Lemtrada® (alemtuzumab) (Intravenous)

Effective Date:01/01/2020
Review Date:4/10/2019, 9/18/2019, 12/20/2019, 1/22/20, 6/10/2021, 6/16/2022, 7/13/2023, 12/07/2023, 01/10/2024, 06/04/2025
Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage will be approved initially for 5 doses and may be renewed for 3 doses annually thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- First Course
  - 12 billable units daily for 5 days during the first 12 months
- Second/Subsequent Courses
  - 12 billable units daily for 3 days every 12 months thereafter

III. Summary of Evidence

Lemtrada is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease and active secondary progressive disease, in adults. The approval of Lemtrada is based on two pivotal randomized Phase III open-label rater-blinded studies comparing treatment with Lemtrada to Rebif® (high-dose subcutaneous interferon beta-1a) in patients with relapsing remitting MS who were either new to treatment (CARE-MS I) or who had relapsed while on prior therapy (CARE-MS II). In clinical trials, Lemtrada was shown to significantly reduce the relapse rate for individuals with relapsing-remitting MS, as well as significantly reduce the risk of sustained disability accumulation. In a multi-year extension study of the 334 individuals who participated in the original Phase II study (comparing Lemtrada to Rebif), Lemtrada reduced the risk for sustained accumulation of disability by 73 percent, while 77 percent of Lemtrada-treated patients were relapse-free. A five-year assessment showed that 87 percent were free of sustained disability accumulation, 72 percent were relapse-free, and 65 percent were free of clinical-disease activity. Adverse events from Lemtrada can include infusion reactions to the medication, an increased risk of infection, and emergent autoimmune diseases. Lemtrada requires a Risk Evaluation and Mitigation Strategy (REMS) for Lemtrada due to its safety profile, which includes serious autoimmune conditions, infusion reactions, and an increased risk of certain cancers.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

- Lemtrada is being prescribed by or in consultation with a neurologist; **AND**
- Patient has been evaluated and screened for the presence of varicella zoster virus (VZV) and vaccinated, if required, prior to initiating treatment; **AND**
- Patient has a baseline electrocardiogram (ECG); **AND**

Universal Criteria [1]

- Patient does not have human immunodeficiency virus (HIV) infection; **AND**
- Patient has been evaluated and screened for the presence of tuberculosis (TB) prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; **AND**
- Patient does not have an active infection; **AND**
- Patient will not receive live vaccines while on therapy or within 6 weeks prior to initiation of treatment; **AND**
- Patient has received a baseline skin exam for melanoma and will receive yearly skin exams while on therapy; **AND**
- Patient has a baseline urine protein to creatinine ratio AND thyroid-stimulating hormone (TSH) level prior to initiation of treatment and will receive ongoing laboratory monitoring during treatment; **AND**
- Medicare & Commercial members must have a documented failure, intolerance, or contraindication to with Ocrevus (ocrelizumab) and Tysabri (natalizumab); OR
- Medicaid members must have an inadequate response, intolerance, or contraindication to Tysabri (natalizumab) and one more drug indicated for MS; **AND**
- Patient will receive anti-viral prophylaxis for herpetic viral infections initiated on the first day of treatment and continued for two months following treatment (*or until the CD4+ lymphocyte count is ≥ 200 cells/mcL*); **AND**
- Prescriber and patient must be enrolled in and meet the conditions of the LEMTRADA REMS program; **AND**
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Multiple Sclerosis (MS) † [1,10,14]

- Patient has been diagnosed with a relapsing form of multiple sclerosis [i.e., relapsing-remitting disease (RRMS)***** or active secondary progressive MS (SPMS)******]; **AND**
- Patient must have a confirmed diagnosis of MS as documented by laboratory report (i.e., MRI); **AND**
- Used as single agent therapy; **AND**
- Patient must have had an inadequate response to an adequate trial of two or more drugs indicated for the treatment of MS; **AND**
- Will not be used for the treatment of clinically isolated syndrome (CIS)

