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).

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

For Select formulary (Commercial), Glatopa is excluded.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
1/16/2023	

FDA APPROVED 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		1
Avonex® (interferon β-1a) Injection for intramuscular use	Treatment of relapsing forms of 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, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults		4
Copaxone®[a]	Treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	a- Generic available	5

Agent(s)	FDA Indication(s)	Notes	Ref#
(glatiramer acetate)[a] Injection for subcutaneous use			
Extavia® (interferon b-1b) Injection for subcutaneous use	Treatment of relapsing forms of Multiple Sclerosis, 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 equivalent 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 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 b-1a) 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		12

Agent(s)	FDA Indication(s)	Notes	Ref#
Injection for intramuscular use			
Ponvory™ (Ponesomid) 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 b-1a) 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 ODT™ (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 pediatric patients 10 years of age and older and weighing less than or equal to 40 kg		29
Tecfidera®[a] (dimethyl fumarate)[a] Capsule	Treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	a- 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, impaired mobility, mood and cognitive changes, pain and other sensory problems, visual disturbances, and elimination dysfunction),

	resulting in a significant impact on quality of life for patients and their families. Diagnosis of MS is primarily based on clinical presentation. The core requirement for the diagnosis is demonstration of CNS lesion dissemination and presence of symptoms such as visual loss, motor function loss, difficulty with balancing, and vertigo. There are currently four major types of MS: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).(23)
Clinically isolated syndrome	CIS is a first episode of neurologic symptoms caused by inflammation and demyelination in the central nervous system. The episode, which by definition must last for at least 24 hours, is characteristic of multiple sclerosis but does not yet meet the criteria for a diagnosis of MS because people who experience a CIS may or may not go on to develop MS. When CIS is accompanied by lesions on a brain MRI that are similar to those seen in MS, the person has a high likelihood of a second episode of neurologic symptoms and diagnosis of relapsing-remitting MS. When CIS is not accompanied by MS-like lesions on brain MRI, the person has a much lower likelihood of developing MS.(23) When caused by an acute inflammatory demyelinating event, approximately 85% of all patients subsequently develop MS. The relationship between conventional brain MRI features and the short-term risk of CIS patients developing definite MS has been assessed by several studies and allows for the diagnosis of MS based on the 2017 McDonald criteria. However, in CIS patients with initial multifocal clinical symptom presentation the abnormal MRI did not stratify the risk for clinically definite disease conversion. (28) CIS cohort studies spanning 7 through 20 years of follow-up investigated the long-term risk of MS development and found conversions rates of 65-80% for patients with an abnormal conventional MRI and 8-20% for those with an inconspicuous baseline MRI. (28)
Relapsing remitting multiple sclerosis (RRMS)	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 (SPMS).(23)
Secondary progressive multiple sclerosis (SPMS)	SPMS begins as RRMS, but over time the disease enters a stage of steady deterioration in function, unrelated to acute attacks. Typically, when SPMS stage is reached, the relapse rate is also reduced. Prior to the era of disease-modifying agents (DMAs), approximately half of patients diagnosed with relapsing MS would progress to SPMS by 10 years, and 80-90% would do so by 25 years.(23)
2017 McDonald Criteria for the diagnosis of Multiple Sclerosis:	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)

Clinical Presentation	**Additional Data needed to make MS diagnosis**
In a person with a typical attack/CIS at onset	
≥ 2 attacks and objective clinical evidence of ≥ 2 lesions OR ≥ 2 attacks and objective clinical evidence of 1 lesion with historical evidence of prior attack involving lesion in different location	None. Dissemination in space[a] and dissemination in time[b] have been met
≥ 2 attacks and objective clinical evidence of 1 lesion	**ONE** of these criteria: Additional clinical attack implicating different CNS site OR ≥ 1 symptomatic or asymptomatic MS-typical T2 lesions in ≥ 2 areas of CNS: periventricular, juxtacortical/cortical, infratentorial, or spinal cord
1 attack and objective clinical evidence of ≥ 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 ≥ 1 MS-Typical symptomatic or asymptomatic T2 lesions in ≥ 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

a - 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)

b - 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) There is a subgroup of RRMS patients who have a more aggressive disease course marked by a rapid accumulation of physical and cognitive deficit, despite treatment with 1 or more DMTs. In the past, this disease phenotype was called aggressive MS; it is now called highly active MS. It is generally agreed that the severe nature of this phenotype requires different treatment decisions. There is no consensus on the definition of highly active MS or the treatment algorithm.(26) 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.(20)
	
