Multiple Sclerosis Agents Prior Authorization with Quantity Limit Program Summary

For BCBS KS, the following preferred generic agents are not subject to prior authorization, and are only subject to quantity limits: dimethyl fumarate (generic Tecfidera), fingolimod (generic Gilenya), glatiramer (generic Copaxone), Glatopa, teriflunomide (generic Aubagio).

A prior authorization only needs to be submitted for dimethyl fumarate, fingolimod, glatiramer, Glatopa or teriflunomide when the request is for a quantity above the quantity limits listed in this document.

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
03-01-2025

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Aubagio® (teriflunomide)* 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 available	1
Avonex® (interferon β-1a) 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® (monomethyl fumarate) 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® (interferon β-1b) 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® (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 available	5

Agent(s)	FDA Indication(s)	Notes	Ref#
Injection for subcutaneous use			
Extavia® (interferon β-1b) 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® (fingolimod)* 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 available	7
Glatopa® (glatiramer acetate) 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® (ofatumumab) 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® (cladribine) Tablet	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease in adults 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. Limitation of Use: Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.		10
Mayzent® (siponimod) 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® (peginterferon β-1a) 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® (ponesimod) 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® (interferon β-1b) 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® (fingolimod) 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® (dimethyl fumarate)* 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 available	14
Vumerity® (diroximel fumarate) 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

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) 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)

The diagnosis of MS requires elimination of more likely diagnoses and demonstration of dissemination of lesions in the CNS in space and time.(21)

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)

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)

The 2017 McDonald criteria to diagnose MS is shown in the chart below.(21,22)

<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
OR
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>
</table>
</td></tr>
</table>

attack involving lesion in different location	
Greater than or equal to 2 attacks and objective clinical evidence of 1 lesion	**ONE** of these criteria: Additional clinical attack implicating different CNS site OR 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: Additional clinical attack OR Simultaneous presence of both enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions OR New T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) OR CSF specific (i.e., not in serum) oligoclonal bands
1 attack and objective clinical evidence of 1 lesion	**ONE** of these criteria: Additional attack implicating different CNS site OR 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 **AND** **ONE** of these criteria: Additional clinical attack OR Simultaneous presence of both enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions OR New T2 enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) OR 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

	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) 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) 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) 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) 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) 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 • No functional impairment (school, work, daily activities, etc.) • No motor/cerebellar/brain stem/sphincter involvement	• Moderate to severe • Functional impairment • Motor/cerebellar/brain stem/sphincter involvement
Recovery	• Full recovery at 6 months • No functional impairment • EDSS change from baseline less than or equal to 1 point at 6 months unless baseline EDSS greater than 5.5	• Incomplete recovery • Functional impairment • If EDSS at baseline was 0 then greater than a 1.5 point change from baseline • If EDSS greater than 0 but less than or equal to 5.5 at baseline then greater than 1 point change at 6 months • If EDSS greater than 5.5 any change would

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

	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)

	○ Recent myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure with hospitalization, or Class III/IV heart failure ○ History of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker ○ Baseline QTc interval greater than or equal to 500 msec ○ Treatment with Class Ia or Class III anti-arrhythmic drugs ○ Hypersensitivity to fingolimod or its excipients • **Glatopa** (glatiramer) is contraindicated in:(8) ○ Known hypersensitivity to glatiramer acetate or mannitol • **Kesimpta** (ofatumumab) is contraindicated in:(9) ○ Active HBV infection • **Mavenclad** (cladribine) contains a boxed warning with the following:(10) ○ 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 ○ 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 • **Mavenclad** (cladribine) is contraindicated in:(10) ○ Patients with current malignancy ○ 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 ○ HIV infection ○ Active chronic infections (e.g., hepatitis or tuberculosis) ○ History of hypersensitivity to cladribine ○ Women intending to breastfeed on a Mavenclad treatment day and for 10 days after the last dose • **Mayzent** (siponimod) is contraindicated in:(11) ○ Patients with a CYP2C9 *3/*3 genotype ○ 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 ○ Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker • **Plegridy** (peginterferon β-1a) is contraindicated in:(12) ○ History of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of Plegridy • **Ponvory** (ponesimod) is contraindicated in:(27) ○ 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 ○ Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker • **Rebif** (interferon β-1a) is contraindicated in:(13) ○ History of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation • **Tascenso ODT** (fingolimod) is contraindicated in:(29) ○ Recent myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization or Class III/IV heart failure ○ History or presence of Mobitz Type II second-degree or third-degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker ○ Baseline QTc interval greater than or equal to 500 msec ○ Cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs ○ Hypersensitivity reaction to fingolimod or any of the excipients in Tascenso ODT. Observed reactions include rash, urticaria, and angioedema