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

***Definitive diagnosis of MS with a relapsing-remitting course is based upon <u>BOTH</u> dissemination in time and space. Unless contraindicated, MRI should be obtained (even if criteria are met). [14]**

<u>Dissemination in time</u> (*Development/ appearance of new CNS lesions over time*)	**<u>Dissemination in space</u>** (*Development of lesions in distinct anatomical locations within the CNS; multifocal*)

• ≥ 2 clinical attacks; **OR**
• 1 clinical attack <u>AND</u> one of the following:
  ○ MRI indicating simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2- hyperintense or gadolinium-enhancing lesion on follow-up MRI compared to baseline scan
  ○ CSF-specific oligoclonal bands
	• ≥ 2 lesions; **OR**
	• 1 lesion <u>AND</u> one of the following:
	  ○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location
	  ○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)

****Active secondary progressive MS (SPMS) is defined as the following: [11,14-16,20]**

- Expanded Disability Status Scale (EDSS) score ≥ 3.0; **AND**
- Disease is progressive ≥ 3 months following an initial relapsing-remitting course (i.e., EDSS score increase by 1.0 in patients with EDSS ≤5.5 or increase by 0.5 in patients with EDSS ≥6); **AND**
  - ≥ 1 relapse within the previous 2 years; **OR**
  - Patient has gadolinium-enhancing activity OR new or unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

V. Renewal Criteria [1,13,19]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section IV; **AND**
- Patient has not received a dose of alemtuzumab within the past 12 months; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: immune thrombocytopenia, glomerular nephropathies including anti-glomerular basement membrane (anti-GBM) disease, thyroid disorders, autoimmune conditions (hepatitis, cytopenias [e.g., neutropenia, hemolytic anemia, and pancytopenia], encephalitis, etc.), severe infusion reactions including anaphylaxis, ischemic or hemorrhagic strokes, cervicocephalic (e.g., vertebral, carotid) arterial dissection, malignancies (e.g., thyroid cancer, melanoma, lymphoproliferative disorders/lymphoma, etc.), progressive multifocal leukoencephalopathy, thrombotic thrombocytopenic purpura, hemophagocytic lymphohistiocytosis, Adult Onset Still's Disease (AOSD), acquired hemophilia A, acute acalculous cholecystitis, pneumonitis, immune- mediated colitis, etc.; **AND**
- Continuous monitoring of response to therapy indicates a beneficial response***** [manifestations of MS disease activity include, but are not limited to, an increase in annualized relapse rate (ARR), development of new/worsening T2 hyperintensities or enhancing lesions on brain/spinal MRI, and progression of sustained impairment as evidenced by expanded disability scale (EDSS), timed 25-foot walk (T25-FW), 9-hole peg test (9-HPT)].

*****Note:
Inadequate response, in those who have been adherent and receiving therapy for sufficient time to realize the full treatment effect, is defined as ≥ 1 relapse, ≥ 2 unequivocally new MRI-detected lesions, or increased disability on examination over a one-year period.

VI. Dosage/Administration [1]

Indication	Dose
Multiple Sclerosis	Administer by intravenous (IV) infusion over 4 hours: ▪ First course: 12 mg/day on 5 consecutive days (60 mg total dose) ▪ Second course: 12 mg/day on 3 consecutive days (36 mg total dose), administered 12 months after the first treatment course. ▪ Subsequent courses: 12 mg/day on 3 consecutive days (36 mg total dose) administered, as needed, at least 12 months after the last dose of any prior treatment course.

VII. Billing Code/Availability Information

HCPCS Code:

- J0202 - Injection, alemtuzumab, 1 mg; 1mg = 1 billable unit

NDC:

- Lemtrada 12 mg/1.2 mL single-dose vial: 58468-0200-xx

VIII. References

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Accessed October 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G35	Multiple Sclerosis

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage- database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Jurisdiction	NCD/LCA/ LCD Document(s)	Contractor
J, M	A55310	Palmetto GBA

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale: Lemtrada was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Lemtrada according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.