# Multiple Sclerosis Agents Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

For Medicaid, the preferred products are the MN Medicaid Preferred Drug List (PDL) preferred drugs: Avonex, Avonex pen, Betaseron kit, Betaseron vial, Copaxone 20 mg/mL, Dimethyl fumarate, fingolimod, Rebif, Rebif Rebidose pen, and teriflunomide tablet.

The BCBS MN Step Therapy Supplement also applies for Medicaid.

## POLICY REVIEW CYCLE

| Effective Date | Date of Origin |
|---|---|
| 06-01-2024 | 06-01-2018 |

## FDA APPROVED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Aubagio®<br><br>(teriflunomide)*<br><br>Tablet | Treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | *generic equivalent available | 1 |
| Avonex®<br><br>(interferon β-1a)<br><br>Injection for intramuscular use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 2 |
| Bafiertam®<br><br>(monomethyl fumarate)<br><br>Delayed-release capsule | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 3 |
| Betaseron®<br><br>(interferon β-1b)<br><br>Injection for subcutaneous use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 4 |
| Copaxone®<br><br>(glatiramer acetate)* | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | *generic equivalent available | 5 |

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Injection for subcutaneous use | | | |
| Extavia®<br><br>(interferon β-1b)<br><br>Injection for subcutaneous use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 6 |
| Gilenya®<br><br>(fingolimod)*<br><br>Capsule | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older | *generic equivalent available | 7 |
| Glatopa®<br><br>(glatiramer acetate)<br><br>Injection for subcutaneous use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 8 |
| Kesimpta®<br><br>(ofatumumab)<br><br>Injection for subcutaneous use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 9 |
| Mavenclad®<br><br>(cladribine)<br><br>Tablet | Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease in adults<br><br>Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug indicated for the treatment of MS<br><br>Limitation of Use:<br>Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile | | 10 |
| Mayzent®<br><br>(siponimod)<br><br>Tablet | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 11 |
| Plegridy®<br><br>(peginterferon β-1a)<br><br>Injection for subcutaneous | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 12 |

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| use or intramuscular use | | | |
| Ponvory®<br><br>(ponesimod)<br><br>Tablet | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 27 |
| Rebif®<br><br>(interferon β-1b)<br><br>Injection for subcutaneous use | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 13 |
| Tascenso®<br><br>(fingolimod)<br><br>Oral disintegrating tablet | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 10 years of age and older | | 29 |
| Tecfidera®<br><br>(dimethyl fumarate)*<br><br>Capsule | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | *generic equivalent available | 14 |
| Vumerity®<br><br>(diroximel fumarate)<br><br>Delayed-release capsule | Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults | | 15 |

*See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm*

## CLINICAL RATIONALE

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| Multiple sclerosis | Multiple sclerosis (MS) is a disorder of the central nervous system (CNS) characterized by demyelization, inflammation, and degenerative changes. Most people with MS experience relapses and remissions of neurological symptoms, particularly early in the disease, and clinical events are usually associated with areas of CNS inflammation. Gradual worsening or progression, with or without subsequent acute attacks of inflammation or radiological activity, may take place early, but usually becomes more prominent over time. While traditionally viewed as a disease solely of CNS white matter, more advanced imaging techniques have demonstrated significant early and ongoing CNS gray matter damage as well.(16)<br><br>Those diagnosed with MS may have many fluctuating and disabling symptoms (including, but not limited to, fatigue, pain, bladder and bowel issues, sexual dysfunction, movement and coordination problems, visual disturbances, and cognition and emotional changes.(30) There are currently four major types of MS: clinically |

<table>
<tr><td></td><td>isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).(23)</td></tr>
<tr><td>Relapsing remitting multiple sclerosis (RRMS)</td><td>RRMS is characterized by clearly defined attacks (relapses) of new or increasing neurologic symptoms. These relapses are followed by periods of partial or complete recovery. There is no or minimal disease progression during the periods between disease relapses, though individual relapses may result in severe residual disability. The course of MS varies, however, about 85-90% of individuals with MS demonstrate a relapsing pattern at onset, which transitions over time in the majority of untreated patients to a pattern of progressive worsening with few or no relapses or MRI activity.(23)</td></tr>
<tr><td>Secondary progressive multiple sclerosis (SPMS)</td><td>SPMS begins as RRMS, but over time the disease enters a stage of steady deterioration in function, unrelated to acute attacks. Most people with RRMS will transition to SPMS. In SPMS there is no progressive worsening of symptoms over time with no definite periods of remission.(23)</td></tr>
<tr><td>2017 McDonald Criteria for the diagnosis of Multiple Sclerosis:</td><td>Diagnostic criteria for multiple sclerosis combining clinical, imaging, and laboratory evidence have evolved over time. The increasing incorporation of paraclinical assessments, especially imaging, to supplement clinical findings has allowed earlier, more sensitive, and more specific diagnosis.(21,22)<br><br>The diagnosis of MS requires elimination of more likely diagnoses and demonstration of dissemination of lesions in the CNS in space and time.(21)<br><br>Misdiagnosis of multiple sclerosis remains an issue in clinical practice, and several factors that potentially increase this risk have been identified. Multiple sclerosis has heterogeneous clinical and imaging manifestations, which differ between patients over time. There is no single pathognomonic clinical feature or diagnostic test; diagnosis of multiple sclerosis relies on the integration of clinical, imaging, and laboratory findings. MRI abnormalities associated with other diseases and non-specific MRI findings, which are common in the general population, can be mistaken for multiple sclerosis. The increasingly strong focus on timely diagnosis to alleviate uncertainty for patients and allow initiation of disease-modifying therapies might also increase the risk of misdiagnosis.(21)<br><br>With increasing availability and use of MRI, incidental T2 hyperintensities on brain imaging are common, the subset of individuals with MRI findings that are strongly suggestive of multiple sclerosis lesions but with no neurological manifestations or other clear-cut explanation are said to have radiologically isolated syndrome. There is no consensus on whether patients with radiologically isolated syndrome will develop MS. Some practitioners argue that these patients have a high likelihood of developing MS while others argue that up to two-thirds of these patients will not receive a diagnosis of MS in 5 years. A consensus panel decided to require clinical manifestations to make the diagnosis of MS (2017 McDonald Criteria for the diagnosis of Multiple Sclerosis).(21)<br><br>The 2017 McDonald criteria to diagnose MS is shown in the chart below.(21,22)<br><br>
<table>
<tr><th>Clinical Presentation</th><th>Additional Data needed to make MS diagnosis</th></tr>
<tr><td colspan="2">In a person with a typical attack/CIS at onset</td></tr>
<tr><td>Greater than or equal to 2 attacks and objective clinical evidence of greater than or equal to 2 lesions<br>OR<br>Greater than or equal to 2 attacks and objective clinical evidence of 1 lesion with historical evidence of prior</td><td>None. Dissemination in space* and dissemination in time** have been met</td></tr>
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| attack involving lesion in different location | |
| Greater than or equal to 2 attacks and objective clinical evidence of 1 lesion | **ONE** of these criteria:<br>Additional clinical attack implicating different CNS site<br>OR<br>Greater than or equal to 1 symptomatic or asymptomatic MS-typical T2 lesions in greater than or equal to 2 areas of CNS: periventricular, juxtacortical/cortical, infratentorial, or spinal cord |
| 1 attack and objective clinical evidence of greater than or equal to 2 lesions | **ONE** of these criteria:<br>Additional clinical attack<br>OR<br>Simultaneous presence of both enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions<br>OR<br>New T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)<br>OR<br>CSF specific (i.e., not in serum) oligoclonal bands |
| 1 attack and objective clinical evidence of 1 lesion | **ONE** of these criteria:<br>Additional attack implicating different CNS site<br>OR<br>Greater than or equal to 1 MS-Typical symptomatic or asymptomatic T2 lesions in greater than or equal to 2 areas of CNS: periventricular, juxtacortical/cortical, infratentorial, or spinal cord<br><br>**AND**<br>**ONE** of these criteria:<br>Additional clinical attack<br>OR<br>Simultaneous presence of both enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions<br>OR<br>New T2 enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)<br>OR<br>CSF-specific (i.e., not in serum) oligoclonal bands |

