PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date January 1, 2024	
	LEMTRADA (ALEMTUZUMAB)	**Policy #** Lemtrada (alemtuzumab)	
		Review Date 11/29/2023	**Applicable to:** ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan (AHP) applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the disclaimer section below for more information.

POLICY

This policy addresses the coverage of Lemtrada (alemtuzumab) in the treatment relapsing forms of multiple sclerosis (MS) and graft versus host disease (GVHD).

APPLICABLE HCPCS

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

Available as: Lemtrada 12 mg/1.2 mL single-dose vial

CLINICAL CRITERIA

A. INITIAL CRITERIA

Lemtrada (alemtuzumab) may be authorized when **ALL** of the following criteria have been met with documentation (i.e., office chart notes, treatment response to previous therapy or drug regimens, lab results, treatment plan, other relevant clinical information).

1. Documented diagnosis of a **ONE** of the following:

    a. Relapsing Form of Multiple Sclerosis (e.g., Active Secondary Progressive MS (SPMS) [e.g., SPMS with a documented relapse)]; Relapsing-Remitting MS); **and** will not be used for the treatment of clinically isolated syndrome (CIS)

OR

b. Graft Versus Host Disease (GVHD)

AND

2. **ONE** of the following (a or b) is met according to documented diagnosis:

    a. Multiple Sclerosis
    Inadequate response to at least **TWO (2) different medications**, unless clinically significant adverse effects are experienced or all are contraindicated: Aubagio®, Tecfidera®, Gilenya™, an interferon-beta agent (Avonex, Betaseron, Rebif, or Plegridy), glatiramer (Copaxone®, Glatopa®), Mayzent®

    b. GVHD
        i. Member has received an allogeneic stem cell transplant for hematologic malignancies; **and**
        ii. Used for steroid-refractory acute or chronic GVHD; **and**
        iii. Used in combination with systemic corticosteroids as additional therapy following no response to first-line therapy options.

AND

3. Member is not receiving alemtuzumab in combination with another disease-modifying agent for MS (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, teriflunomide, ocrelizumab, etc.); **AND**

4. Member has been evaluated/screened for the presence of the following conditions ***prior to*** initiating treatment and meets **ALL** of the following:
    a. No active infection; **and**
    b. No human immunodeficiency virus (HIV) infection; **and**
    c. No untreated active or latent tuberculosis; **and**
    d. No concurrent treatment with live vaccines while on therapy or within 6 weeks prior to initiation of treatment; **and**

AND

5. Member has been evaluated and screened for the presence of:
    a. Varicella zoster virus (VZV) immunity status and vaccination, if required, prior to initiating treatment; **and**
    b. Tuberculosis (TB) prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment.

AND

6. Prescriber attestation of the following:
    a. Member has received a *baseline* for the following tests as indicated by FDA-approved labeling, including skin exam for melanoma and will receive yearly skin exams; urine protein to creatinine ratio, and thyroid-stimulating hormone (TSH) level prior to initiation of treatment; **AND**
    b. Ongoing laboratory monitoring during treatment as indicated and submit relevant documentation for continuation of therapy request.

AND

7. Prescriber is certified with, and patient is enrolled in, Lemtrada (alemtuzumab) Risk Evaluation and Mitigation Strategy (REMS) Program.

B. REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA

Lemtrada (alemtuzumab) may be authorized for continuation of therapy when the initial criteria have been met **AND** documentation of ALL the following:

1. Absence of intolerance or adverse events from the previous course of treatment [e.g., hypersensitivity to alemtuzumab or any component of the formulation, 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 Disease (AOSD), acquired hemophilia A, acute acalculous cholecystitis, pneumonitis, etc.;]; **AND**

2. Patient has not received a dose of alemtuzumab within the past 12 months; **AND**

3. Not prescribed for, or administered concurrently with, other disease-modifying therapies for MS; **AND**

4. Positive response to therapy indicated by **ONE** of the following as applicable to member's diagnosis:

    a. **Multiple Sclerosis.** Documentation of stabilization or improvement in disease activity, signs and symptoms, or functional capacity as compared to baseline (or prior to treatment with Lemtrada (alemtuzumab):
        i. A decrease in frequency, severity, sequelae relapses from baseline; **or**
        ii. Beneficial effect on MRI measures of disease severity; **or**
        iii. Improvement in patients reported MS related symptoms.

    b. **Graft Versus Host Disease (GVHD).** No reauthorizations.

