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Last P&T Approval/Version: 04/24/2024
Next Review Due By: 04/2025
Policy Number: C6919-A

Lemtrada (alemtuzumab)

PRODUCTS AFFECTED

Lemtrada (alemtuzumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. RELAPSING MULTIPLE SCLEROSIS:
1. Documentation of a definitive diagnosis of a relapsing form of multiple sclerosis including: Relapsing- remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS]

with relapses
AND

2. Documentation of **inadequate response (trial of 3 months) to BOTH of the following:
   (a) ONE of the following: ONE Interferon therapy (Avonex, Rebif, Extavia, Betaseron, Plegridy) OR Glatiramer OR teriflunomide (Aubagio) OR dimethyl fumarate (Tecfidera)
   AND
   (b) ONE of the following: Tysabri (natalizumab) OR Ocrevus (ocrelizumab) OR fingolimod (Gilenya)
   **Inadequate response is defined as meeting at least TWO (2) of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesions progression as measured by MRI, OR 3) Worsening disability (e.g., sustained worsening of EDSS score or neurological exam findings; worsening disability include, but not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or EDSS > 3.5)
   AND
3. Documentation of baseline thyroid function tests, complete blood cell count (CBC) with differential, serum creatinine levels, serum transaminases and total bilirubin, urinalysis with urine cell counts, urine protein to creatinine ratio, and screen for the presence of tuberculosis; skin exam (for melanoma) [APPENDIX] [DOCUMENTATION REQUIRED]
   AND
4. Prescriber attests to perform periodic testing during treatment according to routine patient management per the FDA label (e.g., annual human papillomavirus screening and skin exams; tuberculosis screening; signs/symptoms of infection and progressive multifocal leukoencephalopathy (PML)) [APPENDIX]
   AND
5. Prescriber attests that member is not currently being treated with a disease modifying agent (DMA) other than the requested agent, B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab), or lymphocyte trafficking blocker (e.g., mitoxantrone)
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Lemtrada (alemtuzumab) include: Known hypersensitivity or anaphylactic reactions to alemtuzumab or any of the excipients in Lemtrada, Infection with Human Immunodeficiency Virus, or Active infection]

CONTINUATION OF THERAPY:

A. RELAPSING MULTIPLE SCLEROSIS:

1. Documentation of positive clinical response or stable disease based on ONE of the following:
   (a) Documentation of a stable number or decrease in acute attacks (relapses) within the last 6 months
   OR
   (b) Documentation of lack of progression or sustained disability
   OR
   (c) Recent (within the last 6 months) MRI shows lack of development of new asymptomatic lesions
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., immune thrombocytopenia, glomerular nephropathies, thyroid disorders, autoimmune conditions, severe infusion reactions, ischemic or hemorrhagic strokes, malignancies, etc.)
   AND
3. Member has not received a dose of alemtuzumab within the past 12 months
   AND
4. Prescriber attests to performing periodic testing during treatment (e.g., TSH levels, urine protein to creatinine ratio, etc.) and physical examinations (melanoma exam, malignancies, infection, TB etc.) according to routine patient management as indicated by FDA labeling [APPENDIX]

DURATION OF APPROVAL:
Initial authorization: 5 doses (given on 5 consecutive days), Continuation of therapy: 3 doses (given on 3 consecutive days) annually 12 months following the initial course or subsequent courses

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified neurologist or specialist in multiple sclerosis. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
17 years of age and older

QUANTITY:
Initial authorization: FIVE 12-mg injections, Continuation of therapy: THREE 12-mg injections

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Lemtrada (alemtuzumab). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Multiple Sclerosis Agents - Monoclonal Antibodies

FDA-APPROVED USES:
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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Monitoring/Labs:
Baseline laboratory tests are required prior to treatment with Lemtrada.
Conduct the following laboratory tests at baseline and at periodic intervals until 48 months after the last treatment course of LEMTRADA in order to monitor for early signs of potentially serious adverse effects:

- CBC with differential prior to initiation then monthly until 48 months after last infusion
- serum creatinine prior to initiation then monthly until 48 months after last infusion or at any time during therapy if clinically indicated
- serum transaminases and total bilirubin prior to initiation then periodically until 48 months after the last

infusion or at any time during therapy if clinically indicated

- urinalysis with urine cell counts prior to initiation then monthly until 48 months after last infusion (urine dipstick results of ≥1+ protein warrant assessment of urine protein to creatinine ratio)
- urine protein to creatinine ratio at baseline and then as clinically indicated (evaluate further for nephropathies if urine protein to creatinine ratio >200 mg/g increase in serum creatinine >30%, or unexplained hematuria)
- TSH at baseline and every 3 months until 48 months after last infusion or longer or at any time during therapy if clinically indicated

Additional monitoring:

- Monitor for signs/symptoms of infection
- annual human papillomavirus screening
- tuberculosis screening
- signs/symptoms of progressive multifocal leukoencephalopathy
- baseline and annual skin exams (for melanoma)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Multiple Sclerosis (MS) is a chronic autoimmune disease that degrades the protective myelin sheath that covers nerve cells in the central nervous system, specifically in the areas of the brain, spinal cord, and optic nerves. For most Americans, the risk of developing MS is approximately 0.1% but the risk is increased for individuals with a first-degree relative with MS. MS occurs at least two to three times more commonly in women than in men. Most patients are diagnosed between the ages of 20 to 50 years. Relapsing remitting MS (RRMS) is the most common type of MS affecting approximately 85% of the patients initially diagnosed with MS. Complications of MS include fatigue, loss of coordination, visual problems, cognitive and sexual dysfunction, depression, spasticity, and pain.