	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.(19)
	
	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	• ≥ 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 ≤ 1 point at 6 months unless baseline EDSS >5.5	• Incomplete recovery • Functional impairment • If EDSS at baseline was 0 then > 1.5 point change from baseline • If EDSS > 0 but less than 5.5 at baseline then > 1 point change at 6 months • If EDSS > 5.5 any change would be a major concern
MRI	• One new lesion	• ≥ 3 new lesions during treatment excluding spinal cord lesions • > 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)
Safety (1-15)	• **Aubagio** (teriflunomide) has a black box warning with the following: o 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 o 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: o Severe hepatic impairment o Pregnancy o Hypersensitivity reaction to teriflunomide, leflunomide, or any of the inactive ingredients in Aubagio o Current leflunomide treatment • **Avonex** (interferon β-1a) is contraindicated in: o History of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation • **Bafiertam** (monomethyl fumarate) is contraindicated in: o Known hypersensitivity to monomethyl fumarate, dimethyl fumarate, diroximel fumarate, or any of the excipients of Bafiertam o Co-administration with dimethyl fumarate or diroximel fumarate • **Betaseron** (interferon β-1b) is contraindicated in: o History of hypersensitivity to natural or recombinant interferon beta, albumin or mannitol

	• **Copaxone** (glatiramer) is contraindicated in: o Known hypersensitivity to glatiramer acetate or mannitol • **Extavia** (interferon β-1b) is contraindicated in: o History of hypersensitivity to natural or recombinant interferon beta, Albumin (Human), USP, or any other component of the formulation • **Gilenya** (fingolimod) is contraindicated in: o Recent myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure with hospitalization, or Class III/IV heart failure o History of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome, unless patient has a pacemaker o Baseline QTc interval greater than or equal to 500 msec o Treatment with Class Ia or Class III anti-arrhythmic drugs o Hypersensitivity to fingolimod or its excipients • **Glatopa** (glatiramer) is contraindicated in: o Known hypersensitivity to glatiramer acetate or mannitol • **Kesimpta** (ofatumumab) is contraindicated in: o Active HBV infection • **Mavenclad** (cladribine) contains a black box warning with the following: o 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 o 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: o Patients with current malignancy o 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 o HIV infection o Active chronic infections (e.g., hepatitis or tuberculosis) o History of hypersensitivity to cladribine o Women intending to breastfeed on a Mavenclad treatment day and for 10 days after the last dose • **Mayzent** (siponimod) is contraindicated in: o Patients with a CYP2C9 *3/*3 genotype o 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: ○ History of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of the formulation • **Ponvory** (ponesimod) is contraindicated in: ○ 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: ○ History of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation • **Tascenso** (fingolimod) is contraindicated in: ○ Patients who have in the last 6 months experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization or Class III/IV heart failure ○ Patients who have a history or presence of Mobitz Type II second-degree or third-degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker ○ Patients who have a baseline QTc interval ≥ 500 msec ○ Patients who have cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs ○ Patients who have had a 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: ○ Known hypersensitivity to dimethyl fumarate or any of the excipients of Tecfidera • **Vumerity** (diroximel fumarate) is contraindicated in: ○ Known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of Vumerity ○ Co-administration with dimethyl fumarate For additional clinical information see Prime Therapeutics Formulary Chapter 9.6C Multiple Sclerosis Agents.

REFERENCES

Number	Reference
1	Aubagio prescribing information. Genzyme Corporation. April 2021.
2	Avonex prescribing information. Biogen, Inc. March 2020.
3	Bafiertam prescribing information. Banner Life Sciences LLC. August 2020.

