Oscar Clinical Guideline: Multiple Sclerosis Agents (PG094, Ver. 6)

Multiple Sclerosis Agents

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Multiple Sclerosis (MS) is an autoimmune disease in which the body's immune system attacks its own tissues. This immune system malfunction destroys the fatty substance (myelin) that coats and protects nerve fibers in the brain and spinal cord, as known as the central nervous system. When the protective myelin is damaged and the nerve fiber is exposed, the messages that travel along that nerve fiber may be slowed or blocked. This can cause communication problems between the brain and the rest of the body. Eventually, the disease can cause irreversible damage or deterioration of the nerves leaving a person with the potential for permanent disability and a lack of functionality of the central nervous system.

While the causes of MS are largely unknown, genetics and environmental factors have contributing factors. Some symptoms of MS include numbness, tingling or tremor; vision changes; walking impairment; slurred speech; dizziness; and changes in bowel and bladder function or control. Multiple sclerosis is characterized by a "waxing and waning" course of the disease, meaning there are often periods of relapse or attacks followed by periods of improvement or remission. There is no cure for multiple sclerosis. However, treatments can help speed recovery from attacks, modify the course of the disease and manage symptoms.

This policy references the most recent Food and Drug Administration (FDA) prescribing information for each medication as well as guidelines and reports published by the National Multiple Sclerosis Society (NMSS) for consideration of approval of these medications. The FDA and NMSS set the treatment considerations. Please refer to the FDA website at www.fda.gov/drugs and NMSS website at www.nationalmssociety.org for more information.

Table 1: Immunomodulatory Agents, MS agents with disease-modifying activity

Drug	FDA-Approved Indications
Aubagio (teriflunomide)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
Avonex (Interferon Beta-1a)	
Bafiertam (Monomethyl Fumarate)	
Betaseron (Interferon Beta-1b)	
Copaxone (Glatiramer Acetate)	
Extavia (Interferon Beta-1b)	
Gilenya, TASCENSO ODT (Fingolimod)	is indicated for the 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.
Kesimpta (Ofatumumab)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
Lemtrada (Alemtuzumab)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. Limitations of Use: LEMTRADA is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

Mavenclad (Cladribine)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of MAVENCLAD is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Limitations of Use: MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.
Mayzent (Siponimod)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
Plegridy (Peginterferon Beta-1a)	
Ponvory (Ponesimod)	
Rebif (Interferon Beta-1a)	
Tecfidera (Dimethyl Fumarate)	
Vumerity (Diroximel Fumarate)	

MS Agents with separate drug-specific or adopted guideline		**Clinical Guideline**
Briumvi (ublituximab)	is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.	Briumvi (ublituximab) (PG134)
Mitoxantrone	1. is indicated for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (i.e., patients whose neurologic status is significantly abnormal between relapses). Mitoxantrone injection is not indicated in the treatment of patients with primary progressive multiple sclerosis.	Mitoxantrone (Novantrone) (PG126)

	2. in combination with corticosteroids is indicated as initial chemotherapy for the treatment of patients with pain related to advanced hormone-refractory prostate cancer. 3. in combination with other approved drug(s) is indicated in the initial therapy of acute nonlymphocytic leukemia (ANLL) in adults. This category includes myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.	
Ocrevus (Ocrelizumab)	is indicated for the treatment of: 1. Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults 2. Primary progressive MS, in adults	CVS Caremark Ocrevus 1707-A SGM
Tysabri (Natalizumab)	is indicated: 1. as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. 2. for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-**α**.	CVS Caremark Tysabri 1846-A SGM
Zeposia (Ozanimod)	is indicated for the treatment of: 1. relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. 2. moderately to severely active ulcerative colitis (UC) in adults.	CVS Caremark Zeposia 3747-A SGM

Table 2: Multiple Sclerosis Agents without disease-modifying activity

Preferred Drug	FDA-Approved Indications	
Ampyra (Dalfampridine)	is indicated as a treatment to improve walking in adult patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed.	
MS Agent with drug-specific adopted guideline		**CVS Caremark Clinical Guideline**
Nuedexta (Dextromethorphan and Quinidine)	is indicated for the treatment of pseudobulbar affect (PBA). *PBA occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.*	Nuedexta (dextromethorphan-quinidine) Ref# 870-A

Please note that all Multiple Sclerosis Agents require prior authorization:

- The Plan requires that members be unable to use, or has tried and failed the preferred MS agents first. The Plan's preferred MS agents are:
    - Brand - Aubagio, Betaseron, Copaxone, Gilenya, Mayzent, Rebif, Vumerity, Zeposia
    - generic - dalfampridine (Brand - Ampyra), dimethyl fumarate (Brand - Tecfidera)
- The Plan's preferred IV agent for multiple sclerosis is Tysabri (natalizumab)
- Certain MS agents have adopted CVS Caremark Clinical Guidelines. Please refer to these drug-specific Clinical Guidelines (please refer to Table 1 and Table 2 above).

