on or after March 5, 2020). Effective December 1, 2019, updated coverage criteria for Mayzent (siponimod).</td>
</tr>
<tr>
<td>02/01/20</td>
<td>Interim Review, approved January 14, 2020. Added coverage criteria for Vumerity (diroximel fumarate) and updated coverage criteria for Tecfidera (dimethyl fumarate).</td>
</tr>
</tbody>
</table>
**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2020 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-537-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-5357 (TTY)
Email AppealsDepartmentInquiries@Premera.com

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You must take action by certain deadlines to keep your health coverage or help with costs. You may need to take action by certain deadlines to keep your health coverage or help with costs.

Call 800-722-1471 (TTY: 800-842-5357)

Oromoo (Cushite):

Français (French):

Kreyòl ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan ladan. Avi sila a kapab genyen enfòmasyon enfòmasyon konpyans ayisyen w lan oswa konpyans kouvèti asirians lan atravé Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kék aksyon ayon sèten dat limit pou ka konbè kouvèti asirians sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewa enfòmasyon sa a ak asistans nan lang ou paale a, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):
Tsaab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb koj daim ntawv thov kev pab los yoy koj kev kev pab cuam los ntawv Premera Blue Cross. Tej zaum muaj cov hvub tseem ceeb cuam sau rau hauv daim ntawv no. Tej zaum koj kuy juyu tai uu qee yam uu peb kom koj uu tis pub dhaiu cov caij nyoy uas teev tseg rau hauv daim ntawv no mas koj thaj juyu tai baas kev pab cuam kho hauv daim yoy kev pab them tej niq kho mob ntaawd. Koj muaj cai kom lawv muab cov ntsiab lus no uas tuaw muab sau uak juy kom huu pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):
Daytoy a Pakdaara ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaara mabalini nga adda ket naglaon iti napateg nga impormasion maipanggepp iti aplikasyonu woy ngoy coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelsa iti daytoy a pakdaara. Mabalini nga adda rumbeng nga aramidenyo nga adda rumbeng dagiti partikular a naitunding nga adda tawtaw tapow mapagtalaindoy ti coverage ti salun-aayo woy tungul kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tungul iti bukodyo a pagasago nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Polski (Polish):
Este aviso contiene información importante. Este aviso podrá contener informaciones importantes a respecto de su aplicación o cobertura por medio del Premera Blue Cross. Poderá existir datos importantes neste aviso. Talvez se necesario que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir dados importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Român (Romanian):

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховым покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):
Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้มีข้อมูลสำคัญเกี่ยวกับการขอสาคัญหรือการรับประกันสิทธิ์ของคุณผู้มีสิทธิ์ของ Premera Blue Cross และถ้าคุณพบปัญหาในเอกสารที่นี้ คุณควรจดจำในสาเหตุและผลกระทบการดูแลสุขภาพที่เกี่ยวข้องเพื่อให้คุณได้รับข้อมูลที่ถูกต้อง การโทรติดต่อที่ 800-722-1471 (TTY: 800-842-5357).

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страховального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретній ситуації для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

日本語 (Japanese):
この通報には重要な情報が含まれています。この通報には、Premera Blue Crossの申請または補償範囲に関する重要な情報が含まれている場合があります。この通報には記載されている可能性がある重要な日付をご確認ください。健康保険や補償サポートを維持するには、特定の期間を過ぎて動けるのがもとになる場合があります。ご用意の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357) にお電話ください。