Number	Reference
4	Betaseron prescribing information. Bayer HealthCare Pharmaceuticals, Inc. March 2021.
5	Copaxone prescribing information. Teva Neurosciences, Inc. July 2020.
6	Extavia prescribing information. Novartis Pharmaceuticals Corporation. October 2020.
7	Gilenya prescribing information. Novartis Pharmaceuticals Corporation. December 2019.
8	Glatopa prescribing information. Sandoz. November 2020.
9	Kesimpta prescribing information. Novartis Pharmaceuticals Corporation. August 2020.
10	Mavenclad prescribing information. EMD Serono, Inc. March 2019.
11	Mayzent prescribing information. Novartis Pharmaceuticals Corporation. August 2021.
12	Plegridy prescribing information. Biogen, Inc. January 2021.
13	Rebif prescribing information. EMD Serono, Inc. May 2020.
14	Tecfidera prescribing information. Biogen, Inc. January 2021.
15	Vumerity prescribing information. Alkermes Inc. January 2021.
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27	Ponvory Prescribing Information. Janssen Pharmaceuticals, Inc. April 2021.
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.
29	Tascenso prescribing information. Handa Neuroscience, LLC. December 2021.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Aubagio	Teriflunomide Tab	14 MG ; 7 MG	M ; N ; O ; Y	N	1. Preferred	
Avonex	Interferon Beta-	30 ; 30 MCG/0.5ML	M ; N ; O ; Y	N	1. Preferred	
Avonex pen	Interferon Beta-	30 ; 30 MCG/0.5ML	M ; N ; O ; Y	N	1. Preferred	
BETASERON	Interferon Beta-	0.3 MG	M ; N ; O ; Y	N	1. Preferred	
Gilenya	Fingolimod HCl Cap	0.25 MG ; 0.5 MG	M ; N ; O	N ; O ; Y	1. Preferred	12-01-2022
Kesimpta	Ofatumumab Soln Auto-Injector	20 MG/0.4ML	M ; N ; O ; Y	N	1. Preferred	
Mavenclad	Cladribine Tab Therapy Pack	10 ; 10 MG	M ; N ; O ; Y	N	1. Preferred	
Mayzent ; Mayzent starter pack	Siponimod Fumarate Tab	0.25 MG ; 1 MG ; 2 MG	M ; N ; O ; Y	N	1. Preferred	
Plegridy ; Plegridy starter pack	Peginterferon Beta-	125 MCG/0.5ML ; 63 MCG/0.5ML	M ; N ; O ; Y	N	1. Preferred	
Rebif rebidose ; Rebif rebidose titration	Interferon Beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6 MCG	M ; N ; O ; Y	N	1. Preferred	
Rebif ; Rebif titration pack	Interferon Beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6 MCG	M ; N ; O ; Y	N	1. Preferred	
Vumerity	Diroximel Fumarate Capsule Delayed Release	231 MG	M ; N ; O ; Y	N	1. Preferred	
Bafiertam	Monomethyl Fumarate Capsule Delayed Release	95 MG	M ; N ; O ; Y	N	2. Non-Preferred	
EXTAVIA	Interferon Beta-	0.3 MG	M ; N ; O ; Y	N	2. Non-Preferred	
COPAXONE ; GLATOPA	Glatiramer Acetate Soln Prefilled Syringe	20 MG/ML ; 40 MG/ML	M ; N ; O ; Y	O ; Y	2. Non-Preferred	
Tecfidera ; Tecfidera starter pack	Dimethyl Fumarate Capsule DR Starter Pack ; Dimethyl Fumarate Capsule Delayed Release	120 MG ; 240 MG	M ; N ; O	O ; Y	2. Non-Preferred	
Ponvory ; Ponvory 14-day starter pa	Ponesimod Tab ; Ponesimod Tab Starter Pack	2 & 10 MG ; 20 MG	M ; N ; O ; Y	N	2. Non-Preferred	
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.25 MG ; 0.5 MG	M ; N ; O ; Y	N	2. Non-Preferred	

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.5 MG	30.0	TABS	30	Days				01-16-2023

