Central Nervous System: Multiple Sclerosis Agents, Injectable Utilization Management Criteria

Therapeutic Class:	Central Nervous System: Multiple Sclerosis Agents, Injectable
Non-Preferred Agents:	Betaseron (interferon beta-1b) 0.3 mg vial, Briumvi (ublituximab-xiiy), Copaxone (glatiramer acetate) 40 mg syringe, Glatiramer, Glatopa (glatiramer acetate), Lemtrada (alemtuzumab), Ocrevus (ocrelizumab), Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq), Plegridy (peginterferon beta-1a), Rebif (interferon beta-1a), Tysabri (natalizumab), Tyruko (natalizumab-sztn)
Preferred Agents:	Avonex (interferon beta-1a), Betaseron (interferon beta-1b) 0.3 mg kit, Copaxone (glatiramer acetate) 20 mg syringe, Kesimpta (interferon beta-1a)
Implementation Date:	1/1/2026
Prepared For:	CT
PDL Status:	Non-preferred
Purpose:	Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system characterized by neurologic damage that can affect any part of the body. Symptoms include, but are not limited to, vision problems, numbness or tingling of the face or body, walking difficulties, spasticity, fatigue, or bladder/bowel problems. The exact cause of MS is unknown; however, genetic, infectious, and environmental factors have been identified as potential contributors to the development of this disease. Clinically isolated syndrome (CIS) refers to the first episode of neurologic symptoms of MS. Relapsing-remitting MS (RRMS) is the most common disease course and is characterized by episodes of new or worsening symptoms (relapses) followed by periods of recovery. RRMS often transitions to secondary progressive MS (SPMS), where disability progression steadily occurs over time, independent of relapses. Primary progressive MS (PPMS) is characterized by worsening neurologic function from the onset of symptoms without early relapses or remissions. Disease-modifying treatments (DMTs) are utilized to reduce the number of relapses, delay the progression of disability, and limit new disease activity. The agents in table 1 are all approved by the Food and Drug Administration (FDA) for relapsing forms of MS, including CIS, RRMS, and active SPMS in adults. Alemtuzumab is not recommended for CIS. Ocrelizumab carries an additional indication for PPMS in adults. All agents are administered either by intravenous (IV), intramuscular (IM), or subcutaneous (SC) routes. The 2018 American Academy of Neurology (AAN) guideline recommends

	DMTs for MS and specifically recommends alemtuzumab, natalizumab, or fingolimod (an oral agent) for people with highly active MS. However, the risk of progressive multifocal leukoencephalopathy (PML) should be discussed with patients considering natalizumab, ocrelizumab, rituximab or certain oral agents (i.e., fingolimod, or dimethyl fumarate). Although effective for treating MS, alemtuzumab is associated with notable safety concerns. The prescribing information for alemtuzumab has several boxed warnings, including for autoimmune conditions (e.g., immune thrombocytopenia and anti-glomerular basement membrane disease), infusion reactions, serious and life-threatening stroke, increased risk of malignancies (thyroid cancer, melanoma, and lymphoproliferative disorders), and is only available through a restricted distribution program. Natalizumab has a boxed warning for PML and is also only available through a restricted distribution program. Glatiramer acetate also recently added a boxed warning for anaphylaxis that can occur at any time during treatment, even after the first dose or long after starting the medication. All of the injectable interferon products (beta-1a, beta-1b, and peginterferon beta-1a) have been associated with an increased risk of pulmonary arterial hypertension. None of the injectable MS agents are recommended for use in pediatric patients

Table 1. Central Nervous System: Multiple Sclerosis Agents, Injectable

Generic Name	Brand Name	Approved Indications	Route of Administration	Generic Availability
Alemtuzumab	Lemtrada®	RRMS, SPMS	IV	N
Glatiramer	Copaxone®, Glatopa™*	RRMS, CIS, SPMS	SC	Y
Interferon beta-1a	Avonex®, Rebif®, Rebif® Rebidose®	RRMS, CIS, SPMS	IM, SC	N
Interferon beta-1b	Betaseron®,	RRMS, CIS, SPMS	SC	N
Natalizumab	Tysabri®	RRMS, CIS, SPMS, CD	IV	Y
Natalizumab-sztn	Tyruko	RRMS, CIS, SPMS, CD	IV	N/A
Ocrelizumab	Ocrevus®,	RRMS, CIS, SPMS, PPMS	IV	N
Ocrelizumab and hyaluronidase-ocsq	Ocrevus Zunovo®	RRMS, CIS, SPMS, PPMS	SC	N
Ofatumumab	Kesimpta®	RRMS, CIS, SPMS	SC	N
Peginterferon beta-1a	Plegridy®	RRMS, CIS, SPMS	IM, SC	N
Ublituximab	Briumvi®	RRMS, CIS, SPMS	IV	N

