Pharmacotherapy of Multiple Sclerosis

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

Note: Quantity limits for individual agents can be found in the Dosage and Quantity Limits section below.
### Drug Investigational

**Rituximab (Rituxan®)**  
The use of rituximab in the setting of multiple sclerosis is considered investigational.

### Relapsing Multiple Sclerosis (RMS)

#### Drug Medical Necessity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-CD52</strong></td>
<td><strong>Alemtuzumab may be considered medically necessary for the treatment of relapsing sclerosis when:</strong></td>
</tr>
<tr>
<td>- Alemtuzumab (Lemtrada®)</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), Glatiramer, Copaxone, teriflunomide, dimethyl fumarate, fingolimod, or natalizumab).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>B-Interferons</strong></th>
<th><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 BOTH of the following conditions are met:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Interferon-β 1a (Avonex®, Rebif®, Plegridy®)</td>
<td>• The patient must have an Expended Disability Status Score (EDSS) of less than 6. AND • β-interferons are not to be used concurrently with other MS disease modifying drugs.</td>
</tr>
<tr>
<td>- Interferon-β 1b (Betaseron®, Extavia®)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Copolymers</strong></th>
<th><strong>Glatiramer 20 mg may be considered medically necessary as a first-line agent for the treatment of relapsing forms of multiple sclerosis when BOTH of the following conditions are met:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Glatiramer 20 mg (generic)</td>
<td>• The patient must have an Expended Disability Status Score (EDSS) of less than 6. AND • Glatiramer is not to be used concurrently with other MS disease modifying drugs.</td>
</tr>
<tr>
<td>- Copaxone® 40 mg (not available in generic)</td>
<td></td>
</tr>
</tbody>
</table>

**Copaxone® 40 mg (available as brand only) may be considered medically necessary as a first-line agent for the treatment of relapsing forms of multiple sclerosis when ALL of the following criteria are met:**
• The patient must have an Expended Disability Status Score...
## Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(EDSS) of less than 6. AND</td>
</tr>
<tr>
<td></td>
<td>• Copaxone® is not to be used concurrently with other MS disease modifying drugs.</td>
</tr>
<tr>
<td></td>
<td>AND</td>
</tr>
<tr>
<td></td>
<td>• There has been documented inadequate response to or intolerance of generic glatiramer.</td>
</tr>
</tbody>
</table>

### Dihydroorotate Dehydrogenase Inhibitor

- **Teriflunomide (Aubagio®)**

  Teriflunomide may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when BOTH of the following conditions are met:
  - The patient must have an Expended Disability Status Score (EDSS) of less than 6.
  AND
  - Teriflunomide is not to be used concurrently with other Multiple Sclerosis disease modifying drugs.

### Nrf2 Pathway Activator

- **Dimethyl Fumarate (Tecfidera®)**

  Dimethyl fumarate may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when BOTH of the following conditions are met:
  - The patient must have an Expended Disability Status Score (EDSS) of less than 6.
  AND
  - Dimethyl fumarate is not to be used concurrently with other Multiple Sclerosis disease modifying drugs.

### Sphingosine 1-Phosphate Receptor Modulator

- **Fingolimod (Gilenya®)**

  Fingolimod may be considered medically necessary as a first-line agent in the treatment of relapsing forms of multiple sclerosis when BOTH of the following conditions are met:
  - The patient must have an Expended Disability Status Score (EDSS) of less than 6.
  AND
  - Fingolimod is not to be used concurrently with other Multiple Sclerosis disease modifying drugs.

### α4 Integrin Inhibitors

- **Natalizumab (Tysabri®)**

  Natalizumab may be considered medically necessary as a
### Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **Note:** Due to safety concerns, access to Tysabri® requires enrollment in the TOUCH registry maintained by the manufacturer. (See [https://www.touchprogram.com/TTP/](https://www.touchprogram.com/TTP/)) | first-line agent in the treatment of relapsing forms of multiple sclerosis when BOTH of the following conditions are met:  
- The patient must have an Expended Disability Status Score (EDSS) of less than 6.  
AND  
- Natalizumab is not to be used concurrently with other Multiple Sclerosis disease modifying drugs. |

#### IL-2 receptor Inhibitor
- **Daclizumab (Zinbryta®)**

Daclizumab may be considered medically necessary as a second-line agent in the treatment of relapsing forms of multiple sclerosis when:
- Patient has had an inadequate response to two or more first-line drugs indicated for the treatment of multiple sclerosis (any two of the following: B-interferon(s), Glatiramer, Copaxone, teriflunomide, dimethyl fumarate, fingolimod, or natalizumab).

#### CD20-directed cytolytic antibody
- **Ocrelizumab (Ocrevus®)**

Ocrelizumab may be considered medically necessary as a second-line agent in the treatment of relapsing forms of multiple sclerosis when:
- Patient has had an inadequate response to two or more first-line drugs indicated for the treatment of multiple sclerosis (any two of the following: B-interferon(s), Glatiramer, Copaxone, teriflunomide, dimethyl fumarate, fingolimod, or natalizumab).

### Primary Progressive Multiple Sclerosis (PPMS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **CD20-directed cytolytic antibody**  
- **Ocrelizumab (Ocrevus®)** | Ocrelizumab may be considered medically necessary as a first-line agent in the treatment of primary progressive multiple sclerosis. |

### Dosage and Quantity Limits

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>alemtuzumab (Lemtrada®)</td>
<td></td>
</tr>
</tbody>
</table>
- The first course is 12 mg / day on 5 consecutive days.  
- The second course is 12 mg / day on 3 consecutive days |
# Dosage and Quantity Limits

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>interferon-β 1a (Avonex®)</strong></td>
<td>• Dosing is 30 mcg once a week. This can be titrated starting with 7.5mcg for the first week, then increase by 7.5mcg each week for the next 3 weeks until recommended dose of 30mcg.</td>
</tr>
<tr>
<td><strong>interferon-β 1a (Rebif®)</strong></td>
<td>• Dosing is 22 mcg or 44 mcg three times per week. This can be titrated.</td>
</tr>
<tr>
<td><strong>interferon-β 1a (Plegridy®)</strong></td>
<td>• Dosing is 125 mcg every 14 days (titrate starting with 63 mcg on day 1; 94 mcg on day 15; and, 125 mcg (full dose) on day 29.</td>
</tr>
<tr>
<td><strong>interferon-β 1b (Betaseron®)</strong></td>
<td>• Dosing is 0.25 mg every other day (start at 0.065 mg (0.25mL) every other day, and increase over a six-week period to 0.25mg (1mL) every other day).</td>
</tr>
<tr>
<td><strong>interferon-β 1b (Extavia®)</strong></td>
<td>• Dosing 0.25 mg every other day (start at 0.065mg (0.25mL) every other day, and increase over a six-week period to 0.25mg (1mL) every other day).</td>
</tr>
<tr>
<td><strong>glatiramer (Glatopa®) 20mg (generic Copaxone)</strong></td>
<td>• Dosing is 20mg / mL per day (only available in this strength).</td>
</tr>
</tbody>
</table>
| **Copaxone®** | • Dosing is 20 mg / mL per day (if using 20 mg dose).  
• Dosing is 40 mg / mL three times per week (if using 40mg dose, not available in generic). |
| **teriflunomide (Aubagio®)** | • Dosing is 7mg or 14mg once daily. |
| **dimethyl fumarate (Tecfidera®)** | • Initial dosing is 120mg twice a day for 7 days.  
• Maintenance dosing after 7 days is 240 mg twice a day.  
• Quantity Limit  
  o Quantity is limited to 14 of the 120 mg capsules, to achieve a dosage of one 120mg capsule twice daily for the first week.  
  o Doses of 120 mg 2 or 3 times daily may be approved up to 90 days on a case by case basis for patients having difficulty tolerating the full dose.  
  o After the first week of therapy, 240mg capsules should be dispensed except as noted above, with quantity limited to 60 capsules per 30 day supply, to achieve a dosage of 240 mg twice daily.  
  o Doses in excess of 480 mg per day are considered not |
Dosage and Quantity Limits

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>fingolimod (Gilenya®)</td>
<td>• Dosing is 0.5mg once daily.</td>
</tr>
<tr>
<td></td>
<td>• Quantity Limit</td>
</tr>
<tr>
<td></td>
<td>o Quantity is limited to achieve a dosage of 0.5 mg. per day.</td>
</tr>
<tr>
<td>natalizumab (Tysabri®)</td>
<td>• Dosing is 300mg every 4 weeks</td>
</tr>
<tr>
<td>daclizumab (Zinbryta®)</td>
<td>• Dosing is 150mg Sub-Q once monthly</td>
</tr>
<tr>
<td>ocrelizumab (Ocrevus®)</td>
<td>• Start dose: 300mg intravenous infusion, followed two weeks later by a second 300mg intravenous infusion</td>
</tr>
<tr>
<td></td>
<td>• Subsequent doses: 600mg intravenous infusion every 6 months</td>
</tr>
</tbody>
</table>

