PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis – Lemtrada Prior Authorization Policy
- Lemtrada® (alemtuzumab injection for intravenous use – Genzyme)

REVIEW DATE: 11/11/2020

OVERVIEW

Lemtrada, a CD52-directed cytolytic monoclonal antibody, is indicated for the treatment of patients with 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 injection for intravenous use). The safety and efficacy of Lemtrada have not been established in pediatric patients < 17 years of age.

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] 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,[3] as well as in 2017.[4] The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.[2-4] 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.

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.

A practice guideline recommendation regarding disease-modifying agents for adults with MS from the American Academy of Neurology (2018) states to consider Lemtrada for patients with MS who have highly active disease.[5]

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, stroke, and malignancies.[1] Use of Lemtrada is contraindicated in patients who has infection with human immunodeficiency virus 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 prescription benefit coverage of Lemtrada. All approvals are noted for the duration noted below. 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 magnetic resonance imaging (MRI) reports, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lemtrada injection 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 5 days in patients who meet all of the following criteria (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 or b):
       - **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: Examples include Avonex® (interferon beta-1a injection [intramuscular]), Rebif® (interferon beta-1a injection [subcutaneous]), Betaseron®/Extavia® (interferon beta-1b injection), glatiramer acetate injection (Copaxone®/Glatopa®, generic), Plegridy® (peginterferon beta-1a injection), Gilenya® (fingolimod capsules), Aubagio® (teriflunomide tablets), Mavenclad® (cladribine tablets), Mayzent® (siponimod tablets), Vumerity® (diroximel fumarate delayed-release capsules), Tysabri® (natalizumab injection for intravenous use), Bafiertam™ (monomethyl fumarate delayed-release capsules), dimethyl fumarate delayed-release capsules (Tecfidera®, generic), Zeposia® (ozanimod capsules), Kesimpta® (ofatumumab injection for subcutaneous use), and Ocrevus® (ocrelizumab injection for intravenous use).
       - **b)** 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 (e.g., loss of mobility/or lower levels of ambulation, severe changes in strength or coordination) **[documentation required]**; OR
(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 (e.g., new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions) **[documentation required]**; OR
(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 who specializes in the treatment of multiple sclerosis; OR

B) Patient Who Has Completed a Previous Lemtrada Therapy Course. Approve for 3 days if the patient meets 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. At least 12 months has elapsed from the last dose of any prior Lemtrada treatment course; AND
iv. Medication is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of multiple sclerosis.

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.** Lemtrada should not be given in combination with other disease-modifying agents used for multiple sclerosis. Concomitant use of Lemtrada with immunosuppreisve therapies could increase the risk of immunosuppression.
Note: Examples include Avonex® (interferon beta-1a injection [intramuscular]), Rebif® (interferon beta-1a injection [subcutaneous]), Betaseron®/Extavia® (interferon beta-1b injection), glatiramer acetate injection (Copaxone®/Glatopa®, generic), Plegridy® (peginterferon beta-1a injection), Gilenya® (fingolimod capsules), Aubagio® (teriflunomide tablets), Mavenclad® (cladribine tablets), Mayzent® (siponimod tablets), Vumerity® (diroximel fumarate delayed-release capsules), Tysabri® (natalizumab injection for intravenous use), Bafiertam™ (monomethyl fumarate delayed-release capsules), dimethyl fumarate delayed-release capsules (Tecfidera®, generic), Zeposia® (ozanimod capsules), Kesimpta® (ofatumumab injection for subcutaneous use), and Ocrevus® (ocrelizumab injection for intravenous use).

3. **Human Immunodeficiency Virus (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 multiple sclerosis with non-relapsing forms of the disease.[1]
   Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis.

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® injection for intravenous use [prescribing information]. Cambridge, MA: Genzyme Corporation; September 2020.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated September 2019. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed on November 5, 2020.
3. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
4. 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.
5. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:777-788.