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

REFERENCES

Number	Reference
1	Aubagio prescribing information. Genzyme Corporation. June 2024.
2	Avonex prescribing information. Biogen Inc. July 2023.
3	Bafiertam prescribing information. Banner Life Sciences LLC. December 2023.
4	Betaseron prescribing information. Bayer HealthCare Pharmaceuticals, Inc. July 2023.
5	Copaxone prescribing information. Teva Neuroscience, Inc. November 2023.
6	Extavia prescribing information. Novartis Pharmaceuticals Corporation. July 2023.
7	Gilenya prescribing information. Novartis Pharmaceuticals Corporation. June 2024.
8	Glatopa prescribing information. Sandoz Inc. December 2023.
9	Kesimpta prescribing information. Novartis Pharmaceuticals Corporation. April 2024.
10	Mavenclad prescribing information. EMD Serono, Inc. May 2024.
11	Mayzent prescribing information. Novartis Pharmaceuticals Corporation. June 2024.
12	Plegridy prescribing information. Biogen Inc. July 2023.
13	Rebif prescribing information. EMD Serono, Inc. July 2023.
14	Tecfidera prescribing information. Biogen Inc. April 2024.
15	Vumerity prescribing information. Biogen Inc. September 2024.
16	National Institute for Health and Care Excellence (NICE) Guideline. Multiple Sclerosis in Adults: Management (NG220). Published: 22 June 2022. Available at: https://www.nice.org.uk/guidance/ng220
17	McKenna A, Lin GA, Whittington MD, et al. Oral and Monoclonal Antibody Treatments for Relapsing Forms of Multiple Sclerosis: Effectiveness and Value. A Summary from the Institute for Clinical and Economic Review's (ICER) New England Comparative Effectiveness Public Advisory Council. J Manag Care Spec Pharm. 2023 Jul;29(7):10.18553.
18	Rae-Grant A, Day GS, Marrie RA, et al. Practice Guideline Recommendations Summary: Disease-Modifying Therapies for Adults with Multiple Sclerosis. Neurol. 2018 Apr;90(17):777-788.
19	Corboy JR, Weinshenker BG, Wingerchuk DM. Comment on 2018 American Academy of Neurology Guidelines on Disease-Modifying Therapies in MS. Neurol. 2018 Apri;90(24):1106-1112.
20	Reference no longer used.
21	Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of Multiple Sclerosis: 2017 Revisions of the McDonald Criteria. Lancet Neurol. 2018 Feb;17(2):162-173.
22	National Multiple Sclerosis Society 2017 McDonald MS Diagnostic Criteria. Available at: https://www.nationalmssociety.org/for-professionals/for-healthcare-professionals/diagnosing-ms/diagnostic-criteria-workup
23	MS International Federation. Types of MS. Last updated: 12th March 2022. Available at: https://www.msif.org/about-ms/types-of-ms/
24	Conway D, Cohen JA. Combination Therapy in Multiple Sclerosis. Lancet Neurol. 2010 Mar;9(3):299-308.
25	Freedman MS, Devonshire V, Duquette P, et al. Treatment Optimization in Multiple Sclerosis: Canadian MS Working Group Recommendations. Can J Neurol Sci. 2020 Jul;47(4):437-455.
26	Reference no longer used.

