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	Indication	Dosage Form	Quantity Limit
cladribine (Mavenclad)	Relapsing forms of multiple sclerosis (MS)	10 mg tablets (box of 4 tablets)	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

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)	Relapsing forms of multiple sclerosis (MS)	231 mg capsule	120 capsules/30 days
fingolimod (Gilenya, fingolimod)		0.25 mg capsule	30 capsules/30 days
		0.5 mg capsule	30 capsules/30 days
fingolimod lauryl sulfate (Tascenso ODT)		0.25 mg tablet disintegrating	30 tablets/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 (PFS or Solution)	1 pack (12 syringes)/28 days
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
ofatumumab (Kesimpta)		20 mg/0.4mL Auto-injector	Initial: 3 pens/28 days Maintenance: 1 pen/28 days
ozanimod (Zeposia)	Relapsing forms of multiple sclerosis (MS); Ulcerative colitis**	0.23 mg capsules	4 tablets/4 days
		0.46 mg capsules	3 tablets/3 days
		0.92 mg capsules	30 tablets/30 days
ponesimod (Ponvory)	Relapsing forms of multiple sclerosis (MS)	2-10 mg starter pack	Initial: 14 tablets/14 days Maintenance: 30 tablets/30 days
		20 mg tablet	
siponimod (Mayzent)		0.25 mg starter pack (Titrate to 2 mg dose)	12 tablets/5 days
		0.25 mg tablets	28 tablets/28 days
		0.25 mg starter pack (Titrate to 1 mg dose)	7 tablets/4 days
		1 mg tablet	28 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, generic fingolimod, 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.

I. **Cladribine (Mavenclad), daclizumab (Zinbryta), diroximel fumarate (Vumerity), fingolimod lauryl sulfate (Tascenso ODT), interferon beta-1a (Plegridy), interferon beta-1a (Rebif), interferon beta-1b (Betaseron), interferon beta-1b (Extavia), monomethyl fumarate (Bafiertam), ofatumumab (Kesimpta), ozanimod (Zeposia), ponesimod (Ponvory), 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 at least two of the following have been ineffective or not tolerated, or ALL are contraindicated: interferon beta-1a (Avonex), generic dimethyl fumarate, fingolimod (Gilenya), or generic glatiramer acetate/Glatopa

II. **Brand Gilenya, Brand Tecfidera, and Brand Copaxone** may be considered medically necessary when the following criteria below are met:

A. Criteria I(A)-I(D) above are met; **AND**
B. In the absence of a drug shortage, coverage of the multi-source brand drug is to be considered medically necessary when the prescriber is requesting the multi-source brand drug due to a documented adverse reaction to the generic equivalent; **AND**
C. If the provider has not reported this reaction to MedWatch, please acknowledge the Health Plan or Specialty Pharmacy may report the reaction to MedWatch and may need to contact the provider for more information regarding reaction details for adequate reporting; **AND**
    1. The prescriber must document one or more of the following, indicating that the reaction:

i. Was life-threatening; **OR**
ii. Required hospitalization; **OR**
iii. Required intervention to prevent impairment or damage; **OR**

2. The prescriber is requesting the brand name drug due to a documented allergy to the generic equivalent [i.e. skin rashes (particularly hives), itching, respiratory compilations and angioedema] that required medical intervention to prevent impairment or damage; **OR**
3. The prescriber is requesting the brand name drug due to a documented intolerance to the generic equivalent which caused disability, rendering the patient unable to function or perform activities of daily living; **AND**
    i. More than one generic equivalent has been tried, or there is only one generic equivalent for the prescribed brand drug; **AND**

D. **For Brand Gilenya:** Documentation of treatment with all three (1, 2 and 3) of the following have been ineffective, contraindicated, or not tolerated:
    1. interferon beta-1a (Avonex)
    2. glatiramer acetate (Glatopa) or generic glatiramer acetate
    3. generic dimethyl fumarate; **OR**
E. **For Brand Tecfidera:** Documentation of treatment with all three (1, 2 and 3) of the following have been ineffective, contraindicated, or not tolerated:
    1. interferon beta-1a (Avonex)
    2. generic fingolimod
    3. glatiramer acetate (Glatopa) or generic glatiramer acetate; **OR**
F. **For Brand Copaxone**: Documentation of treatment with all three (1, 2 and 3) of the following have been ineffective, contraindicated, or not tolerated:
    1. interferon beta-1a (Avonex)
    2. generic fingolimod
    3. dimethyl fumarate

III. **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

IV. 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. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. 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**

