



Lemtrada® (alemtuzumab) (Intravenous)

Document Number: IC-0223

Last Review Date: 10/03/2022

Date of Origin: 12/16/2014

Dates Reviewed: 12/2014, 10/2015, 06/2016, 09/2016, 12/2016, 03/2017, 06/2017, 09/2017, 12/2017, 03/2018, 06/2018, 10/2018, 01/2019, 10/2019, 10/2020, 10/2021, 10/2022

I. Length of Authorization

- Multiple Sclerosis: Coverage will be approved initially for 5 doses and may be renewed for 3 doses annually thereafter.
- GVHD: Coverage will be approved for 5 doses only and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Multiple Sclerosis

First Course

- Lemtrada 12 mg/1.2 mL single-dose vial: 5 vials per 365 days (1 vial daily x 5 days per year)

Second/Subsequent Courses

- Lemtrada 12 mg/1.2 mL single-dose vial: 3 vials per 365 days (1 vial daily x 3 days per year)

GVHD

- Lemtrada 12 mg/1.2 mL single-dose vial: 5 vials (1 vial daily x 5 days)

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

Multiple Sclerosis

- First Course
 - 60 billable units (*1 dose daily x 5 days*) during the first 12 months
- Second/Subsequent Courses
 - 36 billable units (*1 dose daily x 3 days*) every 12 months thereafter

GVHD

- 10 billable units daily for 5 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **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**
- 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/mL*); **AND**
- Prescriber and patient must be enrolled in and meet the conditions of the LEMTRADA REMS program; **AND**

Multiple Sclerosis † ^{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**
- Confirmed diagnosis of MS as documented by laboratory report (i.e., MRI); **AND**
- Must be 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)

Graft Versus Host Disease (GVHD) ‡ ¹⁹

- Patient has received a hematopoietic stem cell transplant; **AND**
- Used for steroid-refractory acute or chronic GVHD; **AND**
- Used in combination with systemic corticosteroids as additional therapy following no response to first-line therapy options

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

***Definitive diagnosis of MS with a relapsing-remitting course is based upon BOTH dissemination in time and space. Unless contraindicated, MRI should be obtained (even if criteria are met).^{10,14}**

<u>Dissemination in time</u> <i>(Development/appearance of new CNS lesions over time)</i>	<u>Dissemination in space</u> <i>(Development of lesions in distinct anatomical locations within the CNS; multifocal)</i>
<ul style="list-style-type: none"> • ≥ 2 clinical attacks; OR • 1 clinical attack AND one of the following: <ul style="list-style-type: none"> ○ 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 	<ul style="list-style-type: none"> • ≥ 2 lesions; OR • 1 lesion AND one of the following: <ul style="list-style-type: none"> ○ 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}**

- 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 and unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

IV. Renewal Criteria^{1,13}

Authorizations can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **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 encephalopathy, thrombotic thrombocytopenic purpura, hemophagocytic lymphohistiocytosis, Adult Onset Still's Disease (AOSD), acquired hemophilia A, acute acalculous cholecystitis, pneumonitis, etc.; **AND**

Multiple Sclerosis

- 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 EDSS, timed 25-foot walk (T25-FW), 9-hole peg test (9-HPT)].

- 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

Graft Versus Host Disease (GVHD) ‡¹⁹⁻²³

- Coverage may not be renewed. (*Note: Requests for continued therapy beyond the maximum number of doses specified in Section V will be reviewed on a case-by-case basis.*)

V. Dosage/Administration^{1,20-23}

Indication	Dose
Multiple Sclerosis	Administer by intravenous (IV) infusion over 4 hours: <ul style="list-style-type: none"> ▪ 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.
GVHD	Administer by intravenous (IV) infusion up to 10 mg daily for up to 5 doses.

VI. 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

VII. References

1. Lemtrada [package Insert]. Cambridge, MA; Genzyme Corporation.; August 2022. Accessed September 2022.
2. Goodin DS, Frohman EM, Garmany GP Jr, et al. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002 Jan 22;58(2):169-78.
3. Coles AJ, Fox E, Vladic A, et al. Alemtuzumab more effective than interferon β -1a at 5-year follow-up of CAMMS223 clinical trial. *Neurology*. 2012;78(14):1069–1078.
4. Coles AJ, Fox E, Vladic A, et al. Alemtuzumab versus interferon β -1a in early relapsing-remitting multiple sclerosis: post-hoc and subset analyses of clinical efficacy outcomes. *Lancet Neurol*. 2011;10(4):338–348.