*Dissemination in space is defined as one or more T2-hyperintense lesions that are characteristic of multiple sclerosis in 2 or more of four areas of the CNS (periventricular, cortical or juxtacortical, and infratentorial brain regions, and the spinal cord) demonstrated by an additional clinical attack implicating a different CNS site or by MRI.(21)

**Dissemination in time is defined as simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up

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| | MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI. The presence of CSF-specific oligoclonal bands does not demonstrate dissemination in time per se but can substitute for the requirement for demonstration of this measure.(21) |
| Treatment of MS | Both the Multiple Sclerosis Coalition and the American Academy of Neurology recommend initiating treatment with a DMA FDA approved for the patient's phenotype as soon as possible following the diagnosis of multiple sclerosis. There are several DMAs with at least 10 mechanisms of action available to people with MS. The factors affecting choice of therapy at any point in the disease course are complex and most appropriately analyzed and addressed through a shared decision-making process between the individual and the treating clinician.(16,19)<br><br>The Multiple Sclerosis Coalition recommends that clinicians should consider prescribing a high efficacy medication such as alemtuzumab, cladribine, fingolimod, natalizumab or ocrelizumab for newly diagnosed individuals with highly active MS. Clinicians should also consider prescribing a high efficacy medication for individuals who have breakthrough activity on another DMA regardless of the number of previously used agents.(16) The American Academy of Neurology has recommended alemtuzumab, fingolimod, and natalizumab as options for patients with MS with highly active MS. There lacks a consensus for what constitutes as highly active MS, however.(19) The National Institute for Health and Care Excellence (NICE) defines rapidly evolving severe RRMS as two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load compared with a previous MRI.(31)<br><br>Lack of response to DMAs is hard to define, as most patients with MS are not free of all disease activity. Relapses or new MRI detected lesions may develop after initiation of a DMA and before the treatment becomes effective for patients. When determining efficacy, sufficient time for the DMA therapy to take full effect and patient adherence are important considerations. Evidence of one or more relapses, 2 or more unequivocally new MRI-detected lesions, or increased disability on examination while being treated with a DMA for a 1 year period suggests a sub-optimal response, an alternative regimen (e.g., different mechanism of action) should be considered to optimize therapeutic benefit.(18) A National MS Society consensus statement recommends changing from one disease modifying therapy to another only for medically appropriate reasons (e.g., lack of efficacy, adverse effects, or if better treatments options become available).(16)<br><br>Existing MS therapies are partly effective in halting ongoing inflammatory tissue damage and clinical progression. MS pathogenesis is complex and probably heterogeneous among patient, suggesting that combination therapy strategies that target a range of disease mechanisms might be more effective than medications used as monotherapy. Although preliminary studies have provided favorable results, however, several subsequent large, randomized, controlled trials have had negative of conflicting results. There also may be more adverse reactions associated with combination therapies due to the additive effect.(24)<br><br>In 2020 a Canadian MS working group published recommendations on optimal therapy in relapsing forms of MS. This group notes that there are few studies that have directly compared injectable and oral DMTs. A recent network meta-analysis suggested that pegylated interferon-β-1a and dimethyl fumarate have superior efficacy to other base therapies, there are insufficient data to demonstrate that one base injectable or oral DMT is superior to another. As a result, the choice of initial treatment will need to be individualized according to disease activity, severity, and comorbidities.(25)<br><br>In addition to base therapies, the working group considers 5 DMTs to be of higher efficacy which although can be used as initial therapy, they are generally reserved for patients with a poor response or tolerability with a base therapy. Patients presenting with high disease activity or aggressive/rapidly evolving MS at onset could be considered to initiate therapy with one of these more effective therapies, but the most common treatment initiation is to start on a base therapy with the view of switching within 6-12 months. The 5 agents considered to be of higher efficacy are:(25) |

- Oral agents
  - Fingolimod
  - Cladribine
- Monoclonal antibodies
  - Natalizumab
  - Ocrelizumab
  - Alemtuzumab

The MS working group discussed the criteria for switching therapies in RRMS and recommends a change in DMT is indicated for patients who meet any of the Major criteria below:(25)

| | **Minor** | **Major** |
|---|---|---|
| Relapse rate | • One relapse in first 2 years of treatment | • Greater than or equal to 2 relapses in first year of treatment |
| Severity | • Mild<br>• No functional impairment (school, work, daily activities, etc.)<br>• No motor/cerebellar/brain stem/sphincter involvement | • Moderate to severe<br>• Functional impairment<br>• Motor/cerebellar/brain stem/sphincter involvement |
| Recovery | • Full recovery at 6 months<br>• No functional impairment<br>• EDSS change from baseline less than or equal to 1 point at 6 months unless baseline EDSS greater than 5.5 | • Incomplete recovery<br>• Functional impairment<br>• If EDSS at baseline was 0 then greater than a 1.5 point change from baseline<br>• If EDSS greater than 0 but less than or equal to 5.5 at baseline then greater than 1 point change at 6 months<br>• If EDSS greater than 5.5 any change would |

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| | | be a major concern |
| MRI | • One new lesion | • Greater than or equal to 3 new lesions during treatment excluding spinal cord lesions<br>• Greater than 1 spinal cord lesion |

The workgroup does note that on-treatment relapses should only be performed once the drug has achieved a full clinical effect (typically 2-6 months after drug initiation). Relapses that occur before the maximal efficacy of the drug has been reached should be given less weight, but major criteria should take precedence regardless of timing.(25)

For patients with SPMS the workgroup states that is generally advised to continue with the current DMT after onset of SPMS since many patients will have ongoing inflammatory disease and subclinical disease activity may worsen if treatment is withdrawn. A change in treatment may be warranted in patients with active SPMS who continue to have relapses or new MRI lesions, with the caveat that there is insufficient evidence to identify criteria for a suboptimal response in patients with SPMS.(25)

For patients with primary progressive MS clinicians should offer ocrelizumab to patients with active disease provided the benefits outweigh the risks. Caution is recommended when considering treatment for PPMS subgroups that are less likely to benefit from treatment, such as older patients, those with long-standing stable disease, and/or significant neurological deficits, since the limited benefits may not justify the risk associated with treatment. Rituximab may be considered as an alternative therapy for PPMS in regions that permit off-label use in MS due to cost or other considerations.(25)