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Aubagio	Teriflunomide Tab 14 MG	14 MG	30.0	TABS	30	Days				
Aubagio	Teriflunomide Tab 7 MG	7 MG	30.0	TABS	30	Days				
Avonex pen	Interferon Beta-1a IM Auto-Injector Kit 30 MCG/0.5ML	30 ; 30 MCG/0.5 ML	1.0	KIT	28	Days				
Avonex pen	Interferon Beta-1a IM Auto-Injector Kit 30 MCG/0.5ML	30 ; 30 MCG/0.5 ML	1.0	KIT	28	Days				
Avonex	Interferon Beta-1a IM Prefilled Syringe Kit 30 MCG/0.5ML	30 ; 30 MCG/0.5 ML	1.0	KIT	28	Days				
Avonex	Interferon Beta-1a IM Prefilled Syringe Kit 30 MCG/0.5ML	30 ; 30 MCG/0.5 ML	1.0	KIT	28	Days				
Bafiertam	Monomethyl Fumarate Capsule Delayed Release	95 MG	120.0	CAPS	30	Days				
Betaseron	Interferon Beta-	0.3 MG	14.0	VIALS	28	Days			50419-0524-01 ; 50419-0524-35	
Extavia	Interferon Beta-	0.3 MG	15.0	VIALS	30	Days			00078-0569-12 ; 00078-0569-61 ; 00078-0569-99	
Copaxone ; Glatiramer acetate	Glatiramer Acetate Soln Prefilled Syringe	20 MG/ML	30.0	SYRNGS	30	Days			00378-6960-32 ; 00378-6960-93 ; 68546-0317-30	
Copaxone ; Glatiramer acetate	Glatiramer Acetate Soln Prefilled Syringe	40 MG/ML	12.0	SYRNGS	28	Days			00378-6961-12 ; 00378-6961-32 ; 68546-0325-06 ; 68546-0325-12	
Gilenya	Fingolimod HCl Cap 0.25 MG (Base Equiv)	0.25 MG	30.0	CAPS	30	Days				
Gilenya	Fingolimod HCl Cap 0.5 MG (Base Equiv)	0.5 MG	30.0	CAPS	30	Days				
Glatopa	Glatiramer Acetate Soln Prefilled Syringe	20 MG/ML	30.0	SYRNGS	30	Days			00781-3234-34 ; 00781-3234-71	
Glatopa	Glatiramer Acetate Soln Prefilled Syringe	40 MG/ML	12.0	SYRNGS	28	Days			00781-3250-71 ; 00781-3250-89	

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Kesimpta	Ofatumumab Soln Auto-Injector	20 MG/0.4 ML	1.0	PEN	28	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (10 Tabs)	10 MG	20.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (4 Tabs)	10 ; 10 MG	8.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (5 Tabs)	10 ; 10 MG	10.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (6 Tabs)	10 ; 10 MG	12.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (7 Tabs)	10 ; 10 MG	14.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (8 Tabs)	10 ; 10 MG	8.0	TABS	301	Days				
Mavenclad	Cladribine Tab Therapy Pack 10 MG (9 Tabs)	10 ; 10 MG	9.0	TABS	301	Days				
Mayzent starter pack	Siponimod Fumarate Tab 0.25 MG (12) Starter Pack	0.25 MG	12.0	TABS	180	Days				
Mayzent starter pack	Siponimod Fumarate Tab	0.25 MG	1.0	PACK	180	Days				
Mayzent	Siponimod Fumarate Tab 0.25 MG (Base Equiv)	0.25 MG	120.0	TABS	30	Days				
Mayzent	Siponimod Fumarate Tab	1 MG	30.0	TABS	30	Days				
Mayzent	Siponimod Fumarate Tab 2 MG (Base Equiv)	2 MG	30.0	TABS	30	Days				
Plegridy starter pack	Peginterferon Beta-1a Soln Pen-inj 63 & 94 MCG/0.5ML Pack	63 MCG/0.5 ML	1.0	KIT	180	Days				
Plegridy starter pack	Peginterferon Beta-1a Soln Pref Syr 63 & 94 MCG/0.5ML Pack	63 MCG/0.5 ML	1.0	KIT	180	Days				
Plegridy	Peginterferon Beta-	125 MCG/0.5 ML	2.0	SYRNGS	28	Days				
Plegridy	Peginterferon Beta-1a Soln Pen-injector 125 MCG/0.5ML	125 MCG/0.5 ML	2.0	PENS	28	Days				
Plegridy	Peginterferon Beta-1a Soln Prefilled Syringe 125 MCG/0.5ML	125 MCG/0.5 ML	2.0	SYRNGS	28	Days				
Ponvory 14-day starter pa	Ponesimod Tab Starter Pack	2 & 10 MG	14.0	TABS	180	Days				
Ponvory	Ponesimod Tab	20 MG	30.0	TABS	30	Days				
Rebif rebidose	Interferon Beta-1a Soln Auto-Inj 22 MCG/0.5ML (12MU/ML)	22 MCG/0.5 ML	12.0	SYRNGS	28	Days				