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>J0202</td>
<td>Injection, alemtuzumab, 1 mg</td>
</tr>
<tr>
<td>J1595</td>
<td>Injection, glatiramer acetate, 20 mg</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>J3490</td>
<td>Unclassified drugs</td>
</tr>
<tr>
<td>J3590</td>
<td>Unclassified biologics</td>
</tr>
<tr>
<td>Q3027</td>
<td>Injection, interferon beta-1a (Avonex®), 1 mcg for intramuscular use</td>
</tr>
</tbody>
</table>

Related Information

N/A
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) is a newly approved oral agent that is indicated for the treatment of relapsing forms of MS (RMS). The exact mechanism whereby it exerts its 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

Daclizumab is a humanized monoclonal antibody that binds to the alpha subunit of the interleukin-2 receptor (IL-2Rα, CD25). The precise mechanism by which daclizumab exerts therapeutic effects in multiple sclerosis is unknown but is presumed to involve modulation of IL-2 mediated activation of lymphocytes through binding to CD25, a subunit of the high-affinity IL-2 receptor.

The efficacy of ZINBRYTA was demonstrated in two randomized, double-blind, controlled studies (Study 1 and Study 2). Both studies evaluated 150 mg of subcutaneous ZINBRYTA taken once every four weeks in patients with relapsing multiple sclerosis (RMS). Study 1: Active-Controlled Trial in RMS Study 1 compared ZINBRYTA to 30 mcg weekly intramuscular doses of AVONEX in 1841 patients. The study included RMS patients who had either: 1) at least 2 relapses during the prior 3 years and at least one relapse in the year prior to randomization; or 2) one or more clinical relapses and one or more new T1 gadolinium (Gd)-enhancing or T2 hyperintense MRI lesions within the prior 2 years with at least one of these events in the prior 12 months. Patients with progressive forms of multiple sclerosis or an Expanded Disability Status Scale (EDSS) score greater than 5 were excluded. Treatment continued for up to 144 weeks until the
The last enrolled patient completed 96 weeks of treatment. Clinical assessments were to occur every 12 weeks and after relapse events. MRI scans were performed at Week 24 and Week 96. The primary outcome measure of Study 1 was the annualized relapse rate (ARR). Additional outcome measures included the proportion of patients relapsed, the proportion of patients who experienced confirmed disability progression, and the number of new or newly enlarging T2 hyperintense lesions. Confirmed disability progression was defined as at least a 1 point increase from baseline EDSS (1.5 point increase for patients with baseline EDSS of 0) sustained for 12 weeks.

In Study 1, randomization assigned 919 patients to ZINBRYTA and 922 patients to AVONEX; 71% of ZINBRYTA- and 70% of AVONEX-treated patients completed at least 96 weeks of treatment with the assigned drug. At baseline, the mean age of patients was 36 years, the mean disease duration since diagnosis was 4.2 years, the mean EDSS score was 2.5, and the mean number of relapses in the prior year was 1.6. At baseline, 68% of patients were female, 46% of patients had MRI scans with T1 Gd-enhancing lesions and 41% of patients had previously taken one or more non-steroid treatments for MS. ZINBRYTA had a statistically significant effect on the annualized relapse rate and on the number of new or newly enlarging T2 hyperintense lesions. There was no statistically significant effect on 12-week confirmed disability progression.

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.

References


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>
</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). ©2017 Premera All Rights Reserved.

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Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

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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:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at:

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Arabic (Amharic):
لَمْ يُهْدَى الْعِلْمُ إِلَّا بِإِذْنٍ هُوَ مَيْلٌ لِلْإِلَهِ وَهُوَ الْأَحْكَامُ
Premera Blue Cross 9-1102, سِيْتِيْتُ، واشنطن، وا. 98111
تَلَّفُ بِكِنْفَة 855-332-4535، فَخْر 425-918-5592، تَّيْت 800-842-5357
إِلْعَابُ إِلَى اثْنَانِيْنْ مُؤُنَّثَينَانِيْنْ بِالْأَكْرَمُ أَوْ سِيْتِيْتَ
فِي ضَغْطِ الْعِلْمِ إِلَّا بِإِذْنٍ هُوَ مَيْلٌ لِلْإِلَهِ وَهُوَ الْأَحْكَامُ
Premera Blue Cross 9-1102، سِيْتِيْتُ، واشنطن، وا. 98111
تَلَّفُ بِكِنْفَة 855-332-4535، فَخْر 425-918-5592، تَّيْت 800-842-5357