Number	Reference
27	Ponvory prescribing information. Janssen Pharmaceuticals, Inc. August 2023.
28	Reference no longer used.
29	Tascenso prescribing information. Handa Neuroscience, LLC. December 2022.
30	MS International Federation. Symptoms. Last updated: 25th October 2021. Available at: https://www.msif.org/about-ms/symptoms-of-ms/
31	National Institute for Health and Care Excellence (NICE). Ofatumumab for Treating Relapsing Multiple Sclerosis: Technology Appraisal Guidance (TA699). 2021 May. Available at: https://www.nice.org.uk/guidance/ta699

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 ; Tecfidera starter pack	dimethyl fumarate capsule delayed release ; dimethyl fumarate capsule dr starter pack	120 & 240 MG ; 120 MG ; 240 MG	M ; N ; O	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	N ; O ; Y		
Tascenso odt	fingolimod lauryl sulfate tablet disintegrating	0.25 MG ; 0.5 MG	M ; N ; O ; Y	N		
Copaxone	glatiramer acetate soln prefilled syringe	20 MG/ML ; 40 MG/ML	M ; N ; O	O ; Y		
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		
Ponvory ; Ponvory 14-day starter pack	ponesimod tab ; ponesimod tab starter pack	2-3-4-5-6-7-8-9 & 10 MG ; 20 MG	M ; N ; O ; Y	N		
Mayzent ; Mayzent starter pack	siponimod fumarate tab	0.25 MG ; 1 MG ; 2 MG	M ; N ; O ; Y	N		
Aubagio	teriflunomide tab	14 MG ; 7 MG	M ; N ; O	O ; Y		
Betaseron	interferon beta-	0.3 MG	M ; N ; O ; Y	N		
Extavia	interferon beta-	0.3 MG	M ; N ; O ; Y	N		

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	14 MG	30	Tablets	30	DAYS			
Aubagio	Teriflunomide Tab 7 MG	7 MG	30	Tablets	30	DAYS			
Avonex	Interferon Beta-1a IM Prefilled Syringe Kit 30 MCG/0.5ML	30 MCG/0.5 ML	1	Kit	28	DAYS			
Avonex pen	Interferon Beta-1a IM Auto-Injector Kit 30 MCG/0.5ML	30 MCG/0.5 ML	1	Kit	28	DAYS			
Bafiertam	Monomethyl Fumarate Capsule Delayed Release	95 MG	120	Capsules	30	DAYS			
Betaseron	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-	0.3 MG	15	Vials	30	DAYS			00078056912 ; 00078056961 ; 00078056999;
Gilenya	Fingolimod HCl Cap 0.25 MG (Base Equiv)	0.25 MG	30	Capsules	30	DAYS			
Gilenya	Fingolimod HCl Cap 0.5 MG (Base Equiv)	0.5 MG	30	Capsules	30	DAYS			
Kesimpta	Ofatumumab Soln Auto-Injector	20 MG/0.4 ML	1	Pen	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			
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			