The Institute for Clinical and Economic Review (ICER) evaluated a new IV treatment, ublituximab against current FDA and accepted use DMT for adults with RRMS. Only in the case of ublituximab vs placebo/no DMT is ublituximab superior rated. The ratings are noted below.(17)

**Adults with RRMS**

| Treatment | Comparator | Evidence Rating |
|---|---|---|
| Ublituximab | Natalizumab | I: Insufficient |
| | Ofatumumab | I: Insufficient |
| | Ocrelizumab | I: Insufficient |
| | Rituximab | I: Insufficient |
| | Fumarate class (dimethyl, diroximel, monomethyl) | C++: comparable or better |
| | Fingolimod | C++: comparable or better |
| | Ozanimod | C++: comparable or better |
| | Ponesimod | C++: comparable or better |

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|---|---|---|
| | Siponimod | I: Insufficient |
| | Teriflunomide | B: Incremental |
| | Placebo/no DMT | A: Superior |

A: Superior - High certainty of a substantial (moderate-large) net health benefit
B: Incremental - High certainty of a small net health benefit
C++: Comparable or better - Moderate certainty of a comparable, small, or substantial net health benefit, with which certainty of at least a comparable net health benefit
I: Insufficient - Any situation where the level of certainty in the evidence is low

ICER does note that payors should consider the following:(17)

- Payors should remove barriers to access to rituximab for RMS patients who are appropriate candidates for this therapy. This includes coverage of biosimilar rituximab with little or no prior authorization given the lack of concern regarding use in appropriate patients and how inexpensive it is compared with other monoclonal antibodies of equal effectiveness
- Payors should not unilaterally implement policies to switch RMS patients who are stable on their chosen DMT over to lower-cost biosimilar rituximab

Safety

- **Aubagio** (teriflunomide) has a boxed warning with the following:(1)
  - Hepatotoxicity: clinically significant and potentially life-threatening liver injury, including acute liver failure requiring transplant, has been reported in patients treated with Aubagio in the post marketing setting. Concomitant use of Aubagio with other hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of Aubagio and monitor ALT levels at least monthly for six months. If drug induced liver injury is suspected, discontinue Aubagio and start accelerated elimination procedure
  - Embryofetal toxicity: teratogenicity and embryolethality occurred in animals administered teriflunomide. Exclude pregnancy prior to initiating Aubagio therapy. Advise use of effective contraception in females of reproductive potential during treatment and during an accelerated drug elimination procedure. Stop Aubagio and use an accelerated drug elimination procedure if the patient becomes pregnant
- **Aubagio** (teriflunomide) is contraindicated in:(1)
  - Severe hepatic impairment
  - Pregnant women and females of reproductive potential not using effective contraception. Aubagio may cause fetal harm
  - Hypersensitivity reaction to teriflunomide, leflunomide, or any of the inactive ingredients in Aubagio
  - Coadministration with leflunomide
- **Avonex** (interferon β-1a) is contraindicated in:(2)
  - History of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation
- **Bafiertam** (monomethyl fumarate) is contraindicated in:(3)
  - Known hypersensitivity to monomethyl fumarate, dimethyl fumarate, diroximel fumarate, or any of the excipients of Bafiertam
  - Co-administration with dimethyl fumarate or diroximel fumarate
- **Betaseron** (interferon β-1b) is contraindicated in:(4)
  - History of hypersensitivity to natural or recombinant interferon beta, albumin or mannitol
- **Copaxone** (glatiramer) is contraindicated in:(5)
  - Known hypersensitivity to glatiramer acetate or mannitol
- **Extavia** (interferon β-1b) is contraindicated in:(6)
  - History of hypersensitivity to natural or recombinant interferon beta, albumin (human), or mannitol
- **Gilenya** (fingolimod) is contraindicated in:(7)

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| | ○ Recent myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure with hospitalization, or Class III/IV heart failure<br>○ History of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker<br>○ Baseline QTc interval greater than or equal to 500 msec<br>○ Treatment with Class Ia or Class III anti-arrhythmic drugs<br>○ Hypersensitivity to fingolimod or its excipients<br>• **Glatopa** (glatiramer) is contraindicated in:(8)<br>○ Known hypersensitivity to glatiramer acetate or mannitol<br>• **Kesimpta** (ofatumumab) is contraindicated in:(9)<br>○ Active HBV infection<br>• **Mavenclad** (cladribine) contains a boxed warning with the following:(10)<br>○ Malignancies: Mavenclad may increase the risk of malignancy. Mavenclad is contraindicated in patients with current malignancy; evaluate the benefits and risks on an individual basis for patients with prior or increased risk of malignancy<br>○ Risk of teratogenicity: Mavenclad is contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the risk of fetal harm<br>• **Mavenclad** (cladribine) is contraindicated in:(10)<br>○ Patients with current malignancy<br>○ Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during Mavenclad dosing and for 6 months after the last dose in each treatment course<br>○ HIV infection<br>○ Active chronic infections (e.g., hepatitis or tuberculosis)<br>○ History of hypersensitivity to cladribine<br>○ Women intending to breastfeed on a Mavenclad treatment day and for 10 days after the last dose<br>• **Mayzent** (siponimod) is contraindicated in:(11)<br>○ Patients with a CYP2C9 *3/*3 genotype<br>○ Patients who in the last 6 months have experienced: myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure<br>○ Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker<br>• **Plegridy** (peginterferon β-1a) is contraindicated in:(12)<br>○ History of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of Plegridy<br>• **Ponvory** (ponesimod) is contraindicated in:(27)<br>○ Patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure<br>○ Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker<br>• **Rebif** (interferon β-1a) is contraindicated in:(13)<br>○ History of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation<br>• **Tascenso ODT** (fingolimod) is contraindicated in:(29)<br>○ Recent myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization or Class III/IV heart failure<br>○ History or presence of Mobitz Type II second-degree or third-degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker<br>○ Baseline QTc interval greater than or equal to 500 msec<br>○ Cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs<br>○ Hypersensitivity reaction to fingolimod or any of the excipients in Tascenso ODT. Observed reactions include rash, urticaria, and angioedema |

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| | ○ Concomitant use with other products containing fingolimod<br>• **Tecfidera** (dimethyl fumarate) is contraindicated in:(14)<br>○ Known hypersensitivity to dimethyl fumarate or any of the excipients of Tecfidera<br>• **Vumerity** (diroximel fumarate) is contraindicated in:(15)<br>○ Known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of Vumerity<br>○ Co-administration with dimethyl fumarate |

