Utilization Review Policy 139

POLICY: Multiple Sclerosis (Injectable – Other) – Lemtrada Utilization Management Medical Policy

- Lemtrada® (alemtuzumab intravenous infusion – Genzyme)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 07/23/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Lemtrada, a CD52-directed cytolytic monoclonal antibody, is indicated for the treatment of relapsing forms of **multiple sclerosis** (MS) to include relapsing remitting disease and active secondary progressive MS in adults.[1] Lemtrada is not recommended for use in patients with clinically isolated syndrome because of its safety profile.

Due to its safety profile, use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more medications indicated for the treatment of MS.[1] Lemtrada contains the same active ingredient found in Campath® (alemtuzumab intravenous infusion). The safety and efficacy of Lemtrada have not been established in patients less than 17 years of age. Lemtrada is administered by intravenous infusion over 4 hours for two or more treatment courses. The dose for the first course is 12 mg/day on five consecutive days. The second course is 12 mg/day on three consecutive days 12 months after the first treatment course. Subsequent treatment courses of 12 mg per day on three consecutive days (36 mg total) may be given, as needed, at least 12 months after the last dose of any prior treatment course.

Disease Overview

MS is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system that impacts almost 1,000,000 people in the US.[2-4] The condition is marked by inflammation and demyelination, as well as degenerative alterations. Patients usually experience relapses and remissions in their neurological symptoms. For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults. The MS disease course is heterogeneous but has some patterns. Approximately 85% to 90% of patients have a relapsing pattern at onset. However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS). Around 10% to 15% of patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity. Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age), and the distribution is equivalent among the two genders. Advances in the understanding of the MS disease process, as well as in MRI technology, spurned updated disease course descriptions in 2013,[5] as well as in 2017.[6] The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.[2-6] Clinically isolated syndrome is now more recognized among the course descriptions of MS. It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be

MS but has yet to fulfill diagnostic criteria. It is notable that the other MS designations can be further characterized considering whether patients have active disease (or not active), as well as if disease is worsening or stable. Disability in MS is commonly graded on the deterioration of mobility per the Expanded Disability Status Scale (EDSS), an ordinal scale that ranges from 0 to 10, with higher scores indicating greater disability.

Guidelines

In September 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.[2] Many options from various disease classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.

Safety

Lemtrada is available only through a restricted Risk Evaluation Mitigation Strategy (REMS) program called the LEMTRADA REMS Program due to the risks of autoimmunity, infusion reactions, and malignancies.[1] Use of Lemtrada is contraindicated in patients who have infection with human immunodeficiency virus (HIV) and those with active infection. Progressive multifocal leukoencephalopathy has occurred in a patient with MS who received Lemtrada.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Lemtrada. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for 30 days which is an adequate duration for the patient to receive the recommended number of doses. Because of the specialized skills required for evaluation and diagnosis of patients treated with Lemtrada, as well as the monitoring required for adverse events and long-term efficacy, approval requires Lemtrada to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Lemtrada at initiation as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, MRI reports, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lemtrada is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Multiple Sclerosis.** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy (this includes patients who have started but not completed the first course of Lemtrada therapy). Approve for five doses in patients who meet ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 17 years of age; AND

ii. Patient has a relapsing form of multiple sclerosis; AND
Note: Examples of relapsing forms of multiple sclerosis include relapsing remitting disease and active secondary progressive disease.

iii. Patient meets ONE of the following (a, b, c, or d):

a) According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to two disease-modifying agents used for multiple sclerosis; OR
Note: See Appendix for examples.

b) According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to one of Kesimpta (ofatumumab subcutaneous injection), a natalizumab intravenous product (Tysabri, biosimilar), Briumvi (ublituximab-xiiy intravenous infusion), Mavenclad (cladribine tablets), Ocrevus (ocrelizumab intravenous infusion), or Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq subcutaneous injection); OR

c) Patient has received Lemtrada in the past; OR

d) According to the prescriber, the patient has highly-active or aggressive multiple sclerosis by meeting ONE of the following [(1), (2), (3), or (4)]:

1. Patient has demonstrated rapidly advancing deterioration(s) in physical functioning **[documentation required]**; OR
Note: Examples include loss of mobility or lower levels of ambulation and severe changes in strength or coordination.

2. Disabling relapse(s) with suboptimal response to systemic corticosteroids **[documentation required]**; OR

3. Magnetic resonance imaging (MRI) findings suggest highly active or aggressive multiple sclerosis **[documentation required]**; OR
Note: Examples include new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions.