Definitions

"CIS" or "clinically isolated syndrome" refers to the first symptomatic episode lasting at least 24 hours caused by inflammation and demyelination in the central nervous system. This episode is characteristic of multiple sclerosis but does not always result in a person developing MS. Early treatment of CIS has been shown to delay the onset of MS.

"**Compendia**" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"Disease modifying therapy" refers to treatments found to reduce the number of relapses, delay progression of disability, and limit new disease activity according to research and clinical trials.

"EDSS" or "Expanded Disability Status Scale" refers to the most widely utilized MS assessment tool that consists of an ordinal clinical rating scale with half point increments ranging from 0 (normal neurologic examination) to 10 (death due to MS).

"MRI" or "Magnetic Resonance Imaging" refers to a medical imaging technique that creates detailed three-dimensional (3D) images of the organs and tissues in your body. A brain MRI can reveal areas of active MS disease called lesions within the central nervous system.

"Relapse" refers to an attack or exacerbation of MS (also known as a flare-up) resulting in the occurrence of new symptoms or the worsening of old symptoms.

"RRMS" or "relapsing-remitting MS" refers to the most common type of MS in which there are clearly defined attacks or relapses of increasing neurologic symptoms followed by periods of partial or complete recovery or remissions.

"SPMS" or "secondary progressive MS" refers to a version of disease progression that can follow an initial relapsing-remitting course in which there is a worsening of neurologic function and increased disability over time.

"25 foot timed walk" or "T25-FW" refers to a quantitative mobility and leg function performance test whereby a patient is directed to walk 25 feet as quickly and safely as possible. This test is typically the first component of the MS functional composite (MSFC) score to be performed at an office visit. Administration time will vary depending upon the ability of the patient.

Medical Necessity Criteria for Initial Authorization

The Plan considers Multiple Sclerosis Agents medically necessary when the agent-specific criteria below are met:

Ampyra (dalfampridine)

The Plan considers dalfampridine medically necessary when ALL of the following criteria are met:

1. The member has a confirmed diagnosis of multiple sclerosis***; AND***
2. dalfampridine is being used for relief of symptoms (to improve walking)***; AND***
3. Prior to initiation of therapy with dalfampridine, the member is ambulatory and has experienced sustained walking impairment, defined as ONE of the following:
    a. 25-foot timed walk completed within 8 to 45 seconds***; or***
    b. For a 25-foot timed walk less than 8 seconds, the Expanded Disability Status Scale (EDSS) must be between 4.5 and 6.5***; AND***
4. The requested medication is for ONE of the following:
    a. generic dalfampridine (the Plan's preferred product)***; or***
    b. Brand Ampyra AND the member is unable to use, or has tried and failed generic dalfampridine from two or more (≥ 2) manufacturers***; AND***
5. The requesting provider has submitted the necessary clinical documentation (e.g., chart notes, laboratory reports, disease progression, previous medications tried and failed, etc) for review***; AND***
6. The medication is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.

If the above prior authorization criteria are met, the requested medication will be approved for 90 days.

Immunomodulatory Agents:

Aubagio⇅ (Teriflunomide)	**Gilenya⇅ (Fingolimod)**	Ponvory (Ponesimod)
Avonex (Interferon Beta-1a)	Kesimpta (Ofatumumab)	**Rebif** (Interferon Beta-1a)
Bafiertam (Monomethyl Fumarate)	Lemtrada (Alemtuzumab)	Tascenso ODT (fingolimod)
Betaseron (Interferon Beta-1b)	Mavenclad (Cladribine)	Tecfidera (**Dimethyl Fumarate**)

Copaxone (Glatiramer Acetate)	**Mayzent** (Siponimod)	**Vumerity** (Diroximel Fumarate)
Extavia (Interferon Beta-1b)	Plegridy (Peginterferon Beta-1a)	

⇵This product is only included in the formulary for certain plans. Please check the Plan's specific Formulary.