5. Coles AJ, Twyman CL, Arnold DL, et al; for CARE-MS II investigators. Alemtuzumab for patients with relapsing multiple sclerosis after disease-modifying therapy: a randomised controlled phase 3 trial. *Lancet*. 2012;380(9856):1829–1839.
6. Coles AJ, Compston DA, Selmaj KW, et al; for CAMMS223 Investigators. Alemtuzumab vs interferon beta-1a in early multiple sclerosis. *N Engl J Med*. 2008;359(17):1786–1801.
7. Cohen JA, Coles AJ, Arnold DL, et al; for CARE-MS I investigators. Alemtuzumab versus interferon beta 1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: a randomised controlled phase 3 trial. *Lancet*. 2012;380(9856):1819–1828.
8. Fox EJ, Sullivan HC, Gazda SK, et al. A single-arm, open-label study of alemtuzumab in treatment-refractory patients with multiple sclerosis. *Eur J Neurol*. 2012;19(2):307–311.
9. Freedman MS, Selchen D, Arnold DL, et al. Treatment optimization in MS: Canadian MS Working Group updated recommendations. *Can J Neurol Sci*. 2013 May;40(3):307-23.
10. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. *Ann Neurol*. 2011 Feb; 69(2): 292–302. doi: 10.1002/ana.22366.
11. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014 Jul 15;83(3):278-86. doi: 10.1212/WNL.0000000000000560.
12. Montalban X, Gold R, Thompson AJ, et al. (2018),ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis. *Eur J Neurol*, 25 Iss 2, Jan2018: 215–237. doi:10.1111/ene.13536
13. 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.
14. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018 Feb;17(2):162-173. doi: 10.1016/S1474-4422(17)30470-2.
15. Kappos L, Bar-Or A, Cree BAC, et al. Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomised, phase 3 study. *Lancet*. 2018;391(10127):1263. Epub 2018 Mar 23.
16. Lorscheider J, Buzzard K, Jokubaitis V, et al, on behalf of the MSBase Study Group. Defining secondary progressive multiple sclerosis. *Brain*, Volume 139, Issue 9, September 2016, Pages 2395–2405, <https://doi.org/10.1093/brain/aww173>.
17. Cohen JA, Coles AJ, Arnold DL, et al; CARE-MS I investigators. Alemtuzumab versus interferon beta 1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: a randomised controlled phase 3 trial. *Lancet*. 2012 Nov 24;380(9856):1819-28. doi: 10.1016/S0140-6736(12)61769-3. Epub 2012 Nov 1. PMID: 23122652.
18. Coles AJ, Twyman CL, Arnold DL, et al; CARE-MS II investigators. Alemtuzumab for patients with relapsing multiple sclerosis after disease-modifying therapy: a randomised

controlled phase 3 trial. *Lancet*. 2012 Nov 24;380(9856):1829-39. doi: 10.1016/S0140-6736(12)61768-1. Epub 2012 Nov 1. PMID: 23122650.

19. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) alemtuzumab. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2022.
20. Gómez-Almaguer D, Ruiz-Argüelles GJ, del Carmen Tarín-Arzaga L, et al. Alemtuzumab for the treatment of steroid-refractory acute graft-versus-host disease. *Biol Blood Marrow Transplant*. 2008 Jan;14(1):10-5. doi: 10.1016/j.bbmt.2007.08.052.
21. Schnitzler M, Hasskarl J, Egger M, et al. Successful treatment of severe acute intestinal graft-versus-host resistant to systemic and topical steroids with alemtuzumab. *Biol Blood Marrow Transplant*. 2009 Aug;15(8):910-8. doi: 10.1016/j.bbmt.2009.04.002. Erratum in: *Biol Blood Marrow Transplant*. 2010 Jan;16(1):128.
22. Nikiforow S, Kim HT, Bindra B, et al. Phase I study of alemtuzumab for therapy of steroid-refractory chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2013 May;19(5):804-11. doi: 10.1016/j.bbmt.2013.02.009.
23. Gutiérrez-Aguirre CH, Cantú-Rodríguez OG, Borjas-Almaguer OD, et al. Effectiveness of subcutaneous low-dose alemtuzumab and rituximab combination therapy for steroid-resistant chronic graft-versus-host disease. *Haematologica*. 2012 May;97(5):717-22. doi: 10.3324/haematol.2011.054577.
24. Palmetto GBA. Local Coverage Article: Billing and Coding: Instructions for Lemtrada® (alemtuzumab) When Used in the Treatment of Relapsing Multiple Sclerosis (A55310). Centers for Medicare & Medicaid Services, Inc. Updated on 10/14/2019 with effective date 10/24/2019. Accessed September 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G35	Multiple Sclerosis

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): J, M	NCD/LCD Document (s): A55310
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a55310&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMCD%2C6%2C3%2C5%2C1%2CF%2CP	

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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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