4. Manifestations of multiple sclerosis-related cognitive impairment **[documentation required]**; AND

iv. Medication is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of multiple sclerosis; OR

B) Patient Who Has Completed a Previous Course of Lemtrada Therapy. Approve for three doses if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. Patient is ≥ 17 years of age; AND

ii. Patient has a relapsing form of multiple sclerosis; AND
Note: Examples of relapsing forms of multiple sclerosis include relapsing remitting disease and active secondary progressive disease.

iii. Patient meets ONE of the following (a or b):

a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
Note: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization

or reduced worsening on the Expanded Disability Status Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-3 (NEDA-3) or NEDA-4; improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Item MS Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and/or attenuation of brain volume loss.

b) Patient experienced stabilization, slowed progression, or improvement in at least one symptom such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation; AND

iv. At least 12 months has elapsed from the last dose of any prior Lemtrada treatment course; AND

v. Medication is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of multiple sclerosis.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) First treatment course is 12 mg/day by intravenous infusion on 5 consecutive days (60 mg total dose); OR

B) For additional treatment courses, the dose is 12 mg/day by intravenous infusion on 3 consecutive days (36 mg total dose) administered 12 months after the last Lemtrada treatment course.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Lemtrada is not recommended in the following situations:

1. **Clinically Isolated Syndrome.** Lemtrada is not recommended for use in patients with clinically isolated syndrome due to its safety profile.[1]

2. **Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis.** These agents are not indicated for use in combination (See Appendix for examples). Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.

3. **HIV Infection.** Use of Lemtrada is contraindicated in patients who are infected with HIV because Lemtrada causes prolonged reductions of CD4+ lymphocyte counts.[1]

4. **Non-Relapsing Forms of Multiple Sclerosis.** The efficacy of Lemtrada has not been established in patients with MS with non-relapsing forms of the disease.[1]
   Note: An example of a non-relapsing form of MS is primary progressive MS.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Lemtrada® intravenous infusion [prescribing information]. Cambridge, MA: Genzyme; May 2024.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. September 2019.
3. McGinley MP, Goldschmidt C, Rae-Grant AD. Diagnosis and treatment of multiple sclerosis. A review. *JAMA*. 2021;325(8):765-779.
4. No authors listed. Drugs for multiple sclerosis. *Med Lett Drugs Ther*. 2021;63(1620):42-48.
5. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
6. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/30/2022
Annual Revision	**Multiple Sclerosis:** The following agents were added to the list allowing an exception with previous use: Tyruko (natalizumab-sztn intravenous infusion), Briumvi (ublituximab-xiij intravenous infusion), Mavenclad (cladribine tablets), and Lemtrada.	11/15/2023
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
Annual Revision	Ocrevus Zunovo was added to the Appendix.	10/09/2024
Selected Revision	**Multiple Sclerosis:** For initial therapy, for the criteria that requires the patient to try one alternative it was added that the patient has experienced inadequate efficacy or significant intolerance (according to the prescriber) to this agent. Also, Ocrevus Zunovo was added to the list of disease-modifying multiple sclerosis drugs that count toward meeting this requirement. The individual listing of Tysabri and Tyruko among these alternatives was changed to state "a natalizumab intravenous product (Tysabri, biosimilar)". Lemtrada was separated from this listing of agents into an individual criterion in which receipt of Lemtrada in the past counts (without requiring inadequate efficacy or significant intolerance [according to the prescriber]).	10/16/2024
Early Annual Revision	**Multiple Sclerosis:** Extavia was removed from the Appendix. The name of the policy was changed to add "Injectable – Other".	07/23/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025

APPENDIX

Medication	Mode of Administration
Aubagio® (teriflunomide tablets, generic)	Oral
Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Briumvi® (ublituximab-xiiy intravenous infusion)	Intravenous infusion
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)
Gilenya® (fingolimod capsules, generic)	Oral
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)
Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion
Mavenclad® (cladribine tablets)	Oral
Mayzent® (siponimod tablets)	Oral
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq subcutaneous injection)	Subcutaneous Injection (not self-administered)
Plegridy® (peginterferon beta-1a subcutaneous or intramuscular injection)	Injection (self-administered)
Ponvory® (ponesimod tablets)	Oral
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)
Tascenso ODT® (fingolimod orally disintegrating tablets)	Oral
Tecfidera® (dimethyl fumarate delayed-release capsules, generic)	Oral
Tyruko® (natalizumab-sztn intravenous infusion)	Intravenous infusion
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral