Multiple Sclerosis

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO047

Description

Medications included in this policy are subcutaneous and oral disease modifying therapies for the treatment of multiple sclerosis.

Length of Authorization

Cladribine (Mavenclad) only

- Initial: 12 months
- Renewal: Two months, maximum of one renewal per lifetime

All other agents

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
cladribine (Mavenclad)	10 mg tablets (box of 4 tablets)	Relapsing forms of multiple sclerosis (MS)	1 box (4 tablets)/26 days*
	10 mg tablets (box of 5 tablets)		1 box (5 tablets)/26 days*
	10 mg tablets (box of 6 tablets)		1 box (6 tablets)/26 days*
	10 mg tablets (box of 7 tablets)		1 box (7 tablets)/26 days*
	10 mg tablets (box of 8 tablets)		1 box (8 tablets)/26 days*
	10 mg tablets (box of 9 tablets)		1 box (9 tablets)/26 days*
	10 mg tablets (box of 10 tablets)		1 box (10 tablets)/26 days*
daclizumab (Zinbryta)	150mg/mL single-dose PFS±		1 syringe/28 days

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PHARMACY
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dimethyl fumarate (Tecfidera, dimethyl fumarate)	30 day starter pack		1 starter pack/30 days (60 capsules/30 days)
	120 mg capsule		60 capsules/30 days
	240 mg capsule		60 capsules/30 days
monomethyl fumarate (Bafiertam)	95 mg capsule		120 capsules/30 days
diroximel fumarate (Vumerity)	231 mg capsule		120 capsules/30 days
fingolimod (Gilenya)	0.25 mg capsule		30 capsules/30 days
	0.5 mg capsule		30 capsules/30 days
glatiramer acetate (Copaxone, Glatopa, glatiramer acetate)	20 mg/mL single dose PFS		30 syringes per/30 days
glatiramer acetate (Copaxone, Glatopa, glatiramer acetate)	40 mg/mL single dose PFS		12 syringes/28 days
interferon beta-1a (Avonex)	30 mcg/0.5mL PFS		4 syringes (1 kit)/28 days
	30 mcg/0.5mL pen		4 pens/28 days
interferon beta-1a (Plegridy)	Starter Pack – (Pen Injector or PFS)		1 starter pack/28 days
	125 mcg/0.5mL (Pen Injector or PFS)		2 pens (or PFS)/28 days
interferon beta-1a (Rebif)	22 mcg/0.5mL (Auto-injector or PFS)		12 syringes/28 days
	44 mcg/0.5mL (Auto-injector or PFS)		12 syringes/28 days
	Titration Pack		1 pack (12 syringes)/28 days

	(PFS or Solution)		
interferon beta-1b (Betaseron)	0.3 mg powder for reconstitution		14 syringes/28 days
interferon beta-1b (Extavia)	0.3 mg powder for reconstitution		15 syringes/30 days
ozanimod (Zeposia)	0.23 mg capsules		4 tablets/4 days
	0.46 mg capsules		3 tablets/3 days
	0.92 mg capsules		30 tablets/30 days
siponimod (Mayzent)	0.25 mg starter pack		12 tablets/5 days
	0.25 mg tablets		112 tablets/28 days
	2 mg tablets		30 tablets/30 days
teriflunomide (Aubagio)	7 mg tablets		28 tablets/28 days
	14 mg tablets		28 tablets/28 days

*Maximum of 2 boxes/331 days

‡PFS: Prefilled Syringe

Initial Evaluation

Interferon beta-1a (Avonex), generic dimethyl fumarate, fingolimod (Gilenya), glatiramer acetate (Glatopa), and generic glatiramer acetate are the preferred agents.

- There is no prior authorization* required on these preferred agents, unless requesting over the allowed quantity limits noted above.

**Brand Copaxone and Tecfidera do not require prior authorization; however, step therapy or non-formulary requirements apply*

I. **Cladribine (Mavenclad), daclizumab (Zinbryta), diroximel fumarate (Vumerity), interferon beta-1a (Plegridy), interferon beta-1a (Rebif), interferon beta-1b (Betaseron), interferon beta-1b (Extavia), monomethyl fumarate (Bafiertam), ozanimod (Zeposia), and teriflunomide (Aubagio)** may be considered medically necessary when the following criteria below are met:

A. Medication is prescribed by, or in consultation with, a neurologist; **AND**

B. Medication will be used as monotherapy for multiple sclerosis; **AND**

C. Multiple sclerosis (MS) diagnosis is confirmed and documented by a laboratory report (e.g. MRI); **AND**

D. A diagnosis of one of the following:
    1. **Relapsing-Remitting MS (RRMS); OR**
    2. **Clinically Isolated Syndrome (CIS)**; **OR**
    3. **Active Secondary Progressive MS (SPMS)**; **AND**
        i. Active disease confirmed by one of the following: clinical relapses, MRI evidence of contrast enhancing lesions, or new or unequivocally enlarging T2 lesions; **AND**

E. Documentation of treatment with two of the following have been ineffective, contraindicated, or not tolerated: interferon beta-1a (Avonex), generic dimethyl fumarate, fingolimod (Gilenya), glatiramer acetate (Glatopa), or generic glatiramer acetate

II. **Siponimod (Mayzent)** may be considered medically necessary when the following criteria below are met:
    A. Criteria I(A)-I(E) above are met; **AND**
    B. CYP2C9 genotype has been confirmed; **AND**
    C. Member does not have a CYP2C9*3/*3 genotype

III. Medications listed above are considered investigational when used for all other conditions, including but not limited to:
    A. Primary Progressive MS (PPMS)