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Rebif rebidose	Interferon Beta-1a Soln Auto-inj 44 MCG/0.5ML (24MU/ML)	44 MCG/0.5 ML	12.0	SYRNGS	28	Days				
Rebif titration pack	Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML	6 MCG	1.0	KIT	180	Days				
Rebif titration pack	Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML	6 MCG	1.0	KIT	180	Days				
Rebif	Interferon Beta-1a Soln Pref Syr 22 MCG/0.5ML (12MU/ML)	22 MCG/0.5 ML	12.0	SYRNGS	28	Days				
Rebif	Interferon Beta-1a Soln Pref Syr 44 MCG/0.5ML (24MU/ML)	44 MCG/0.5 ML	12.0	SYRNGS	28	Days				
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.25 MG	30.0	TABS	30	Days				
Tecfidera starter pack	Dimethyl Fumarate Capsule DR Starter Pack 120 MG & 240 MG	120 MG	60.0	CAPS	180	Days				
Tecfidera	Dimethyl Fumarate Capsule Delayed Release 120 MG	120 MG	56.0	CAPS	180	Days				
Tecfidera	Dimethyl Fumarate Capsule Delayed Release 240 MG	240 MG	60.0	CAPS	30	Days				
Vumerity	Diroximel Fumarate Capsule Delayed Release 231 MG	231 MG	120.0	CAPS	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
Avonex	Interferon Beta-	30 ; 30 MCG/0.5ML	
Avonex pen	Interferon Beta-	30 ; 30 MCG/0.5ML	Commercial ; HIM
Bafiertam	Monomethyl Fumarate Capsule Delayed Release	95 MG	Commercial ; HIM
BETASERON	Interferon Beta-	0.3 MG	Commercial ; HIM
EXTAVIA	Interferon Beta-	0.3 MG	Commercial ; HIM
COPAXONE ; GLATOPA	Glatiramer Acetate Soln Prefilled Syringe	20 MG/ML ; 40 MG/ML	Commercial ; HIM
Tecfidera ; Tecfidera starter pack	Dimethyl Fumarate Capsule DR Starter Pack ; Dimethyl Fumarate Capsule Delayed Release	120 MG ; 240 MG	Commercial ; HIM
Gilenya	Fingolimod HCl Cap	0.25 MG ; 0.5 MG	Commercial ; HIM
Kesimpta	Ofatumumab Soln Auto-Injector	20 MG/0.4ML	Commercial ; HIM
Mavenclad	Cladribine Tab Therapy Pack	10 ; 10 MG	Commercial ; HIM
Mayzent ; Mayzent starter pack	Siponimod Fumarate Tab	0.25 MG ; 1 MG ; 2 MG	Commercial ; HIM
Plegridy ; Plegridy starter pack	Peginterferon Beta-	125 MCG/0.5ML ; 63 MCG/0.5ML	Commercial ; HIM
Ponvory ; Ponvory 14-day starter pa	Ponesimod Tab ; Ponesimod Tab Starter Pack	2 & 10 MG ; 20 MG	Commercial ; HIM

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Rebif rebidose ; Rebif rebidose titration	Interferon Beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6 MCG	Commercial ; HIM
Rebif ; Rebif titration pack	Interferon Beta-	22 MCG/0.5ML ; 44 MCG/0.5ML ; 6 MCG	Commercial ; HIM
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.25 MG ; 0.5 MG	Commercial ; HIM
Vumerity	Diroximel Fumarate Capsule Delayed Release	231 MG	Commercial ; HIM