Clinically, MS presents with four relatively distinguishable patterns based on the course of disease. Of the four clinical subtypes of MS (primary progressive, progressive relapsing, RRMS and secondary progressive), RRMS is the most common and is characterized by acute relapses followed by partial or full recovery.

1. Relapsing–remitting MS: the most common form, affecting about 85% of MS patients. It is marked by flare-ups (relapses or exacerbations) of symptoms followed by periods of remission when symptoms improve or disappear.
2. Secondary progressive MS: may develop in some patients with relapsing–remitting disease. For many patients, treatment with disease-modifying agents helps delay such progression. The disease course continues to worsen with or without periods of remission or leveling off of symptom severity (plateaus).
3. Primary progressive MS affects approximately 10% of MS patients. Symptoms continue to worsen gradually from the beginning. There are no relapses or remissions, but there may be occasional plateaus. This form of MS is more resistant to the drugs typically used to treat the disease.
4. Progressive-relapsing MS: PRMS affects about 5% of patients. It is characterized by continuous neurologic decline from the time of diagnosis, accompanied by distinct attacks. Itis progressive from the start, with intermittent flare-ups of worsening symptoms along the way. There are no periods of remission.

Lemtrada, a CD52-directed cytolytic monoclonal antibody, is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). 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. The recommended dose of Lemtrada is 12 mg/day given by intravenous (IV) infusion for two treatment courses. The first treatment course is 12 mg/day IV on 5 consecutive days (60 mg total dose) and the second treatment course is 12 mg/day IV on 3 consecutive days (36 mg total dose) given 12 months after the first treatment course. Infuse Lemtrada over 4 hours and administer the agent in a setting that has equipment and personnel to appropriately manage anaphylaxis or serious infusion

reactions. Observe patients for infusion reactions during and for at least 2 hours after each Lemtrada infusion. Patients should complete any needed immunizations at least 6 weeks prior to Lemtrada therapy initiation.

Lemtrada REMS (Risk Evaluation and Mitigation Strategy) Program:
LEMTRADA is available only through a restricted program under a REMS called the LEMTRADA REMS Program because of the risks of autoimmunity, infusion reactions, and malignancies.
Notable requirements of the LEMTRADA REMS Program include the following:
• Prescribers must be certified with the program by enrolling and completing training.
• Patients must enroll in the program and comply with ongoing monitoring requirements.
• Pharmacies must be certified with the program and must only dispense to certified healthcare facilities that are authorized to receive LEMTRADA.
• Healthcare facilities must enroll in the program and verify that patients are authorized before infusing LEMTRADA. Healthcare facilities must have on-site access to equipment and personnel trained to manage infusion reactions.
Further information, including a list of qualified healthcare facilities, is available at 1-855-676-6326.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Lemtrada (alemtuzumab) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Lemtrada (alemtuzumab) include: Hypersensitivity to alemtuzumab or any of its components, HIV infection (due to prolonged reduction of CD4+ lymphocyte counts) or any other uncontrolled active infection, Live virus vaccine: Live viral vaccines should not be administered following a course of Lemtrada. Concurrent therapy with other disease-modifying multiple sclerosis agents, Post-transplant antibody induction therapy, any cancer indication, including, but not limited to B-cell chronic lymphocytic leukemia.

OTHER SPECIAL CONSIDERATIONS:
Lemtrada (alemtuzumab) has a black box warning for autoimmunity, infusion reactions, stroke, and malignancies. Lemtrada causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts before starting treatment and then at monthly intervals until 48 months after the last dose of Lemtrada. Lemtrada causes serious and life-threatening infusion reactions. Lemtrada must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for two hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period. Serious and life-threatening stroke (including ischemic and hemorrhagic stroke) has been reported within 3 days of Lemtrada administration. Instruct patients to seek immediate medical attention if symptoms of stroke occur. Lemtrada may cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams. Because of the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) Program. Call 1-855-676-6326 to enroll in the Lemtrada REMS program.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0202	Injection, alemtuzumab, 1 mg

AVAILABLE DOSAGE FORMS:
Lemtrada SOLN 12MG/1.2ML single-dose vial

REFERENCES

1. Lemtrada™ (alemtuzumab) injection for intravenous use [prescribing information]. Cambridge, MA: Genzyme Corporation; February 2024.
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3. Coles AJ, Twyman CL, Arnold DL, et al, for the CARE-MS II Investigators. Alemtuzumab for patients with relapsing multiple sclerosis after disease-modifying therapy: a randomized controlled phase 3 study. Lancet. 2012;380:1829-1839.
4. Campath® injection for intravenous use [prescribing information]. Cambridge, MA: Genzyme Corporation; September 2014.
5. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. Rosalind Kalb and Nancy Reitman. © 2012 National Multiple Sclerosis Society.
6. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence. July 2014. Available at: http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition .pdf
7. McGraw CA, Lublin FD. Interferon beta and glatiramer acetate therapy. Neurotherapeutics. 2013;10:2-18.
8. O'Connor PW, Oh J. Disease-modifying agents in multiple sclerosis. Handb Clin Neurol.2014;122:465-501
9. 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.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Appendix Background Other Special Considerations References	Q2 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Background Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q2 2023
REVISION- Notable revisions: Duration of Approval Billing/Coding Information	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file