Lemtrada (Alemtuzumab)

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 a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults (generally diagnosed before 50 years of age) with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS (occurring in about 85% of patients), characterized by acute

attacks followed by periods of remission. Treatment goals include reducing relapses, slowing disability progression, and managing symptoms. Disease-modifying therapies are the primary treatment approach and include injectable medications (e.g., interferons, glatiramer acetate), oral medications (e.g., dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (e.g., natalizumab, ocrelizumab).

MS is a progressive disease, meaning that symptoms tend to worsen over time, and it can be classified into several types, including relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).

Currently, there is no cure for MS, but various treatment options are available to manage symptoms, slow the progression of the disease, and improve quality of life.

- Disease-modifying therapies (DMTs) are a class of medications that target the immune system to reduce inflammation and slow down the progression of the disease. The type of DMT prescribed will depend on the type and severity of MS, as well as the individual's medical history and preferences. Some common DMTs include interferon beta, glatiramer acetate, dimethyl fumarate, and fingolimod.
- High dose corticosteroids, such as high dose intravenous methylprednisolone or oral prednisone can be prescribed to reduce inflammation during acute MS relapses.
- Symptomatic treatments are also available to manage specific symptoms of MS, such as muscle spasms, bladder problems, and depression. Physical therapy, occupational therapy, and speech therapy can help individuals with MS maintain mobility, independence, and communication skills.

Lemtrada (alemtuzumab) is a CD52-directed cytolytic monoclonal antibody indicated for relapsing forms of MS, to include relapsing-remitting disease and active secondary progressive disease, in adults. Due to its safety profile, including risks of autoimmune conditions, infusion reactions, stroke, and malignancies, Lemtrada (alemtuzumab) is generally reserved for those who have had an inadequate response to two (2) or more MS medications. It is administered as two (2) treatment courses 12 months apart, with potential additional courses as needed. Lemtrada (alemtuzumab) is not indicated for those with clinically isolated syndrome (CIS).

Due to the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada (alemtuzumab) is available only through restricted distribution under the Risk Evaluation Mitigation Strategy (REMS) program.

Definitions

"Clinically isolated syndrome or CIS" refers to a first episode of neurologic symptoms lasting at least 24 hours caused by inflammation or demyelination in the central nervous system.

"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" is a medication that modifies the course of MS by reducing relapses and slowing disability progression.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"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.

"Multiple sclerosis" is a chronic autoimmune disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Primary progressive MS" refers to worsening neurologic function from the onset of symptoms, without early relapses or remissions.

"Relapse" is defined as the appearance of new symptoms or the worsening of existing symptoms lasting at least 24 hours in the absence of fever or infection.

"Relapsing-remitting MS" refers to a disease course characterized by clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery.

"[s]" indicates state mandates may apply.

"Secondary progressive MS or SPMS" 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.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Lemtrada (alemtuzumab) medically necessary when ONE of the following criteria are met:

1. Authorization may be granted for pediatric members less than 18 years of age with multiple sclerosis when there is documentation that the benefits outweigh the risks*; OR*
   Note: If approved, the requested product will be authorized for up until the member reaches 18 years of age.
2. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Lemtrada (alemtuzumab) medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates the member meets ALL of the following:

1. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has ONE (1) of the following forms of multiple sclerosis:
   a. Relapsing-remitting (RRMS)*; or*
   b. Active secondary progressive disease (SPMS); *AND*
4. The member is unable to use, or has tried and failed BOTH of the following:[s]
   a. Tysabri (natalizumab) or Tyruko (natalizumab-sztn)*; and*
   b. Is unable to use, or has tried and failed at least ONE (1) of the following:
      i. Dimethyl Fumarate (generic Tecfidera)*; and/or*
      ii. Fingolimod (generic Gilenya); *and/or*
      iii. Teriflunomide (generic Aubagio); *AND*
5. The member meets ALL of the following:
   a. No evidence of Human immunodeficiency virus (HIV) infection*; or*
   b. No evidence of active infections; *AND*
6. Lemtrada (alemtuzumab) will be used as monotherapy for multiple sclerosis (i.e., member is not using and will not use other disease-modifying MS therapies while on Lemtrada); *AND*
7. Lemtrada (alemtuzumab) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

- *The recommended dosage of Lemtrada is 12 mg/day administered by intravenous infusion for 2 treatment courses:*
    i. *First course: 12 mg/day on 5 consecutive days (total 60 mg).*
    ii. *Second course: 12 mg/day on 3 consecutive days (total 36 mg) administered 12 months after the first treatment course.*
    iii. *Additional 3-day (total 36 mg) courses may be administered as needed with a minimum of 12 months between courses.*
    iv. *Corticosteroids premedication is recommended prior to infusion for the first 3 days of each treatment course.*
    v. *Administration of antiviral agents for herpetic prophylaxis is recommended, starting on the first day of Lemtrada (alemtuzumab) dosing and continuing for a minimum of two months after completion of Lemtrada (alemtuzumab) dosing or until CD4+ lymphocyte count is more than 200 cells/microliter, whichever occurs later.*

If the above prior authorization criteria are met, the requested medication will be authorized for one treatment course (5 consecutive days of 12 mg/day, for a total of 60 mg).[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Lemtrada (alemtuzumab) medically necessary when recent (within the last 6-months) clinical chart documentation provided indicates the member meets ALL of the following:

1. The requested medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member has experienced at least ONE (1) of the following:
    a. Improvement in at least ONE (1) objective measure, such as:
        i. Reduced disease activity on MRI*; and/or*
        ii. Improved or stable disability scores*; and/or*
        iii. Reduced relapse rate*; and/or*
        iv. Improved fatigue or walking assessments; *or*
    b. The member has shown stabilization or improvement in at least ONE (1) MS symptom, such as:
        i. Motor function*; and/or*
        ii. Fatigue*; and/or*
        iii. Vision*; and/or*
        iv. Bowel/bladder function*; and/or*

v. Spasticity*; and/or*
vi. Walking/gait*; and/or*
vii. Pain/numbness/tingling; *AND*

3. At least 12 months have passed since the last dose of Lemtrada.

<u>If the above reauthorization criteria are met, the requested medication will be authorized for one treatment course (3 consecutive days of 12 mg/day, for a total of 36 mg).</u>[5]

[5] *<u>NOTE:</u> The Plan may consider authorizing additional treatment courses of Lemtrada beyond the initial two courses on a case-by-case basis, based on documented evidence of continued disease activity and the prescriber's clinical judgment. However, the safety and efficacy of more than two treatment courses have not been well established in clinical trials. The Plan recommends that healthcare providers carefully weigh the potential benefits against the increased risks of autoimmune disorders, infusion reactions, stroke, and malignancies associated with additional Lemtrada courses. Members experiencing disease activity after completing two courses should discuss the risks and benefits of additional Lemtrada treatment versus alternative MS therapies with their healthcare provider.*

Experimental or Investigational / Not Medically Necessary[5]

Lemtrada (alemtuzumab) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Use in combination with other disease-modifying therapies for MS. There is limited knowledge about the use of combining DMTs for MS.
- Use for the treatment of clinically isolated syndrome. Lemtrada (alemtuzumab) has not been studied and is not recommended for use in those with CIS, due to the safety profile of Lemtrada (alemtuzumab).
- Use for the treatment of other autoimmune conditions not related to MS. There is no high quality evidence to support the safety and efficacy of Lemtrada (alemtuzumab) for the management of other autoimmune conditions (e.g., Crohn's disease).
- Use for the treatment of primary progressive MS. The safety and efficacy of Lemtrada (alemtuzumab) has not been established in those with PPMS.
- Use in members with active infections, including HIV. Lemtrada (alemtuzumab) is contraindicated in those with HIV infection and active infections.

Applicable Billing Codes

Table 1
CPT/HCPCS codes for Multiple Sclerosis considered medically necessary if criteria are met:

Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J0202	Injection, alemtuzumab, 1 mg

Table 2	
ICD-10 diagnosis codes considered medically necessary for Multiple Sclerosis with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
G35	Multiple sclerosis
G35.A	Relapsing-remitting multiple sclerosis
G35.C1	Active secondary progressing multiple sclerosis
G35.D	Multiple sclerosis, unspecified

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