CLIENT SUMMARY – QUANTITY LIMITS

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

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Plegridy starter pack	Peginterferon Beta-1a Soln Pref Syr 63 & 94 MCG/0.5ML Pack	63 MCG/0.5ML	Commercial ; HIM
Plegridy	Peginterferon Beta-	125 MCG/0.5ML	Commercial ; HIM
Plegridy	Peginterferon Beta-1a Soln Pen-injector 125 MCG/0.5ML	125 MCG/0.5ML	Commercial ; HIM
Plegridy	Peginterferon Beta-1a Soln Prefilled Syringe 125 MCG/0.5ML	125 MCG/0.5ML	Commercial ; HIM
Ponvory 14-day starter pa	Ponesimod Tab Starter Pack	2 & 10 MG	Commercial ; HIM
Ponvory	Ponesimod Tab	20 MG	Commercial ; HIM
Rebif rebidose	Interferon Beta-1a Soln Auto-Inj 22 MCG/0.5ML (12MU/ML)	22 MCG/0.5ML	Commercial ; HIM
Rebif rebidose	Interferon Beta-1a Soln Auto-inj 44 MCG/0.5ML (24MU/ML)	44 MCG/0.5ML	Commercial ; HIM
Rebif titration pack	Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML	6 MCG	Commercial ; HIM
Rebif titration pack	Interferon Beta-1a Pref Syr 6X8.8 MCG/0.2ML & 6X22 MCG/0.5ML	6 MCG	Commercial ; HIM
Rebif	Interferon Beta-1a Soln Pref Syr 22 MCG/0.5ML (12MU/ML)	22 MCG/0.5ML	Commercial ; HIM
Rebif	Interferon Beta-1a Soln Pref Syr 44 MCG/0.5ML (24MU/ML)	44 MCG/0.5ML	Commercial ; HIM
Tascenso odt	Fingolimod Lauryl Sulfate Tablet Disintegrating	0.25 MG	Commercial ; HIM
Tecfidera starter pack	Dimethyl Fumarate Capsule DR Starter Pack 120 MG & 240 MG	120 MG	Commercial ; HIM
Tecfidera	Dimethyl Fumarate Capsule Delayed Release 120 MG	120 MG	Commercial ; HIM
Tecfidera	Dimethyl Fumarate Capsule Delayed Release 240 MG	240 MG	Commercial ; HIM
Vumerity	Diroximel Fumarate Capsule Delayed Release 231 MG	231 MG	Commercial ; HIM

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Through Preferred - Mavenclad	**TARGET AGENT(S)** **Preferred generic agent(s)** **Dimethyl fumarate** **Fingolimod** **Glatiramer** **Preferred brand agent(s)** **Aubagio** (teriflunomide) **Avonex** (interferon b-1a) **Betaseron** (interferon b-1b) **Gilenya** (fingolimod) **Kesimpta** (ofatumumab) **Mavenclad** (cladribine) **Mayzent** (siponimod) **Plegridy** (peginterferon b-1a) **Rebif** (interferon b-1a) **Vumerity** (diroximel fumarate) **Non-Preferred agent(s)** **Bafiertam** (monomethyl fumarate)

Module	Clinical Criteria for Approval
	Copaxone (glatiramer) **Extavia** (interferon b-1b) **Glatopa** (glatiramer) **Ponvory** (ponesimod) **Tascenso ODT** (fingolimod) **Tecfidera** (dimethyl fumarate) **Mavenclad (cladribine) Initial Evaluation** **Mavenclad (cladribine)** 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: 1. Information has been provided that 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**

Agents Eligible for Continuation of Therapy
Mavenclad (cladribine)

B. The patient has an FDA approved diagnosis for the requested agent **AND**
2. ONE of the following:
A. The patient has highly active MS disease activity AND BOTH of the following:
1. The patient has greater than or equal to 2 relapses in the previous year **AND**
2. ONE of the following:
A. The patient has greater than or equal to 1 gadolinium enhancing lesion on MRI **OR**
B. The patient has significant increase in T2 lesion load compared with a previous MRI **OR**
B. The patient has NOT been previously treated with the requested agent AND ONE of the following:
1. The patient has been treated with at least 3 MS agents from different drug classes **OR**
2. The patient has tried and had had an inadequate response to ONE preferred generic agent FDA approved for the treatment of the requested indication **OR**
3. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to ONE preferred generic agent FDA approved for the treatment of the requested indication **OR**
4. The patient has FDA labeled contraindication to ALL preferred generic agents FDA approved for the treatment of the requested indication **OR**
5. The prescriber has provided information in support of using the requested agent over ALL preferred generic agents FDA approved for the treatment of the requested indication **OR**
C. The patient has been previously treated with the requested agent AND BOTH of the following:
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**
2. 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**