## REFERENCES


| Number | Reference |
|---|---|
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| 3 | Bafiertam prescribing information. Banner Life Sciences LLC. January 2023. |
| 4 | Betaseron prescribing information. Bayer HealthCare Pharmaceuticals, Inc. July 2023. |
| 5 | Copaxone prescribing information. Teva Neuroscience, Inc. February 2023. |
| 6 | Extavia prescribing information. Novartis Pharmaceuticals Corporation. July 2023. |
| 7 | Gilenya prescribing information. Novartis Pharmaceuticals Corporation. August 2023. |
| 8 | Glatopa prescribing information. Sandoz Inc. March 2023. |
| 9 | Kesimpta prescribing information. Novartis Pharmaceuticals Corporation. September 2022. |
| 10 | Mavenclad prescribing information. EMD Serono, Inc. September 2022. |
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| 12 | Plegridy prescribing information. Biogen, Inc. July 2023. |
| 13 | Rebif prescribing information. EMD Serono, Inc. July 2023. |
| 14 | Tecfidera prescribing information. Biogen, Inc. February 2023. |
| 15 | Vumerity prescribing information. Biogen Inc. February 2023. |
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|---|---|
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| 28 | Kitzler HH, Wahl H, Eisele JC, et al. Multi-component relaxation in clinically isolated syndrome; Lesion myelination may predict multiple sclerosis conversion. NeuroImage:Clinical 20 (2018)61-70. |
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| 31 | National Institute for Health and Care Excellence. NICE Guidance - Conditions and diseases - Neurological conditions - Multiple sclerosis. Ofatumumab for treating relapsing multiple sclerosis. Technology appraisal guidance [TA699] Published:19 May 2021. Accessed at 3 Committee discussion \| Ofatumumab for treating relapsing multiple sclerosis \| Guidance \| NICE. |


## POLICY AGENT SUMMARY PRIOR AUTHORIZATION

| Target Brand Agent(s) | Target Generic Agent(s) | Strength | Targeted MSC | Available MSC | Final Age Limit | Preferred Status |
|---|---|---|---|---|---|---|
| | | | | | | |
| Mavenclad | cladribine tab therapy pack | 10 MG | M ; N ; O ; Y | N | | |
| Tecfidera | dimethyl fumarate capsule delayed release | 120 MG ; 240 MG | M ; N ; O ; Y | O ; Y | | |
| Tecfidera starter pack | dimethyl fumarate capsule dr starter pack | 120 & 240 MG | M ; N ; O ; Y | O ; Y | | |
| Vumerity | diroximel fumarate capsule delayed release | 231 MG | M ; N ; O ; Y | N | | |
| Gilenya | fingolimod hcl cap | 0.25 MG ; 0.5 MG | M ; N ; O ; Y | N ; O ; Y | | |
| Tascenso odt | fingolimod lauryl sulfate tablet disintegrating | 0.25 MG ; 0.5 MG | M ; N ; O ; Y | N | | |
| Rebif rebidose ; Rebif rebidose titration | interferon beta- | 22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG | M ; N ; O ; Y | N | | |
| Rebif ; Rebif titration pack | interferon beta- | 22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG | M ; N ; O ; Y | N | | |
| Avonex pen | interferon beta- | 30 MCG/0.5ML | M ; N ; O ; Y | N | | |
| Avonex | interferon beta- | 30 MCG/0.5ML | M ; N ; O ; Y | N | | |
| Bafiertam | Monomethyl Fumarate Capsule Delayed Release | 95 MG | M ; N ; O ; Y | N | | |
| Kesimpta | ofatumumab soln auto-injector | 20 MG/0.4ML | M ; N ; O ; Y | N | | |
| Plegridy ; Plegridy starter pack | peginterferon beta- | 125 MCG/0.5ML ; 63 & 94 MCG/0.5ML | M ; N ; O ; Y | N | | |
| Plegridy ; Plegridy starter pack | peginterferon beta- | 125 MCG/0.5ML ; 63 & 94 MCG/0.5ML | M ; N ; O ; Y | N | | |
| Ponvory | ponesimod tab | 20 MG | M ; N ; O ; Y | N | | |
| Ponvory 14-day starter pa | ponesimod tab starter pack | 2-3-4-5-6-7-8-9 & 10 MG | M ; N ; O ; Y | N | | |
| Mayzent | siponimod fumarate tab | 0.25 MG ; 1 MG ; 2 MG | M ; N ; O ; Y | N | | |

| Target Brand Agent(s) | Target Generic Agent(s) | Strength | Targeted MSC | Available MSC | Final Age Limit | Preferred Status |
|---|---|---|---|---|---|---|
| Mayzent starter pack | siponimod fumarate tab | 0.25 MG | M ; N ; O ; Y | N | | |
| Aubagio | teriflunomide tab | 14 MG ; 7 MG | M ; N ; O ; Y | O ; Y | | |
| Betaseron | Interferon Beta- ; interferon beta- | 0.3 MG | M ; N ; O ; Y | N | | |
| Copaxone | glatiramer acetate soln prefilled syringe | 20 MG/ML ; 40 MG/ML | M ; N ; O ; Y | O ; Y | | |
| Extavia | Interferon Beta- ; interferon beta- | 0.3 MG | M ; N ; O ; Y | N | | |
| Glatopa | glatiramer acetate soln prefilled syringe | 20 MG/ML ; 40 MG/ML | M ; N ; O ; Y | O ; Y | | |

## POLICY AGENT SUMMARY QUANTITY LIMIT

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| Aubagio | teriflunomide tab | 14 MG ; 7 MG | 30 | Tablets | 30 | DAYS | | | |
| Avonex | interferon beta- | 30 MCG/0.5 ML | 4 | Syringes | 28 | DAYS | | | |
| Avonex pen | interferon beta- | 30 MCG/0.5 ML | 4 | Pens | 28 | DAYS | | | |
| Bafiertam | Monomethyl Fumarate Capsule Delayed Release | 95 MG | 120 | Capsules | 30 | DAYS | | | |
| Betaseron | Interferon Beta- ; interferon beta- | 0.3 MG | 14 | Vials | 28 | DAYS | | | 50419052401 ; 50419052435 |
| Copaxone ; Glatopa | Glatiramer Acetate Soln Prefilled Syringe 20 MG/ML | 20 MG/ML | 30 | Syringes | 30 | DAYS | | | |
| Copaxone ; Glatopa | Glatiramer Acetate Soln Prefilled Syringe 40 MG/ML | 40 MG/ML | 12 | Syringes | 28 | DAYS | | | |
| Extavia | Interferon Beta- ; interferon beta- | 0.3 MG | 15 | Vials | 30 | DAYS | | | 00078056912 ; 00078056961 ; 00078056999 |
| Gilenya | fingolimod hcl cap | 0.25 MG ; 0.5 MG | 30 | Capsules | 30 | DAYS | | | |
| Kesimpta | Ofatumumab Soln Auto-Injector | 20 MG/0.4 ML | 1 | Syringe | 28 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (10 Tabs) | 10 MG | 20 | Tablets | 301 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (4 Tabs) | 10 MG | 8 | Tablets | 301 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (5 Tabs) | 10 MG | 10 | Tablets | 301 | DAYS | | | |

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (6 Tabs) | 10 MG | 12 | Tablets | 301 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (7 Tabs) | 10 MG | 14 | Tablets | 301 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (8 Tabs) | 10 MG | 8 | Tablets | 301 | DAYS | | | |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (9 Tabs) | 10 MG | 9 | Tablets | 301 | DAYS | | | |
| Mayzent | Siponimod Fumarate Tab | 1 MG | 30 | Tablets | 30 | DAYS | | | |
| Mayzent | Siponimod Fumarate Tab 0.25 MG (Base Equiv) | 0.25 MG | 120 | Tablets | 30 | DAYS | | | |
| Mayzent | Siponimod Fumarate Tab 2 MG (Base Equiv) | 2 MG | 30 | Tablets | 30 | DAYS | | | |
| Mayzent starter pack | Siponimod Fumarate Tab | 0.25 MG | 7 | Tablets | 180 | DAYS | | | |
| Mayzent starter pack | Siponimod Fumarate Tab 0.25 MG (12) Starter Pack | 0.25 MG | 12 | Tablets | 180 | DAYS | | | |
| Plegridy | Peginterferon Beta- | 125 MCG/0.5 ML | 2 | Syringes | 28 | DAYS | | | |
| Plegridy | Peginterferon Beta-1a Soln Pen-injector 125 MCG/0.5ML | 125 MCG/0.5 ML | 2 | Pens | 28 | DAYS | | | |
| Plegridy | Peginterferon Beta-1a Soln Prefilled Syringe 125 MCG/0.5ML | 125 MCG/0.5 ML | 2 | Syringes | 28 | DAYS | | | |
| Plegridy starter pack | Peginterferon Beta-1a Soln Pen-inj 63 & 94 MCG/0.5ML Pack | 63 & 94 MCG/0.5 ML | 1 | Kit | 180 | DAYS | | | |
| Plegridy starter pack | Peginterferon Beta-1a Soln Pref Syr 63 & 94 MCG/0.5ML Pack | 63 & 94 MCG/0.5 ML | 1 | Kit | 180 | DAYS | | | |
| Ponvory | Ponesimod Tab | 20 MG | 30 | Tablets | 30 | DAYS | | | |
| Ponvory 14-day starter pa | Ponesimod Tab Starter Pack | 2-3-4-5-6-7-8-9 & 10 MG | 14 | Tablets | 180 | DAYS | | | |
| Rebif | Interferon Beta-1a Soln Pref Syr 22 MCG/0.5ML (12MU/ML) | 22 MCG/0.5 ML | 12 | Syringes | 28 | DAYS | | | |
| Rebif | Interferon Beta-1a Soln Pref Syr 44 MCG/0.5ML (24MU/ML) | 44 MCG/0.5 ML | 12 | Syringes | 28 | DAYS | | | |
| Rebif rebidose | Interferon Beta-1a Soln Auto-Inj 22 MCG/0.5ML (12MU/ML) | 22 MCG/0.5 ML | 12 | Syringes | 28 | DAYS | | | |
| Rebif rebidose | Interferon Beta-1a Soln Auto-inj 44 MCG/0.5ML (24MU/ML) | 44 MCG/0.5 ML | 12 | Syringes | 28 | DAYS | | | |

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| Rebif rebidose titration | Interferon Beta-1a Auto-inj 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML | 6X8.8 & 6X22 MCG | 1 | Kit | 180 | DAYS | | | |
| Rebif titration pack | Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML | 6X8.8 & 6X22 MCG | 1 | Kit | 180 | DAYS | | | |
| Tascenso odt | fingolimod lauryl sulfate tablet disintegrating | 0.25 MG ; 0.5 MG | 30 | Tablets | 30 | DAYS | | | |
| Tecfidera | Dimethyl Fumarate Capsule Delayed Release 120 MG | 120 MG | 56 | Capsules | 180 | DAYS | | | |
| Tecfidera | Dimethyl Fumarate Capsule Delayed Release 240 MG | 240 MG | 60 | Capsules | 30 | DAYS | | | |
| Tecfidera starter pack | dimethyl fumarate capsule dr starter pack | 120 & 240 MG | 1 | Kit | 180 | DAYS | | | |
| Vumerity | Diroximel Fumarate Capsule Delayed Release 231 MG | 231 MG | 120 | Capsules | 30 | DAYS | | | |

## CLIENT SUMMARY – PRIOR AUTHORIZATION

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Aubagio | teriflunomide tab | 14 MG ; 7 MG | Medicaid |
| Avonex | interferon beta- | 30 MCG/0.5ML | Medicaid |
| Avonex pen | interferon beta- | 30 MCG/0.5ML | Medicaid |
| Bafiertam | Monomethyl Fumarate Capsule Delayed Release | 95 MG | Medicaid |
| Betaseron | Interferon Beta- ; interferon beta- | 0.3 MG | Medicaid |
| Copaxone | glatiramer acetate soln prefilled syringe | 20 MG/ML ; 40 MG/ML | Medicaid |
| Extavia | Interferon Beta- ; interferon beta- | 0.3 MG | Medicaid |
| Gilenya | fingolimod hcl cap | 0.25 MG ; 0.5 MG | Medicaid |
| Glatopa | glatiramer acetate soln prefilled syringe | 20 MG/ML ; 40 MG/ML | Medicaid |
| Kesimpta | ofatumumab soln auto-injector | 20 MG/0.4ML | Medicaid |
| Mavenclad | cladribine tab therapy pack | 10 MG | Medicaid |
| Mayzent | siponimod fumarate tab | 0.25 MG ; 1 MG ; 2 MG | Medicaid |
| Mayzent starter pack | siponimod fumarate tab | 0.25 MG | Medicaid |
| Plegridy ; Plegridy starter pack | peginterferon beta- | 125 MCG/0.5ML ; 63 & 94 MCG/0.5ML | Medicaid |
| Plegridy ; Plegridy starter pack | peginterferon beta- | 125 MCG/0.5ML ; 63 & 94 MCG/0.5ML | Medicaid |
| Ponvory | ponesimod tab | 20 MG | Medicaid |
| Ponvory 14-day starter pa | ponesimod tab starter pack | 2-3-4-5-6-7-8-9 & 10 MG | Medicaid |
| Rebif ; Rebif titration pack | interferon beta- | 22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG | Medicaid |
| Rebif rebidose ; Rebif rebidose titration | interferon beta- | 22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG | Medicaid |
| Tascenso odt | fingolimod lauryl sulfate tablet disintegrating | 0.25 MG ; 0.5 MG | Medicaid |

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Tecfidera | dimethyl fumarate capsule delayed release | 120 MG ; 240 MG | Medicaid |
| Tecfidera starter pack | dimethyl fumarate capsule dr starter pack | 120 & 240 MG | Medicaid |
| Vumerity | diroximel fumarate capsule delayed release | 231 MG | Medicaid |
| Vumerity | diroximel fumarate capsule delayed release | 231 MG | Medicaid |