**FDA-approved branded generic to Copaxone.*
Abbreviations: CIS, clinically isolated syndrome; CD, Crohn's Disease; IM, intramuscular; IV, intravenous; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SC, subcutaneous; SPMS, secondary progressive multiple sclerosis

All authorizations must be prescribed in accordance with FDA approved labeling. Use of samples to initiate therapy does not meet step therapy and/or continuation of therapy prior authorization requirements. Prior therapies will be verified through pharmacy claims and/or submitted chart notes.

General Approval Criteria:

- Requested quantity in accordance with FDA approved product labelling
- For specific formulation requests
    - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used
    - **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used
    - **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Initial Therapy – All the following must be met for the diagnosis of Multiple Sclerosis:

- Prescribed by or in consultation with a neurologist or other specialist familiar with the treated disease state
- Patient age is 18 years and older
- Claim is for a preferred agent **OR**
- Patient has a documented diagnosis of clinically isolated syndrome (CIS) (with the exception of Lemtrada) or Multiple Sclerosis (MS) **AND** Failure to achieve desired therapeutic outcome with a trial of **ONE** preferred oral (excluding dalfampridine) **OR** injectable MS agent (defined as 30 day trial) **OR** documented adverse drug event/adverse drug reaction or contraindication to preferred products **AND**

Additional Criteria for Lemtrada

- Trial and failure of one additional medication approved for the treatment of MS (in addition to a preferred agent for a total of 2 trials) **OR** documented medical reason trial of 1 agent is appropriate
- Provider attests to having met the REMS requirements for counseling and monitoring
- Provider attests that patient is not pregnant
- Provider attests that Lemtrada will not be administered during active infections
- Therapy will deny if
    - Being used for CIS
    - Documented human immunodeficiency virus (HIV) infection

Additional Criteria for Tysabri and Tyruko

- Tysabri and Tyruko will not be combined with immunosuppressants and will be used as monotherapy for the treatment of Multiple Sclerosis
- Provider attests to having met the REMS requirements for counseling and monitoring
- Therapy will deny if patient has or has had progressive multifocal leukoencephalopathy (PML)

Additional Criteria for Briumvi

- Documentation of all of the following prior to starting therapy:
  - Hepatitis B screening
  - Quantitative serum immunoglobulins
  - Liver function tests
- Therapy will deny if patient has active hepatitis B virus infection

Additional Criteria For Ocrevus and Ocrevus Zunovo

- *Trial and failure of a preferred agent not required for a diagnosis of primary progressive multiple sclerosis (documentation required of PPMS diagnosis)*
- Documentation of all of the following prior to starting therapy:
  - Hepatitis B screening
  - Quantitative serum immunoglobulins
  - Liver function tests
- Therapy will deny if patient has active hepatitis B virus infection

For the diagnosis of Moderate to Severe Crohn's disease – all of the following must be met

- Claim is for Tysabri or Tyruko
- Documented diagnosis (listed above)
- Prescribed by or in consultation with a gastroenterologist
- Trial of a preferred tumor necrosis factor inhibitor (TNFi) **AND** conventional Crohn's disease therapies OR documented adverse event/adverse drug reaction or contraindication to both classes of drug
- Tysabri or Tyruko will not be combined with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or TNFi
- Provider attests to having met the REMS requirements for counseling and monitoring
- Therapy will deny if patient has or has had progressive multifocal leukoencephalopathy (PML)

Initial PA length: 1 year for MS indications (6 months for Tysabri or Tyruko for Crohn's disease indication)

Exclusion Criteria: Approval criteria not met

Continuation Therapy: Documented compliance on current therapy regimen **AND**
Documented continued clinical benefit **AND**

- For specific formulation requests
  - **For brand requests when a therapeutically equivalent generic is preferred:** Provider must provide a documented medical reason the preferred generic formulation cannot be used
  - **For generic requests when a therapeutically equivalent brand is preferred:** Provider must provide a documented medical reason the preferred brand formulation cannot be used
  - **For non-preferred dosage or formulation requests:** Provider must provide a documented medical reason the preferred dosage or formulation cannot be used

Continuation Length: 1 year

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Revision History

Date	Version	Revisions
11/19/2025	V1	Document approved by DSS