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
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	1	Pack	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 pack	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			
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	30	Tablets	30	DAYS			
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.5 MG	30	Tablets	30	DAYS			
Tecfidera	Dimethyl Fumarate Capsule Delayed Release 120 MG	120 MG	56	Capsules	180	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
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	60	Capsules	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	Commercial ; HIM ; ResultsRx
Avonex	interferon beta-	30 MCG/0.5ML	Commercial ; HIM ; ResultsRx
Avonex pen	interferon beta-	30 MCG/0.5ML	Commercial ; HIM ; ResultsRx
Bafiertam	monomethyl fumarate capsule delayed release	95 MG	Commercial ; HIM ; ResultsRx
Betaseron	interferon beta-	0.3 MG	Commercial ; HIM ; ResultsRx
Copaxone	glatiramer acetate soln prefilled syringe	20 MG/ML ; 40 MG/ML	Commercial ; HIM ; ResultsRx
Extavia	interferon beta-	0.3 MG	Commercial ; HIM ; ResultsRx
Gilenya	fingolimod hcl cap	0.25 MG ; 0.5 MG	Commercial ; HIM ; ResultsRx
Kesimpta	ofatumumab soln auto-injector	20 MG/0.4ML	Commercial ; HIM ; ResultsRx
Mavenclad	cladribine tab therapy pack	10 MG	Commercial ; HIM ; ResultsRx
Mayzent ; Mayzent starter pack	siponimod fumarate tab	0.25 MG ; 1 MG ; 2 MG	Commercial ; HIM ; ResultsRx
Plegridy ; Plegridy starter pack	peginterferon beta-	125 MCG/0.5ML ; 63 & 94 MCG/0.5ML	Commercial ; HIM ; ResultsRx
Ponvory ; Ponvory 14-day starter pack	ponesimod tab ; ponesimod tab starter pack	2-3-4-5-6-7-8-9 & 10 MG ; 20 MG	Commercial ; HIM ; ResultsRx
Rebif ; Rebif titration pack	interferon beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG	Commercial ; HIM ; ResultsRx
Rebif rebidose ; Rebif rebidose titration	interferon beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6X8.8 & 6X22 MCG	Commercial ; HIM ; ResultsRx
Tascenso odt	fingolimod lauryl sulfate tablet disintegrating	0.25 MG ; 0.5 MG	Commercial ; HIM ; ResultsRx
Tecfidera ; Tecfidera starter pack	dimethyl fumarate capsule delayed release ; dimethyl fumarate capsule dr starter pack	120 & 240 MG ; 120 MG ; 240 MG	Commercial ; HIM ; ResultsRx
Vumerity	diroximel fumarate capsule delayed release	231 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

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

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

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Mavenclad	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** **Mavenclad** (cladribine) 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. BOTH 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. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. If the patient has been previously treated with the requested agent, BOTH of the following: 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**

Module	Clinical Criteria for Approval
	B. The patient has NOT completed 2 courses of the requested agent (one course consists of 2 cycles of 4-5 days each) **AND** 3. A complete CBC with differential including lymphocyte count has been performed **AND** 4. The lymphocyte count is within normal limits **AND** 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** 6. ONE of the following: A. The patient will NOT be using the requested agent with an additional disease modifying agent (DMA) for the requested indication (please refer to "MS Disease Modifying Agents (DMAs)" list in the "Contraindicated for Concomitant Therapy" table) **OR** B. BOTH of the following: 1. The patient is currently using the requested agent **AND** 2. There is support for the use of the additional DMA (e.g., relapse between cycles) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 8. The requested quantity (dose) does NOT exceed the FDA labeled maximum dose based on the patient's weight **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) NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 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** 2. The patient has had clinical benefit with the requested agent **AND** 3. A complete CBC with differential including lymphocyte count has been performed **AND** 4. The patient has a lymphocyte count of at least 800 cells/microliter **AND** 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** 6. ONE of the following: A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication (please refer to "MS Disease Modifying Agents (DMAs)" list in the "Contraindicated for Concomitant Therapy" table) **OR** B. There is support for the use of the additional DMA (e.g., relapse between cycles) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 8. It has been at least 35 weeks but not more than 67 weeks since the last dose of the requested agent **AND** 9. BOTH of the following: 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** B. The patient has NOT completed 2 courses with the requested agent (one course consists of 2 cycles of 4-5 days each) **AND** 10. The requested dose does NOT exceed the maximum FDA labeled dose for the patient's weight **Length of Approval:** 3 months

Module	Clinical Criteria for Approval
	NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria
MS Agents other than Mavenclad	

Preferred Agent(s)	Non-Preferred Agent(s)
Avonex (interferon β-1a) **Betaseron** (interferon β-1b) dimethyl fumarate fingolimod glatiramer **Glatopa** (glatiramer) **Kesimpta** (ofatumumab) **Mavenclad** (cladribine) **Mayzent** (siponimod) **Plegridy** (peginterferon β-1a) **Rebif** (interferon β-1a) teriflunomide **Vumerity** (diroximel fumarate) **Zeposia** (ozanimod)**	**Aubagio** (teriflunomide)* **Bafiertam** (monomethyl fumarate) **Copaxone** (glatiramer)* **Extavia** (interferon β-1b) **Gilenya** (fingolimod)* **Ponvory** (ponesimod) **Tascenso ODT** (fingolimod) **Tecfidera** (dimethyl fumarate)*