STEP THERAPY

Step therapy criteria do not apply for members who are currently being treated with the requested medications. Step therapy is only applied for members that are new to therapy (have not received the requested drug in the last 365 days.

NOTE: Step therapy is only applicable for the multiple sclerosis indication (does not apply to GVHD).

A. **PREFERRED PRODUCT(S): OCREVUS (OCRELIZUMAB); TYSABRI (NATALIZUMAB)**

B. NONPREFERRED PRODUCT, Lemtrada (alemtuzumab), may be authorized when all of the clinical criteria above are met **AND** ONE of the following:

1. Information has been provided that indicates the patient has been treated with the request medication in the past 365 days; **OR**

2. Documentation that the member has had an ineffective treatment response to the active ingredient(s) of preferred medication(s); **OR**

3. Documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of preferred medication(s); **OR**

4. Clinical rationale from Prescriber indicating preferred medication(s) are likely to be ineffective, likely to cause an adverse reaction or harm, or likely to be of no clinical benefit.

DOSAGE AND AUTHORIZATION TIMEFRAMES

1. Recommended Dosage / Maximum Quantity

Indication	Dose	Maximum Quantity
Multiple Sclerosis (MS)	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.	MS: 3 vials per 12 months • Initial course of therapy (first 12 months): May authorize two additional vials for a total of 5 vials per year; 60 billable units. • Second/Subsequent courses (every 12 months after initial course): 3 vials per year; 36 billable units every 12 months thereafter
GVHD	Administer by intravenous (IV) infusion up to 10 mg daily for up to 5 doses.	5 vials; 10 billable units daily for 5 days

2. Authorization Period

   a. MS: May authorize for 12 months (3 doses annually)
   *ONE time initial authorization of FIVE (5) doses.

   b. GVHD: ONE time authorization only (total of FIVE doses) and may not be reauthorized.

   c. Requests for continued therapy beyond the maximum number of doses specified in the 'Quantity and Authorization Period' section will be reviewed on a case-by-case basis.

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Monoclonal Antibody, Anti-CD52

FDA-APPROVED USES:

MS, relapsing: Treatment of relapsing-remitting and active secondary progressive MS; generally reserved for patients who have had an inadequate response to ≥ 2 medications indicated for the treatment of MS.

Limitations of use: Alemtuzumab is not recommended for use in patients with clinically isolated syndrome due to its safety profile

COMPENDIAL APPROVED OFF-LABELED USES: None

Off-Label / Investigational Uses: Requests for off-label uses with a paucity of clinical evidence, or uses that are not generally accepted by the medical community (such as professional guidelines or consensus), CMS-recognized compendia, or peer-reviewed literature is considered investigational and will not be authorized due to insufficient evidence of overall therapeutic value of safety and efficacy.

ROUTE OF ADMINISTRATION: Intravenous Infusion

BOXED WARNING: Autoimmunity, infusion reactions, stroke and malignancies. May cause serious autoimmune diseases including immune thrombocytopenia and anti-glomerular basement membrane disease.

OTHER CONSIDERATIONS

- Monitor complete blood counts with differential, serum creatinine levels and urinalysis with urine counts before starting treatment and then at monthly intervals until 48 months after the last dose. Perform baseline and yearly skin exams.

- May cause serious, life-threatening infusion reactions. Administer in a setting equipped to manage anaphylaxis and serious infusion reactions. Individuals should be monitored for two hours after each infusion and informed infusion reactions can also occur after the monitoring period. Serious, life-threatening stroke has been reported within three days of administration. May also cause an increased risk of malignancies, including thyroid cancer, melanoma and lymphoproliferative disorders. Due to these safety risks, Lemtrada should generally be reserved for patients who have had an inadequate response to two or more agents indicated for the treatment of MS.