Renewal Evaluation

I. Prescriber attestation that the patient has demonstrated a clinical benefit with therapy, , as defined by: no relapses, less than two unequivocally new MRI-detected lesions, or lack of increased disability on examination over a one-year period; **AND**
II. If the request is for a branded Copaxone product, documentation of treatment with Glatopa or glatiramer acetate has been ineffective, contraindicated, or not tolerated; **OR**
III. If the request is for siponimod (Mayzent) and treatment has been interrupted for four or more consecutive daily doses, a re-titration starter package is allowed

Supporting Evidence

I. **Siponimod (Mayzent):** Per the package label, if treatment with siponimod (Mayzent) is interrupted for FOUR or more consecutive daily doses after completion of initial titration, treatment should be reinitiated with Day 1 of the titration regimen, including first-dose monitoring when appropriate.
II. American Academy of Neurology (AAN) guidelines recommend clinicians should offer DMTs to people with relapsing forms of MS with recent clinical relapses or MRI activity – guidelines do not contain treatment sequencing recommendations.

III. AAN guidelines recommend clinicians should discuss switching from one DMT to another in people with MS who have been using a DMT long enough for the treatment to take full effect and are adherent to their therapy when they experience one or more relapses, two or more unequivocally new MRI-detected lesions, or increased disability on examination, over a one-year period of using a DMT.

IV. DMTs take a variable amount of time to become clinically active, due to this, new lesion formations may occur after initiation but before the time of full efficacy; thus confounding interpretation of follow-up MRI scans. Consequently, many clinicians obtain anew baseline MRI three to six months after initiating DMTs to monitor from a treated baseline. The optimal interval for ongoing monitoring is uncertain, as short-term stability, evidenced by clinical and MRI criteria, may not consistently predict long-term stability.

V. Per Lublin, et al. 2014, disease activity is determined by clinical relapses assessed annually and/or MRI activity (contrast-enhancing lesions; new or unequivocally enlarging T2 lesions).

VI. The FDA Summary Review for Regulatory Action on the NDA for siponimod (Mayzent) states the following: In the active secondary progressive phase of the disease, patients can accrue disability both from acute relapses and from the progressive component of the disease. Active secondary progressive disease and relapsing-remitting disease overlap in evolution. Categorization as secondary progressive disease is based on clinical judgment; there are no clinical findings or biomarkers that meaningfully define or predict the phenotypes of relapsing forms of MS. A continued progression of disability with no concurrent inflammatory activity and no clinical relapses is described as non-active secondary progressive MS. Importantly, to support an indication for the treatment of secondary progressive MS (as distinct from active secondary progressive MS), it is critical that efficacy be established in patients who have non-active secondary progressive MS (SPMS), that the drug effect be clearly distinguished from an effect on inflammatory demyelination, and clinical relapses that are present in patients with active SPMS (a relapsing form of MS). Multiple drugs have been approved for the treatment of relapsing forms of MS. Conversely, there is a significant unmet medical need for the treatment of non-active SPMS. The indication supported by the submitted data is for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It must be emphasized that thirteen different therapies have been approved to treat relapsing forms of multiple sclerosis, and that the population for which siponimod will be indicated is the same as for those drugs. The siponimod labeling will be the first explicitly describing that relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, but all sponsors of the drugs approved for the treatment of relapsing forms of multiple sclerosis will be requested to update their indication statements to conform with this contemporary nomenclature.

VII. Tools used in diagnosis of MS:

MS with a relapsing-remitting course

• Based upon two separate areas of damage (dissemination in space) in the CNS that have occurred at different points in time (dissemination in time). Unless contraindicated, MRI should be obtained.	
Dissemination in <u>time</u> (Development/appearance of new CNS lesions over time)	Dissemination in <u>space</u> (Development of lesions in distinct anatomical locations within the CNS)
• ≥ 2 clinical attacks; OR • 1 clinical attack AND one of the following: ○ MRI indicating 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 compared to baseline scan ○ CSF-specific oligoclonal bands	• ≥ 2 lesions; OR • 1 lesion AND one of the following: ○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location ○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)
Secondary progressive MS course	
• MS course characterized by steadily increasing objectively documented neurological disability independent of relapses. Fluctuations, periods of stability, and superimposed relapses might occur. Secondary progressive multiple sclerosis, is further distinguished as a progressive course following an initial relapsing-remitting course. • Diagnosed retrospectively based on previous year's history.	

Investigational Uses or Not Medically Necessary Uses

I. Primary Progressive MS

A. All agents included in this policy have not been evaluated in, or have not been found, to have a positive effect on progression in the setting of PPMS.

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Policy Implementation/Update:

Action and Summary of Changes	Date
Updated preferred products to specify generic dimethyl fumarate upon new generic availability. Removed criteria specific to branded Copaxone. Addition of monomethyl fumarate (Bafiertam) to policy within non-preferred position.	09/2020
Updated to include fingolimod (Gilenya) as a preferred product and included box around preferred agents not requiring prior authorization	07/2020
Updated to include ozanimod (Zeposia) as a non-preferred product	04/2020
Updated to add diroximel fumarate (Vumerity) as a non-preferred agent	02/2020
Removed box around preferred agents not requiring prior authorization	01/2020
Updated to include box around preferred agents not requiring prior authorization	10/2019
Updated to new policy format. Added newly approved drugs Mayzent and Mavencald. Added question requiring diagnosis confirmed and documented by laboratory report (e.g., MRI).	08/2019
New criteria set – consolidated all MS criteria sets to one	11/2017