*generic available
**target in a different program

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
All target agents except the following are eligible for continuation of therapy: Brand Aubagio Brand Copaxone Brand Gilenya 0.5 mg Brand Tecfidera

      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 is at risk if therapy is changed **OR**
   B. BOTH of the following:
      1. ONE of the following:
         A. The patient has a diagnosis of a relapsing form of MS AND ALL of the following:
            1. ONE of the following:
               A. The requested agent is a preferred agent **OR**
               B. The requested agent is a non-preferred agent AND ONE of the following:
                  1. The patient is 17 years of age or younger AND ONE of the following:
                     A. The request is for one of the following brand agents that does NOT have an equipotent preferred generic strength **OR**

Agents that do NOT have an equipotent preferred generic strength

Module	Clinical Criteria for Approval
	Gilenya 0.25 mg Tascenso ODT 0.25 mg B. The patient has tried and had an inadequate response to generic fingolimod (medical records required) **OR** C. The patient has an intolerance (defined as an intolerance to the drug or its excipients, NOT to the route of administration) or hypersensitivity to generic fingolimod (medical records required) **OR** D. The patient has an FDA labeled contraindication to generic fingolimod (medical records required) **OR** E. If the requested agent is Tascenso ODT 0.5 mg, there is support for the use of the requested agent over generic fingolimod (e.g., swallowing difficulties) **OR** 2. The patient is 18 years of age or older AND BOTH of the following: A. ONE of the following: 1. The patient has tried and had an inadequate response to TWO preferred agents that are FDA labeled for the treatment of the requested indication (medical records required) **OR** 2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, NOT to the route of administration) or hypersensitivity to TWO preferred agents FDA labeled for the treatment of the requested indication **OR** 3. The patient has an FDA labeled contraindication to ALL preferred agents FDA labeled for the treatment of the requested indication **AND** B. If the requested agent is Tascenso ODT 0.5 mg, ONE of the following: 1. The patient has tried and had an inadequate response to generic fingolimod (medical records required) **OR** 2. The patient has an intolerance or hypersensitivity to generic

Module	Clinical Criteria for Approval

fingolimod that is NOT expected to occur with the requested agent **OR**

3. The patient has an FDA labeled contraindication to generic fingolimod that is NOT expected to occur with the requested agent **OR**
4. There is support for the use of the requested agent over generic fingolimod (e.g., swallowing difficulties) **OR**

3. The patient has highly active MS disease activity AND BOTH of the following: (medical records including chart notes required)
   A. The patient has greater than or equal to 2 relapses in the previous year **AND**
   B. ONE of the following:
      1. The patient has greater than or equal to 1 gadolinium enhancing lesion of MRI **OR**
      2. The patient has significant increase in T2 lesion load compared with a previous MRI **OR**
4. The patient has been treated with at least 3 MS agents from different drug classes (medical records including chart notes required) (see MS disease modifying agents drug class table) **AND**

2. If the requested agent is Aubagio (teriflunomide), the prescriber has obtained transaminase and bilirubin levels within 6 months prior to initiating treatment **AND**
3. If the requested agent is Gilenya (fingolimod) or Tascenso ODT the prescriber has performed an electrocardiogram within 6 months prior to initiating treatment **OR**

B. The patient has another FDA labeled indication for the requested agent and route of administration **AND**

2. If the patient has an FDA labeled indication, then ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. There is support for using the requested agent for the patient's age for the requested indication **AND**

2. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following (medical records required):

Non-Preferred Agents	Generic Equivalent
Aubagio	teriflunomide
Copaxone	Glatopa/glatiramer
Gilenya 0.5 mg	fingolimod
Tecfidera	dimethyl fumarate