Oromo (Cushite):
Beekisinsin ku oodeffannoo barbaachisaa qaba. Beekisist kun sagantaa
yoona karaa Premera Blue Cross tiin tajajila keessaa ilaachisee
odeffannoo barbaachisaa qabaachuu danda’a. Guyyawaaan muurseessa
ta’an beekisisa kan’a keessatti ilaajaa. Tari kaffaitlidaan deeggarrummu
yoona tajajila fayyaa keessanifi gyyaa dhumaa iratti wanti raawwataan
jiraachuu danda’a. Kaffaitti irraa bilisa haalaa ta’een afaan keessanin
odeffannoo aragachuu fi deeggarsa aragachuu minge ni qabaattu.
Lakkoofsa biibliaa 800-722-1471 (TTY: 800-842-5357) ti biibliaa.

Français (French):
Cet avis a d’importantes informations. Cet avis peut avoir d’importantes
informations sur votre demande ou la couverture par l’intermédiaire de
Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous
devrez peut-être prendre des mesures par certains délais pour maintenir
votre couverture de santé ou d’aide avec les coûts. Vous avez le droit
d’obtenir cette information et de l’aide dans votre langue à aucun coût.
Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):
Aavi sila a gen Enfomasyon Empòtan ladan. Aavi sila a kapab genyen
enfomasyon empòtan konsènan aplikasyon w lan oswa konven kouvèti
asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan
aavi sila a. Ou ka gen pou pran kék aksyon avan sèten dat limit pou ka
kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo.
Se dwa w pou resewa enfomasyon sa a ak asisants nan long ou pale a,
san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):
Diese Benachrichtigung enthält wichtige Informationen. Diese
Benachrichtigung enthält unter Umständen wichtige Informationen
bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera
Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser
Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln
müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten
zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen

Hmoob (Hmong):
Tsbab ntaaw tsjaj xo no muaj cov ntsiab lus tseem ceeb. Tej zaum
ntsaw tsjaj xo no muaj cov ntsiab lus tseem ceeb boj koj daim ntaaw
thov kov pb lus yoj koj hqov kov pb cuam lus ntham Premera Blue
Cross. Tej zaum muaj cov hnub tseem ceeb usas rau hauv daim ntham
no. Tej zaum koj kuy yaw uau u qey yam us peb koj us taas pub
hauv cov caj nyong uas teev taaw hauv daim nthaw no mas koj
thaj yaw taas bas kov pb cuam kho hauv kov pb them tej nqi kho mob
ntaww. Koj muaj cai kom lawv muab cov ntsiab lus no uas tsaw us

Iloko (Ilocano):
Daytoy a Pakdaak ket naglaon iti Napateg nga Impormasion. Daytoy a
pakdaak mabalini nga adda ket naglaon iti napateg nga impormasion
maipanggpe iti aplikasyon wonyen coverage babaen iti Premera Blue
Cross. Daytoy ket mabalini dagiti importante a pelta iti daytoy a pakdaak.
Mabalini nga adda rumbeng nga aramideny nga adda sabbay dagiti
partikular a naituding nga adaaw tapno mapagtalaediy a coverage ti
salu-ayyo woyen tulong kadaagit gastos. Adda karbenganyo a mangala iti
daytoy nga impormasion ken tulong iti bukodyo a pagasasao nga awan ti

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può
contenere informazioni importanti sulla tua domanda o copertura attraverso Premera
Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe
essere necessario un tuo intervento entro una scadenza determinata
per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto
di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.
Chiamate 800-722-1471 (TTY: 800-842-5357).

中文 (Chinese):
本通知有重要的資訊。本通知可能有關於您透過Premera Blue Cross提交的
申請或保險的重要訊息。本通知可能有重要的日期。您可能需要在截止日期
之前採取行動。以保留您的健康保險或費用補貼。您有權利免費以您的母
語得到本資訊和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357).

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This notification may contain important information. If you have any questions, please call 800-722-1471 (TTY: 800-842-5357) at any time.

Premera Blue Cross