## CLIENT SUMMARY – QUANTITY LIMITS

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Aubagio | teriflunomide tab | 14 MG ; 7 MG | Medicaid |
| Avonex | interferon beta- | 30 MCG/0.5ML | Medicaid |
| Avonex pen | interferon beta- | 30 MCG/0.5ML | Medicaid |
| Bafiertam | Monomethyl Fumarate Capsule Delayed Release | 95 MG | Medicaid |
| Betaseron | Interferon Beta- ; interferon beta- | 0.3 MG | Medicaid |
| Copaxone ; Glatopa | Glatiramer Acetate Soln Prefilled Syringe 20 MG/ML | 20 MG/ML | Medicaid |
| Copaxone ; Glatopa | Glatiramer Acetate Soln Prefilled Syringe 40 MG/ML | 40 MG/ML | Medicaid |
| Extavia | Interferon Beta- ; interferon beta- | 0.3 MG | Medicaid |
| Gilenya | fingolimod hcl cap | 0.25 MG ; 0.5 MG | Medicaid |
| Kesimpta | Ofatumumab Soln Auto-Injector | 20 MG/0.4ML | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (10 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (4 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (5 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (6 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (7 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (8 Tabs) | 10 MG | Medicaid |
| Mavenclad | Cladribine Tab Therapy Pack 10 MG (9 Tabs) | 10 MG | Medicaid |
| Mayzent | Siponimod Fumarate Tab | 1 MG | Medicaid |
| Mayzent | Siponimod Fumarate Tab 0.25 MG (Base Equiv) | 0.25 MG | Medicaid |
| Mayzent | Siponimod Fumarate Tab 2 MG (Base Equiv) | 2 MG | Medicaid |
| Mayzent starter pack | Siponimod Fumarate Tab | 0.25 MG | Medicaid |
| Mayzent starter pack | Siponimod Fumarate Tab 0.25 MG (12) Starter Pack | 0.25 MG | Medicaid |
| Plegridy | Peginterferon Beta- | 125 MCG/0.5ML | Medicaid |
| Plegridy | Peginterferon Beta-1a Soln Pen-injector 125 MCG/0.5ML | 125 MCG/0.5ML | Medicaid |
| Plegridy | Peginterferon Beta-1a Soln Prefilled Syringe 125 MCG/0.5ML | 125 MCG/0.5ML | Medicaid |
| Plegridy starter pack | Peginterferon Beta-1a Soln Pen-inj 63 & 94 MCG/0.5ML Pack | 63 & 94 MCG/0.5ML | Medicaid |
| Plegridy starter pack | Peginterferon Beta-1a Soln Pref Syr 63 & 94 MCG/0.5ML Pack | 63 & 94 MCG/0.5ML | Medicaid |
| Ponvory | Ponesimod Tab | 20 MG | Medicaid |
| Ponvory 14-day starter pa | Ponesimod Tab Starter Pack | 2-3-4-5-6-7-8-9 & 10 MG | Medicaid |
| Rebif | Interferon Beta-1a Soln Pref Syr 22 MCG/0.5ML (12MU/ML) | 22 MCG/0.5ML | Medicaid |

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Rebif | Interferon Beta-1a Soln Pref Syr 44 MCG/0.5ML (24MU/ML) | 44 MCG/0.5ML | Medicaid |
| Rebif rebidose | Interferon Beta-1a Soln Auto-Inj 22 MCG/0.5ML (12MU/ML) | 22 MCG/0.5ML | Medicaid |
| Rebif rebidose | Interferon Beta-1a Soln Auto-inj 44 MCG/0.5ML (24MU/ML) | 44 MCG/0.5ML | Medicaid |
| Rebif rebidose titration | Interferon Beta-1a Auto-inj 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML | 6X8.8 & 6X22 MCG | Medicaid |
| Rebif titration pack | Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML | 6X8.8 & 6X22 MCG | Medicaid |
| Tascenso odt | fingolimod lauryl sulfate tablet disintegrating | 0.25 MG ; 0.5 MG | Medicaid |
| Tecfidera | Dimethyl Fumarate Capsule Delayed Release 120 MG | 120 MG | Medicaid |
| Tecfidera | Dimethyl Fumarate Capsule Delayed Release 240 MG | 240 MG | Medicaid |
| Tecfidera starter pack | dimethyl fumarate capsule dr starter pack | 120 & 240 MG | Medicaid |
| Vumerity | Diroximel Fumarate Capsule Delayed Release 231 MG | 231 MG | Medicaid |

## PREFERRED AGENTS

## PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td>Mavencl ad</td><td>
TARGET AGENT(S) - Preferred agents are the MN Medicaid Preferred Drug List (PDL) preferred drugs<br><br>
<u>Preferred Agents</u><br>
Avonex® (interferon beta-1a)<br>
Betaseron® (interferon beta-1b)<br>
Copaxone® 20 mg/mL (glatiramer)*<br>
dimethyl fumarate<br>
fingolimod<br>
Rebif® (interferon beta-1a)<br>
teriflunomide<br><br>
<u>Nonpreferred Agents</u><br>
Aubagio® (teriflunomide)*<br>
Bafiertam™ (monomethyl fumarate)<br>
Copaxone® 40 mg/mL (glatiramer)*<br>
dimethyl fumarate Starter Pack<br>
Extavia® (interferon beta-1b)Glatiramer 20 mg/mL<br>
Gilenya® (fingolimod)*<br>
Glatiramer 40 mg/mL<br>
Glatopa® (glatiramer)*<br>
Kesimpta® (ofatumumab)<br>
Mavenclad® (cladribine)<br>
Mayzent® (siponimod)<br>
Plegridy® (peginterferon beta-1a)<br>
Ponvory™ (ponesimod)<br>
Tecfidera® (dimethyl fumarate)*<br>
Tascenso ODT™ (fingolimod)<br>
Vumerity® (diroximel fumarate)<br>
* -generic available<br><br>
<table>
<tr><th>FDA Labeled Indication</th><th>FDA Approved Agent(s)</th></tr>
<tr><td>Clinically Isolated Syndrome (CIS)</td><td>Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa,</td></tr>
</table>
</td></tr>
</table>

| Module | Clinical Criteria for Approval |
|---|---|

| | |
|---|---|
| | Kesimpta, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity |
| Relapsing Remitting Multiple Sclerosis (RRMS) | Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity |
| Active Secondary Progressive Multiple Sclerosis (SPMS) | Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity |

**Initial Evaluation**

**Mavenclad (cladribine)** will be approved when ALL of the following are met:

1. ONE of the following:
   A. ONE of the following:
      1. The patient has been treated with the requested agent within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent within the past 90 days AND the patient is at risk if therapy is changed **OR**
   B. ALL of the following
      1. The patient has ONE of the following relapsing forms of multiple sclerosis (MS):
         A. Relapsing-remitting disease (RRMS) **OR**
         B. Active secondary progressive disease (SPMS) **AND**
      2. The request is for a non-preferred agent in the Minnesota Medicaid Preferred Drug List (PDL) and ONE of the following:
         A. The patient is currently being treated with the requested agent as indicated by ALL of the following:
            1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
            2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
            3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
         B. The patient's medication history includes two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) AND ONE of the following:
            1. The patient had an inadequate response to two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) **OR**
            2. The prescriber has submitted an evidence-based and peer reviewed clinical practice guideline supporting the use of the requested agent over the preferred agent(s) **OR**
         C. The patient has an intolerance or hypersensitivity to two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent **OR**
         D. The patient has an FDA labeled contraindication to ALL preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent **OR**
         E. The prescriber has provided information that the required preferred agent(s) cannot be used due to a documented medical