Module	Clinical Criteria for Approval
	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 **OR** B. BOTH of the following: 1. The patient is currently using the requested agent **AND** 2. Information has been provided supporting the use of the additional DMA (e.g., relapse between cycles) **AND** 7. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 8. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 9. 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 section below. **Mavenclad (cladribine) Renewal Evaluation** **Mavenclad (cladribine)** 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 **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/µL 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 **OR** B. Information has been provided supporting 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) **AND** 10. The requested dose does not exceed the maximum FDA labeled dose for the patient's weight

Module	Clinical Criteria for Approval
	Length of Approval: 3 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.
Through Preferred - Target Agent(s) (excluding Mavenclad [cladribine])	**TARGET AGENT(S)** **Preferred generic agent(s)** **Dimethyl fumarate** **Fingolimod** **Glatiramer** **Preferred brand agent(s)** **Aubagio** (teriflunomide) **Avonex** (interferon b-1a) **Betaseron** (interferon b-1b) **Gilenya** (fingolimod) **Kesimpta** (ofatumumab) **Mavenclad** (cladribine) **Mayzent** (siponimod) **Plegridy** (peginterferon b-1a) **Rebif** (interferon b-1a) **Vumerity** (diroximel fumarate) **Non-Preferred agent(s)** **Bafiertam** (monomethyl fumarate) **Copaxone** (glatiramer) **Extavia** (interferon b-1b) **Glatopa** (glatiramer) **Ponvory** (ponesimod) **Tascenso ODT** (fingolimod) **Tecfidera** (dimethyl fumarate) **Initial Evaluation** **Target Agent(s) (excluding Mavenclad [cladribine])** 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: 1. Information has been provided that 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** **Agents Eligible for Continuation of Therapy** All target agents except the following are eligible for continuation of therapy: Brand Copaxone

Module	Clinical Criteria for Approval
	Glatopa Brand Tecfidera

B. The patient has a diagnosis of a relapsing form of MS AND ALL of the following:
   1. The patient has an FDA labeled indication for the requested agent **AND**
   2. ONE of the following:
      A. The patient has a diagnosis of clinically isolated syndrome (CIS) AND ALL of the following:
         1. The patient had a single event that lasted at least 24 hours **AND**
         2. The event was not due to fever or infection **AND**
         3. The patient has MS-like brain lesion(s) confirmed by magnetic resonance imaging (MRI) **OR**
      B. The patient has a diagnosis of relapsing remitting multiple sclerosis (RRMS) or secondary progressive multiple sclerosis (SPMS) **AND**
   3. ONE of the following:
      A. The requested agent is a preferred generic agent **OR**
      B. The requested agent is a preferred brand agent AND ONE of the following:
         1. The patient has highly active MS disease activity AND BOTH of the following:
            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**
         2. The patient has been treated with at least 3 MS agents from different drug classes **OR**
         3. The patient has tried and had an inadequate response to ONE preferred generic agent FDA approved for the treatment of the requested indication **OR**
         4. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to ONE preferred generic agent FDA approved for the treatment of the requested indication **OR**
         5. The patient has an FDA labeled contraindication to ALL preferred generic agents FDA approved for the treatment of the requested indication **OR**
         6. The prescriber has provided information in support of using the requested agent over ALL preferred generic agents FDA approved for the treatment of the requested indication **OR**
      C. The requested agent is a non-preferred agent AND BOTH of the following:
         1. ONE of the following:
            A. The patient has tried and had an inadequate response to ONE preferred generic agent FDA approved for the treatment of the requested indication (medical records required) **OR**
            B. The patient has an intolerance (defined as an intolerance to drug or its excipients, not to the route of administration) or hypersensitivity to ONE preferred generic agent FDA approved for the requested indication **OR**

Module	Clinical Criteria for Approval

C. The patient has an FDA labeled contraindication to ALL preferred generic agents FDA approved for the requested indication **AND**

2. ONE of the following:
   A. The patient has tried and had an inadequate response to ONE preferred brand agent or Zeposia (ozanimod) that is FDA approved for the treatment of the requested indication **OR**
   B. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to ONE preferred brand agent or Zeposia (ozanimod) FDA approved for the treatment of the requested indication **OR**
   C. The patient has an FDA labeled contraindication to ALL preferred brand agents AND Zeposia (ozanimod) FDA approved for the treatment of the requested indication **OR**