- Risk Evaluation Mitigation Strategy (REMS) Program: Because of the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada is available only through restricted distribution under a REMS Program.

OVERVIEW / APPENDIX

The American Academy of Neurology (AAN) published practice guidelines in 2018 regarding disease-modifying therapies for adults with MS. The guidelines recommended initiation disease-modifying therapy in patients with relapsing forms of MS with recent clinical relapses or MRI activity. The guideline does not indicate the preference of one DMT over another. However, some DMTs were recommended for certain MS subpopulations, including a recommendation for Lemtrada for highly active disease.

Micromedex noted that 'evidence favors efficacy' for the off-label use of alemtuzumab for the diagnosis of GVHD in patients receiving allogeneic stem cell transplant for hematologic malignancies that are steroid-refractory. 'The European Society of Blood and Marrow Transplantation (EBMT) and European Leukaemia Net working group have created recommendations for the prevention and management of graft versus host disease (GVHD). This guideline includes recommendations for allogeneic stem-cell transplantation in patients with standard risk hematological malignant disease using an HLA-matched sibling or unrelated donor and bone marrow or peripheral blood as stem-cell source in adults, and in pediatric patients in the haploidentical setting (Penack et al. 2020).' According to the clinical practice guidelines, 'There are no established standard treatments. Current practice is to use of the following therapies [list includes alemtuzumab]. Data are lacking from well-designed studies to compare the efficacy of different second-line options (evidence 2A).

REFERENCES

Government Agency

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database: National coverage determination (NCD) (search: Lemtrada (alemtuzumab). Available from CMS. No NCD identified (LCD available but not applicable to MAC)**.**
2. CMS IOM, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50.4.5
3. CMS Transmittal 96, Change Request (CR) 6191 .

Prescribing Information

1. Lemtrada (alemtuzumab) [prescribing information]. Cambridge, MA: Genzyme Corporation; May 2023.
2. Lemtrada Risk Evaluation and Mitigation Strategy (REMS) [website]. Genzyme Corporation. https://www.lemtradahcp.com/rems

Peer Reviewed Literature, Guidelines

1. Milliman Care Guidelines (MCG). Ambulatory Care 27th Edition ACG: A-0577 (AC). 2023.
2. Martínez C, Solano C, Ferrá C, Sampol A, Valcárcel D, Pérez-Simón JA; Spanish Group for Stem Cell Transplantation (Grupo Español de Trasplante Hemopoyético y Terapia Celular). Alemtuzumab as treatment of steroid-refractory acute graft-versus-host disease: results of a phase II study. Biol Blood Marrow Transplant. 2009;15(5):639-642. doi: 10.1016/j.bbmt.2009.01.014.[PubMed 19361757]
3. DRUGDEX. Micromedex [Internet]. Greenwood Village, CO: Truven Health Analytics, Inc. 2023. Alemtuzumab. Accessed September 2023. Available from: Micromedex.
4. Olek MJ, Howard J. Clinical presentation, course and prognosis of multiple sclerosis in adults. Last updated: Aug 30, 2023. In: UpToDate, González-Scarano, F (Ed), UpToDate, Waltham, MA. Accessed: September 2023.
5. Penack O, Marchetti M, Ruutu T, et al: Prophylaxis and management of graft versus host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2020 Feb;7(2):e157-e167. doi: 10.1016/S2352-3026(19)30256-X. PMID: 32004485
6. Schnitzler M, Hasskarl J, Egger M, Bertz H, Finke J. Successful treatment of severe acute intestinal graft-versus-host resistant to systemic and topical steroids with alemtuzumab [published correction appears in Biol Blood Marrow Transplant. 2010;16(1):128.]. Biol Blood Marrow Transplant. 2009;15(8):910-918. doi: 10.1016/j.bbmt.2009.04.002.[PubMed 19589480]
7. 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. Available from: AAN. Accessed September 2023.

DISCLAIMER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section below to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

POLICY HISTORY

Version	Date	Revision Author/Title	Summary of Changes
1	11/29/2023		New Policy