| Module | Clinical Criteria for Approval |
|---|---|
| | condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR**<br>F. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s) **AND**<br>3. If the patient has an FDA labeled indication, then ONE of the following:<br>A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**<br>B. There is support for using the requested agent for the patient's age for the requested indication **AND**<br>2. If the patient has been previously treated with the requested agent, BOTH of the following:<br>A. The prescriber has provided the number of courses the patient has completed (one course consists of 2 cycles of 4-5 days each) **AND**<br>B. The patient has NOT completed 2 courses of the requested agent (one course consists of 2 cycles of 4-5 days each) **AND**<br>3. A complete CBC with differential including lymphocyte count has been performed **AND**<br>4. The lymphocyte count is within normal limits **AND**<br>5. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>6. ONE of the following:<br>A. The patient will NOT be using the requested agent with an additional disease modifying agent (DMA) for the requested indication **OR**<br>B. BOTH of the following:<br>1. The patient is currently using the requested agent **AND**<br>2. There is support for the use of the additional DMA (e.g., relapse between cycles) **AND**<br>7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**<br>8. The requested quantity (dose) does not exceed the FDA labeled maximum dose based on the patient's weight<br><br>**Length of Approval:** 36 weeks for new starts OR if patient is currently taking the requested agent, approve for remainder of the annual course (1 course consists of 2 cycles of 4-5 days)<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria<br><br>**Renewal Evaluation**<br><br>**Mavenclad (cladribine)** will be approved when ALL of the following are met:<br><br>1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (Note: patients not previously approved for the requested agent will require initial evaluation review) **AND**<br>2. The patient has had clinical benefit with the requested agent **AND**<br>3. A complete CBC with differential including lymphocyte count has been performed **AND**<br>4. The patient has a lymphocyte count of at least 800 cells/microliter **AND**<br>5. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>6. ONE of the following:<br>A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication **OR**<br>B. There is support for the use of the additional DMA (e.g., relapse between cycles) **AND**<br>7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**<br>8. It has been at least 35 weeks but not more than 67 weeks since the last dose of the requested agent **AND** |

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td></td><td>9. BOTH of the following:<br>1. The prescriber has provided the number of courses the patient has completed (one course consists of 2 cycles of 4-5 days each) AND<br>2. The patient has NOT completed 2 courses with the requested agent (one course consists of 2 cycles of 4-5 days) AND<br>10. The requested quantity (dose) does not exceed the FDA labeled maximum dose based on the patient's weight<br><br>Length of Approval: 3 months<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria</td></tr>
<tr><td>MS Agents other than Mavenclad</td><td>TARGET AGENT(S) - Preferred agents are the MN Medicaid Preferred Drug List (PDL) preferred drugs<br><br><u>Preferred Agents</u><br>Avonex® (interferon beta-1a)<br>Betaseron® (interferon beta-1b)<br>Copaxone® 20 mg/mL (glatiramer)*<br>dimethyl fumarate<br>fingolimod<br>Rebif® (interferon beta-1a)<br>teriflunomide<br><br><u>Nonpreferred Agents</u><br>Aubagio® (teriflunomide)<br>Bafiertam™ (monomethyl fumarate)<br>Copaxone® 40 mg/mL (glatiramer)*<br>dimethyl fumarate Starter Pack<br>Extavia® (interferon beta-1b)<br>Glatiramer 20 mg/mL<br>Gilenya® (fingolimod)*<br>Glatiramer 40 mg/mL<br>Glatopa® (glatiramer)*<br>Kesimpta® (ofatumumab)<br>Mavenclad® (cladribine)<br>Mayzent® (siponimod)<br>Plegridy® (peginterferon beta-1a)<br>Ponvory™ (ponesimod)<br>Tecfidera® (dimethyl fumarate)*<br>Tascenso ODT™ (fingolimod)<br>Vumerity® (diroximel fumarate)<br>* -generic available<br><br><table><tr><th>FDA Labeled Indication</th><th>FDA Approved Agent(s)</th></tr><tr><td>Clinically Isolated Syndrome (CIS)</td><td>Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity</td></tr><tr><td>Relapsing Remitting Multiple Sclerosis (RRMS)</td><td>Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity</td></tr><tr><td>Active Secondary Progressive Multiple Sclerosis (SPMS)</td><td>Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity</td></tr></table></td></tr>
</table>

| Module | Clinical Criteria for Approval |
|---|---|
| | **Initial Evaluation**<br><br>**Target Agent(s) (excluding Mavenclad [cladribine])** will be approved when ALL of the following are met:<br><br>1. ONE of the following:<br>A. Information has been provided that the patient has been treated with the requested agent within the past 90 days **OR**<br>B. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed **OR**<br>C. BOTH of the following:<br>1. ONE of the following:<br>A. The patient has a diagnosis of a relapsing form of MS AND ALL of the following:<br>1. The request is for a non-preferred agent in the Minnesota Medicaid Preferred Drug List (PDL) and ONE of the following:<br>A. The patient is currently being treated with the requested agent as indicated by ALL of the following:<br>1. A statement by the prescriber that the patient is currently taking the requested agent **AND**<br>2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**<br>3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**<br>B. The patient's medication history includes two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) AND ONE of the following:<br>1. The patient had an inadequate response to two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) **OR**<br>2. The prescriber has submitted an evidence-based and peer reviewed clinical practice guideline supporting the use of the requested agent over the preferred agent(s) **OR**<br>C. The patient has an intolerance or hypersensitivity to two preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent **OR**<br>D. The patient has an FDA labeled contraindication to ALL preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent **OR**<br>E. The prescriber has provided information that the required preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in |

| Module | Clinical Criteria for Approval |
|---|---|
| | performing daily activities or cause physical or mental harm **OR**<br>F. The prescriber has provided information supporting the use of the non-preferred agent over the preferred agent(s) **AND**<br>2. If the requested agent is Aubagio (teriflunomide), the prescriber has obtained transaminase and bilirubin levels within 6 months prior to initiating treatment **AND**<br>3. If the requested agent is Gilenya (fingolimod) or Tascenso ODT (fingolimod) the prescriber has performed an electrocardiogram within 6 months prior to initiating treatment **OR**<br>B. The patient has another FDA labeled indication for the requested agent and route of administration **AND**<br>2. If the patient has an FDA labeled indication, the ONE of the following:<br>A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**<br>B. There is support for using the requested agent for the patient's age for the requested indication **AND**<br>2. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>3. ONE of the following:<br>A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication **OR**<br>B. The patient will be using the requested agent in combination with another DMA used for the treatment of the requested indication AND BOTH of the following:<br>1. The requested agent will be used in combination with Mavenclad (cladribine) **AND**<br>2. There is support for the use of the requested agent in combination with Mavenclad (e.g., relapse between cycles of Mavenclad) **AND**<br>4. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 12 months. NOTE: For agents requiring a starter dose for initial use, the starter dose can be approved for the FDA labeled starting dose and the maintenance dose can be approved for the remainder of 12 months.<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria<br><br>**Renewal Evaluation**<br><br>**Target agent(s) (excluding Mavenclad [cladribine])** will be approved when ALL of the following are met:<br><br>1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (Note: patients not previously approved for the requested agent will require initial evaluation review) **AND**<br>2. The patient has had clinical benefit with the requested agent **AND**<br>3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**<br>4. ONE of the following:<br>A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication **OR**<br>B. The patient will be using the requested agent in combination with another DMA used for the requested indication AND BOTH of the following:<br>1. The requested agent will be used in combination with Mavenclad cladribine) **AND**<br>2. There is support for the use of the requested agent in combination with Mavenclad (e.g., relapse between cycles of Mavenclad) **AND** |

| Module | Clinical Criteria for Approval |
|---|---|
| | 5. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 12 months<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria |

## QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
|---|---|
| QL with PA - All agents excluding Mavenclad | **Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met:<br><br>1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**<br>2. ALL of the following:<br>A. The requested quantity (dose) exceeds the program quantity limit **AND**<br>B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**<br>C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR**<br>3. ALL of the following:<br>A. The requested quantity (dose) exceeds the program quantity limit **AND**<br>B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND**<br>C. There is support for therapy with a higher dose for the requested indication<br><br>**Length of Approval**: up to 12 months. **NOTE**: For agents requiring a starter dose for initial use, the starter dose can be approved for the FDA labeled starting dose and the maintenance dose can be approved for the remainder of 12 months. |
| QL with PA Mavenclad | **Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met:<br><br>1. The requested quantity (dose) does not exceed the program quantity limit **OR**<br>2. BOTH of the following<br>A. The requested quantity (dose) exceeds the program quantity limit **AND**<br>B. The requested quantity (dose) cannot be achieved with a lower quantity of packs and a higher pack size (e.g., two 10 tablet packs instead of four 5 tablet packs) that does not exceed the program quantity limit<br><br>**Length of Approval:** Initial: up to 36 weeks for new starts OR if patient is currently taking the requested agent, approve for remainder of the annual course (1 course consists of 2 cycles of 4-5 days); Renewal: up to 3 months |

## CLASS AGENTS

| Class | Class Drug Agents |
|---|---|
| **Class Ia antiarrhythmics** | |
| Class Ia antiarrhythmics | NORPACE*Disopyramide Phosphate Cap |
| Class Ia antiarrhythmics | Pronestyl (procainamide) |
| Class Ia antiarrhythmics | quinidine |
| **Class III antiarrhythmics** | |
| Class III antiarrhythmics | BETAPACE*Sotalol HCl Tab |
| Class III antiarrhythmics | Cordarone, Pacerone (amiodarone) |
| Class III antiarrhythmics | CORVERT*Ibutilide Fumarate Inj |
| Class III antiarrhythmics | MULTAQ*Dronedarone HCl Tab |
| Class III antiarrhythmics | TIKOSYN*Dofetilide Cap |
| **MS Disease Modifying Agents drug class: CD20 monoclonal antibody** | |
| MS Disease Modifying Agents drug class: CD20 monoclonal antibody | BRIUMVI*ublituximab-xiiy soln for iv infusion |
| MS Disease Modifying Agents drug class: CD20 monoclonal antibody | KESIMPTA*Ofatumumab Soln Auto-Injector |

| Class | Class Drug Agents |
|---|---|
| MS Disease Modifying Agents drug class: CD20 monoclonal antibody | OCREVUS*Ocrelizumab Soln For IV Infusion |
| **MS Disease Modifying Agents drug class: CD52 monoclonal antibody** | |
| MS Disease Modifying Agents drug class: CD52 monoclonal antibody | LEMTRADA*Alemtuzumab IV Inj |
| **MS Disease Modifying Agents drug class: Fumarates** | |
| MS Disease Modifying Agents drug class: Fumarates | BAFIERTAM*Monomethyl Fumarate Capsule Delayed Release |
| MS Disease Modifying Agents drug class: Fumarates | TECFIDERA*Dimethyl Fumarate Capsule Delayed Release |
| MS Disease Modifying Agents drug class: Fumarates | VUMERITY*Diroximel Fumarate Capsule Delayed Release |
| **MS Disease Modifying Agents drug class: Glatiramer** | |
| MS Disease Modifying Agents drug class: Glatiramer | COPAXONE*Glatiramer Acetate Soln Prefilled Syringe |
| MS Disease Modifying Agents drug class: Glatiramer | GLATOPA*Glatiramer Acetate Soln Prefilled Syringe |
| **MS Disease Modifying Agents drug class: IgG4k monoclonal antibody** | |
| MS Disease Modifying Agents drug class: IgG4k monoclonal antibody | TYSABRI*Natalizumab for IV Inj Conc |
| **MS Disease Modifying Agents drug class: Interferons** | |
| MS Disease Modifying Agents drug class: Interferons | AVONEX*Interferon beta-1a injection |
| MS Disease Modifying Agents drug class: Interferons | BETASERON*Interferon beta-1b injection |
| MS Disease Modifying Agents drug class: Interferons | EXTAVIA*Interferon beta-1b injection |
| MS Disease Modifying Agents drug class: Interferons | PLEGRIDY*Peginterferon beta-1a injection |
| MS Disease Modifying Agents drug class: Interferons | REBIF*Interferon Beta- |
| **MS Disease Modifying Agents drug class: Purine antimetabolite** | |
| MS Disease Modifying Agents drug class: Purine antimetabolite | MAVENCLAD*Cladribine Tab Therapy Pack |
| **MS Disease Modifying Agents drug class: Pyrimidine synthesis inhibitor** | |
| MS Disease Modifying Agents drug class: Pyrimidine synthesis inhibitor | AUBAGIO*Teriflunomide Tab |
| **MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator** | |
| MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator | GILENYA*Fingolimod HCl Cap |
| MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator | MAYZENT*Siponimod Fumarate Tab |
| MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator | PONVORY*Ponesimod Tab |
| **MS Disease Modifying Agents Drug Class: Sphingosine 1-phosphate (SIP) receptor modulator** | |
| MS Disease Modifying Agents Drug Class: Sphingosine 1-phosphate (SIP) receptor modulator | TASCENSO*fingolimod lauryl sulfate tablet disintegrating |
| **MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator** | |
| MS Disease Modifying Agents drug class: Sphingosine 1-phosphate (SIP) receptor modulator | ZEPOSIA*Ozanimod capsule |

## CONTRAINDICATION AGENTS

| Contraindicated as Concomitant Therapy |
|---|
| **Examples of Contraindicated Concomitant Disease Modifying Agents (DMAs)**<br>**Aubagio** (teriflunomide)*<br>**Avonex** (interferon β-1a)<br>**Bafiertam** (monomethyl fumarate) |

| Contraindicated as Concomitant Therapy |
| --- |
| **Betaseron** (interferon β-1b)<br>**Briumvi** (ublituximab-xiiy)<br>**Copaxone** (glatiramer)*<br>dimethyl fumarate<br>**Extavia** (interferon β-1b)<br>fingolimod<br>**Gilenya** (fingolimod)*<br>**Glatopa** (glatiramer)<br>glatiramer<br>**Kesimpta** (ofatumumab)<br>**Lemtrada** (alemtuzumab)<br>**Mavenclad** (cladribine)<br>**Mayzent** (siponimod)<br>**Ocrevus** (ocrelizumab)<br>**Plegridy** (peginterferon β-1a)<br>**Ponvory** (ponesimod)<br>**Rebif** (interferon β-1a)<br>**Tascenso ODT** (fingolimod)<br>**Tecfidera** (dimethyl fumarate)*<br>teriflunomide<br>**Tysabri** (natalizumab)<br>**Vumerity** (diroximel fumarate)<br>**Zeposia** (ozanimod)<br><br>* -generic available |