Clinical Policy: Alemtuzumab (Lemtrada)

Reference Number: CP.PHAR.243
Effective Date: 08.01.16
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Alemtuzumab (Lemtrada®) is a CD52-directed cytolytic monoclonal antibody.

FDA Approved Indication(s)

Lemtrada is indicated for the treatment with 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.

Limitation(s) of use: Lemtrada is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Lemtrada is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of relapsing-remitting or secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, c, and d):*
   a. **Dimethyl fumarate** (generic Tecfidera®);
   b. **Teriflunomide** (generic Aubagio®);
   c. **Fingolimod** (Gilenya®);
   d. An **interferon-beta agent** (Avonex®, Betaseron®/Extavia®†, Rebif®, or Plegridy®) or **glatiramer** (Copaxone®, Glatopa®);

   **Prior authorization may be required for all disease modifying therapies for MS*
   †Betaseron is preferred for the Commercial and HIM lines of business; Extavia is preferred for the Medicaid line of business
5. Lemtrada is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
6. Documentation of both baseline number of relapses per year and expanded disability status scale (EDSS) score;

7. Dose does not exceed:
   a. First treatment course: 12 mg per day for 5 consecutive days (60 mg total);
   b. Second or subsequent treatment courses: 12 mg per day for 3 consecutive days (36 mg total).

Approval duration:
Medicaid/HIM – 12 months (*1 treatment course only*)
Commercial – 6 months or to the member's renewal date, whichever is longer (*1 treatment course only*)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Sclerosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Member has not had an increase in the number of relapses per year compared to baseline;
   b. Member has not had ≥ 2 new MRI-detected lesions;
   c. Member has not had an increase in EDSS score from baseline;
   d. Medical justification supports that member is responding positively to therapy;
3. Lemtrada is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
4. It has been at least 12 months since completion of the prior treatment course;

5. Dose does not exceed 12 mg per day for 3 consecutive days (36 mg total per treatment course).

Approval duration:
Medicaid/HIM – 12 months (*1 treatment course only*)
Commercial – 6 months or to the member's renewal date, whichever is longer (*1 treatment course only*)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
EDSS: expanded disability status scale
FDA: Food and Drug Administration
MS: multiple sclerosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
teriflunomide (Aubagio®)	7 mg or 14 mg PO QD	14 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
fingolimod (Gilenya®)	0.5 mg PO QD	0.5 mg/day
dimethyl fumarate (Tecfidera®)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity or anaphylactic reactions to alemtuzumab or any of the excipients in Lemtrada, infection with human immunodeficiency virus, active infection
- Boxed warning(s): autoimmunity, infusion reactions, stroke, and malignancies

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®, Tascenso ODT™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®, and biosimilar Tyruko®), ocrelizumab (Ocrevus®), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ponesimod (Ponvory™), ublituximab-xiiy (Briumvi™), and ofatumumab (Kesimpta®).
- 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Relapsing MS	IV infusion for 2 or more treatment courses: • First course: 12 mg/day on 5 consecutive days • Second course: 12 mg/day on 3 consecutive days 12 months after first course • Subsequent courses as needed: 12 mg/day on 3 consecutive days 12 months after any prior course	See regimen

VI. Product Availability

Single-use vial: 12 mg/1.2 mL

VII. References

1. Lemtrada Prescribing Information. Cambridge, MA: Genzyme Corporation; May 2023. Available at http://www.lemtrada.com. Accessed January 30, 2024.
2. 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(17): 777-788. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/904. Reaffirmed on September 18, 2021.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0202	Injection, alemtuzumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; clarified that only 1 treatment course may be approved per authorization; references reviewed and updated.	01.27.20	05.20
Added requirements for documentation of baseline relapses/EDSS and objective measures of positive response upon re-authorization; references reviewed and updated.	05.27.20	08.20
Per November and December SDC and prior clinical guidance, removed redirection to Mayzent; for RRMS modified redirection to require generic dimethyl fumarate, Aubagio, Gilenya, and either an interferon-beta agent or glatiramer.	01.11.21	
2Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; updated Appendix C with additional contraindications per revised PI; references reviewed and updated.	02.08.21	05.21
2Q 2022 annual review: no significant changes; clarified interferon-beta product redirections for each line of business per SDC; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.31.23	05.23
Per August SDC, added generic references to Aubagio and Gilenya redirections.	08.22.23	11.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2024 annual review: no significant changes; references reviewed and updated.	01.30.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.