Module	Clinical Criteria for Approval

A. The patient has an intolerance or hypersensitivity to the generic equivalent that is not expected to occur with the brand agent **OR**
B. The patient has an FDA labeled contraindication to the generic equivalent that is not expected to occur with the brand agent **OR**
C. There is support for the use of the brand agent over the generic equivalent **AND**

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**
4. ONE of the following:
   A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication (please refer to "MS Disease Modifying Agents (DMAs)" list in the "Contraindicated for Concomitant Therapy" table) **OR**
   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:
      1. The requested agent will be used in combination with Mavenclad (cladribine) **AND**
      2. There is support for the use of the requested agent in combination with Mavenclad (e.g., relapse between cycles of Mavenclad) **AND**
5. The patient does NOT have any FDA labeled contraindications to the requested agent

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.

NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

FDA Labeled Indication	FDA Approved Agent(s)
Clinically Isolated Syndrome (CIS)	Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, 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

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

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**
2. If the requested agent is a brand product with a generic equivalent (listed below) AND ONE of the following:

Non-preferred Agents	Generic Equivalent
Aubagio	teriflunomide

Module	Clinical Criteria for Approval
	<table><tr><td>Copaxone</td><td>Glatopa/glatiramer</td></tr><tr><td>Gilenya 0.5 mg</td><td>fingolimod</td></tr><tr><td>Tecfidera</td><td>dimethyl fumarate</td></tr></table> A. The patient has an intolerance to hypersensitivity to the generic equivalent that is NOT expected to occur with the requested agent **OR** B. The patient has an FDA labeled contraindication to the generic equivalent that is NOT expected to occur with the requested agent **OR** C. There is support for the use of the requested agent over the generic equivalent **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. 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** 5. ONE of the following: A. The patient will NOT be using the requested agent in combination with an additional disease modifying agent (DMA) for the requested indication (please refer to "MS Disease Modifying Agents (DMAs)" list in the "Contraindicated for Concomitant Therapy" table) **OR** B. The patient will be using the requested agent in combination with another DMA used for the requested indication AND BOTH of the following: 1. The requested agent will be used in combination with Mavenclad (cladribine) AND 2. There is support for the use of the requested agent in combination with Mavenclad (e.g., relapse between cycles of Mavenclad) **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA Mavenclad	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** 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 **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
Universal QL - excluding Mavenclad	**Quantity limit for Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**

Module	Clinical Criteria for Approval
	2. There is support why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **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

CLASS AGENTS

Class	Class Drug Agents
Class Ia antiarrhythmics	
Class Ia antiarrhythmics	Pronestyl (procainamide)
Class Ia antiarrhythmics	quinidine
Class Ia antiarrhythmics	NORPACE*Disopyramide Phosphate Cap
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
MS Disease Modifying Agents drug class: CD20 monoclonal antibody	OCREVUS*Ocrelizumab Soln For IV Infusion
MS Disease Modifying Agents drug class: CD20 monoclonal antibody	OCREVUS*ZUNOVO*ocrelizumab-hyaluronidase-ocsq inj
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

Class	Class Drug Agents
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
MS Disease Modifying Agents (DMAs) **Aubagio** (teriflunomide) **Avonex** (interferon β-1a) **Bafiertam** (monomethyl fumarate) **Betaseron** (interferon β-1b) **Briumvi** (ublituximab-xiiy) **Copaxone** (glatiramer) dimethyl fumarate **Extavia** (interferon β-1b) fingolimod **Gilenya** (fingolimod) glatiramer **Glatopa** (glatiramer) **Kesimpta** (ofatumumab) **Lemtrada** (alemtuzumab) **Mavenclad** (cladribine) **Mayzent** (siponimod) **Ocrevus** (ocrelizumab) **Ocrevus Zunovo** (ocrelizumab-hyaluronidase) **Plegridy** (peginterferon β-1a) **Ponvory** (ponesimod) **Rebif** (interferon β-1a) **Tascenso ODT** (fingolimod) **Tecfidera** (dimethyl fumarate) teriflunomide **Tysabri** (natalizumab)

Contraindicated as Concomitant Therapy
Vumerity (diroximel fumarate) **Zeposia** (ozanimod)