The Plan considers the above listed Immunomodulatory Agents medically necessary when ALL of the following criteria are met:

1. The requested medication is for ONE of the following:
    a. a **preferred MS agent** by the Plan and the member has ONE of the following forms of multiple sclerosis:
        i. relapsing-remitting (RRMS)***; or***
        ii. secondary progressive (SPMS)***; or***
        iii. clinically isolated syndrome (CIS)***; or***
    b. Avonex (Interferon Beta-1a) or Plegridy (Peginterferon Beta-1a) and the member meets BOTH of the following:
        i. the member has ONE of the following forms of multiple sclerosis:
            1. relapsing-remitting (RRMS)***; or***
            2. secondary progressive (SPMS)***; or***
            3. clinically isolated syndrome (CIS)***; and***
        ii. The member is unable to use, or has tried and failed Rebif (Interferon Beta-1a) AND two other preferred Immunomodulatory Agents***; or***
    c. Extavia (Interferon Beta-1b) and the member meets BOTH of the following:
        i. the member has ONE of the following forms of multiple sclerosis:
            1. relapsing-remitting (RRMS)***; or***
            2. secondary progressive (SPMS)***; or***
            3. clinically isolated syndrome (CIS)***; and***
        ii. The member is unable to use, or has tried and failed Betaseron (Interferon Beta-1b) AND two other preferred Immunomodulatory Agents***; or***
    d. glatiramer or Glatopa and the member meets BOTH of the following:
        i. the member has ONE of the following forms of multiple sclerosis:
            1. relapsing-remitting (RRMS)***; or***
            2. secondary progressive (SPMS)***; or***
            3. clinically isolated syndrome (CIS)***; and***

ii. The member is unable to use, or has tried and failed Brand Copaxone AND two other preferred Immunomodulatory Agents***; or***

e. Bafiertam (Monomethyl Fumarate), Kesimpta (Ofatumumab), or Ponvory (Ponesimod) and the member meets BOTH of the following:
   i. the member has ONE of the following forms of multiple sclerosis:
      1. relapsing-remitting (RRMS)***; or***
      2. secondary progressive (SPMS)***; or***
      3. clinically isolated syndrome (CIS)***; and***
   ii. The member is unable to use, or has tried and failed three (3) preferred Immunomodulatory Agents***; or***

f. Lemtrada (Alemtuzumab) and the member meets ALL of the following:
   i. the member has ONE of the following forms of multiple sclerosis:
      1. relapsing-remitting (RRMS)***; or***
      2. secondary progressive (SPMS)***; and***
   ii. The member currently does not have evidence of active infection (such as human immunodeficiency [HIV], hepatitis B [HBV], hepatitis C [HCV], or tuberculosis [TB])***; and***
   iii. The member is unable to use, or has tried and failed Tysabri (Natalizumab) AND two other preferred Immunomodulatory Agents***; or***

g. Mavenclad (Cladribine) and the member meets ALL of the following:
   i. the member has ONE of the following forms of multiple sclerosis:
      1. relapsing-remitting (RRMS)***; or***
      2. secondary progressive (SPMS)***; and***
   ii. The member currently does not have evidence of active infection (such as human immunodeficiency [HIV], hepatitis B [HBV], hepatitis C [HCV], or tuberculosis [TB])***; and***
   iii. The member is unable to use, or has tried and failed three (3) preferred Immunomodulatory Agents***; or***

h. Tascenso ODT (fingolimod) and the member meets ALL of the following:
   i. the member has ONE of the following forms of multiple sclerosis:
      1. relapsing-remitting (RRMS)***; or***
      2. secondary progressive (SPMS)***; or***
      3. clinically isolated syndrome (CIS)***; and***
   ii. The member is between 10 to less than 18 years of age***; and***
   iii. The member weighs less than or equal to 40 kg***; AND***

2. The member is not or will not be taking the requested medication with any other disease modifying multiple sclerosis agents (see Table 1)***; AND***
3. The requesting provider has submitted the necessary clinical documentation (e.g., chart notes, laboratory reports, disease progression, previous medications tried and failed, etc) for review***; AND***
4. The medication is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.

If the above prior authorization criteria are met, the requested medication will be approved for 12 months.

Medical Necessity Criteria for Reauthorization

Ampyra (dalfampridine)

Reauthorization for 12 months will be granted if BOTH of the following are met:

1. the member still meets the applicable initial criteria; ***AND***
2. chart documentation shows ONE of the following:
    a. The member has shown improvement in the 25 foot walk time with faster speeds by at least 20% compared to baseline since starting the requested medication***; or***
    b. The member has experienced general improvement in walking ability since starting the requested medication.

Immunomodulatory Agents

Reauthorization for 12 months will be granted if BOTH of the following are met:

1. the member still meets the applicable initial criteria; ***AND***
2. chart documentation shows ONE of the following:
    a. The member has shown a clinical improvement (e.g., reduction in neurologic disability and/or the frequency of clinical relapses) in symptoms since starting the requested medication***; or***
    b. The member has experienced disease stability since starting the requested medication.

Experimental or Investigational / Not Medically Necessary

The Plan will not cover the medications listed in this policy to be used for any other indication outside of what is FDA approved or a generally accepted standard of medical care as evidenced in medical literature and/or treatment guidelines, as this would be considered experimental, investigational, or unproven.

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