IV. If the request is **for Brand Gilenya, Brand Tecfidera, or Copaxone:**

- A. In the absence of a drug shortage, coverage of the multi-source brand drug is to be considered medically necessary when the prescriber is requesting the multi-source brand drug due to a documented adverse reaction to the generic equivalent; **AND**
- B. If the provider has not reported this reaction to MedWatch, please acknowledge the Health Plan or Specialty Pharmacy may report the reaction to MedWatch and may need to contact the provider for more information regarding reaction details for adequate reporting; **AND**
  - a. The prescriber must document one or more of the following, indicating that the reaction:
    - i. Was life-threatening; **OR**
    - ii. Required hospitalization; **OR**
    - iii. Required intervention to prevent impairment or damage; **OR**
  - b. The prescriber is requesting the brand name drug due to a documented allergy to the generic equivalent [i.e. skin rashes (particularly hives), itching, respiratory compilations and angioedema] that required medical intervention to prevent impairment or damage; **OR**
  - c. The prescriber is requesting the brand name drug due to a documented intolerance to the generic equivalent which caused disability, rendering the patient unable to function or perform activities of daily living; **AND**
    - i. More than one generic equivalent has been tried, or there is only one generic equivalent for the prescribed brand drug; **OR**

V. 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 covered by the manufacturer

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. Siponimod (Mayzent) manufacturer, Novartis, confirmed 5-day titration packs/starter pack will be shipped from HomeScripts mail order pharmacy at no charge to commercial plans. Even in cases where the member needs to re-titrate the starter pack is covered by Novartis via HomeScripts.

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 a new 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. In the United States, the Office of Generic Drugs at the Food and Drug Administration (FDA) follows a rigorous review process to make sure that, compared to the brand name (or innovator) medications, the proposed generic medications:

- Contain the same active/key ingredient
- Have the same strength
- Use the same dosage form (for instance, a table, capsule, or liquid) and
- Use the same route of administration (for instance, oral, topical, or injectable)

VIII. The FDA's review process also ensures that generic medications perform the same way in the human body and have the same intended use as the name brand medication. Healthcare professionals and consumers can be assured that FDA-approved generic drug products have met the same rigid manufacturing standards as the innovator drug. In addition, FDA inspects facilities to make certain the generic manufacturing, packaging, and testing sites pass the same quality standards as those of brand-name drugs.

- Thus, when an adverse reaction or allergy occurs to any medication (brand or generic), it is important to report to MedWatch.
- In order to keep effective medical products available on the market, the FDA relies on the voluntary reporting of these events. This information is used to maintain safety surveillance and to monitor if modifications in use or design of the product are warranted to increase patient safety.

IX. It can be difficult to distinguish an allergy from a distinct adverse event related to the generic, therefore any event thought to be related to the medication should be reported to MedWatch.

- As defined by the American Academy of Allergy, Asthma, and Immunology, an allergic reaction occurs when the immune system overreacts to a substance, triggering an allergic reaction. Sensitivities to drugs may produce similar symptoms, but do not involve the immune system. Only 5-20% of adverse reactions to drugs are considered true allergic reactions. The chances of developing an allergy are higher when you take the medication frequently or when it is rubbed on the skin or given by injection, rather than taken by mouth. The most frequent types of allergic symptoms to medications include skin rashes (particularly hives), itching, respiratory

complications and angioedema. The most severe form of immediate allergic reactions is anaphylaxis, and symptoms include hives, facial or throat swelling, wheezing, light-headedness, vomiting and shock.

X. 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.

References

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Policy Implementation/Update:

Action and Summary of Changes	Date
Included newly available generic fingolimod as preferred product, replacing brand formulation. Branded product updated to align with requirements for other multi-source brands (i.e., Copaxone, Tecfidera).	11/2022
Added Tascenso ODT to policy	09/2022
Added 0.25 (1mg) starter pack and 1 mg dose of Mayzent to policy	04/2022
Added renewal of brand Copaxone into policy aligning with requirements for brand Tecfidera requiring medical necessity for brand over generic	11/2021
Update to initial requests for brand Tecfidera or brand Copaxone to require trial of Avonex, Gilenya, and glatiramer acetate (Glatopa)/generic glatiramer acetate for brand Tecfidera requests; and trial of Avonex, Gilenya, and generic dimethyl fumarate for brand Copaxone requests	05/2021
Adding loading dose to QL table for kesimpta	02/2021
Addition of brand Copaxone into policy aligning with requirements for brand Tecfidera requiring medical necessity for brand over generic.	12/2020
Addition of ofatumumab (Kesimpta) and ponesimod to policy within non-preferred position. Addition of brand Tecfidera criteria requiring medical necessity for brand over generic.	11/2020
Updated preferred products to specify generic dimethyl fumarate upon new generic availability (effective 10/2020). 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