D. The patient has highly active MS disease activity AND BOTH of the following: (medical records including chart notes required)
   1. The patient has greater than or equal to 2 relapses in the previous year **AND**
   2. ONE of the following:
      A. The patient has greater than or equal to 1 gadolinium enhancing lesion of MRI **OR**
      B. The patient has significant increase in T2 lesion load compared with a previous MRI **OR**

E. The patient has been treated with at least 3 MS agents from different drug classes (medical records including chart notes required) **AND**

4. If the requested agent is Aubagio, the prescriber has obtained transaminase and bilirubin levels within 6 months prior to initiating treatment **AND**
5. If the requested agent is Gilenya the prescriber has performed an electrocardiogram within 6 months prior to initiating treatment **AND**

2. ONE of the following:
   A. The requested agent is Glatopa or a brand product with a corresponding generic equivalent (listed below) AND ONE of the following:
      1. The patient has an intolerance or hypersensitivity to the corresponding generic equivalent that is not expected to occur with the requested agent **OR**
      2. The patient has an FDA labeled contraindication to the corresponding generic equivalent that is not expected to occur with the requested agent **OR**
      3. The prescriber has provided information to support the use of the requested agent over the corresponding generic equivalent **OR**

Non-Preferred products	Corresponding generic equivalent
Copaxone, Glatopa	Glatiramer
Tecfidera	Dimethyl fumarate

   B. The requested agent is another targeted agent **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 **OR**
   B. ALL of the following:
      1. The patient will be using the requested agent in combination with another DMA used for the treatment of MS **AND**

Module	Clinical Criteria for Approval

2. The requested agent will be used in combination with Mavenclad (cladribine) **AND**
3. Information has been provided supporting the use of the requested agent in combination with Mavenclad (e.g., relapse between cycles of Mavenclad) **AND**

5. ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**
6. 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 section below.

Renewal Evaluation

Target Agent(s) (excluding Mavenclad [cladribine]) 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 AND ONE of the following:
   A. The requested agent is Glatopa or a brand product with a generic equivalent AND ONE of the following: (listed below)
      1. The patient has an intolerance to hypersensitivity to the corresponding generic equivalent that is not expected to occur with the requested agent **OR**
      2. The patient has an FDA labeled contraindication to the corresponding generic equivalent that is not expected to occur with the requested agent **OR**
      3. The prescriber has provided information to support the use of the requested agent over the corresponding generic equivalent **OR**

Non-Preferred products	Corresponding generic equivalent
Copaxone, Glatopa	Glatiramer
Tecfidera	Dimethyl fumarate

   B. The requested agent is any other targeted agent **AND**
2. The patient has had clinical benefit with the requested agent **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 **OR**
   B. BOTH of the following:
      1. The requested agent will be used in combination with Mavenclad **AND**
      2. Information has been provided supporting 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

Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Through Preferred - 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 FDA labeled maximum dose based on the patient's weight **AND** 2. ONE of the following: A. The requested quantity (dose) does not exceed the program quantity limit **OR** B. BOTH of the following 1. The requested quantity (dose) is greater than the program quantity limit **AND** 2. 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: 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: 3 months
Through Preferred - Target Agent(s) (excluding Mavenclad [cladribine])	**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. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 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** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **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.

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Examples of Contraindicated Concomitant Disease Modifying Agents (DMAs)

Aubagio (teriflunomide)
Avonex (interferon β-1a)
Bafiertam (monomethyl fumarate)
Betaseron (interferon β-1b)
Copaxone (glatiramer)

Contraindicated as Concomitant Therapy
Extavia (interferon β-1b)
Gilenya (fingolimod)
Glatopa (glatiramer)
Kesimpta (ofatumumab)
Lemtrada (alemtuzumab)
Mavenclad (cladribine)
Mayzent (siponimod)
Ocrevus (ocrelizumab)
Plegridy (peginterferon β-1a)
Ponvory (ponesimod)
Rebif (interferon β-1a)
Tascenso ODT (fingolimod)
Tecfidera (dimethyl fumarate)
Tysabri (natalizumab)
Vumerity (diroximel fumarate)
Zeposia (ozanimod)

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).

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

For Select formulary (Commercial), Glatopa is excluded.