Clinical Policy Title:	alemtuzumab
Policy Number:	RxA.202
Drug(s) Applied:	Lemtrada®
Original Policy Date:	02/07/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

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

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
alemtuzumab (Lemtrada®)	Relapsing MS (relapsing-remitting disease and active secondary progressive disease)	Intravenous infusion over 4 hours for 2 or more treatment courses: Initial treatment of 2 courses: • First course: 12 mg/day for 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 at least 12 months after any prior course.	Intravenous: 12 mg/dose.

Dosage Forms

- Injection: 12 mg/1.2 mL (10 mg/mL) in a single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of relapsing-remitting MS or active secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Trial and failure of at least 2 preferred disease modifying therapies (Avonex®, Betaseron®, Copaxone®, Vumerity®, Bafiertam®, Kesimpta®), at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization is required for all disease modifying therapies for MS.
5. Lemtrada® is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
6. Dose does not exceed (a or b):
   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
Commercial: 12 months
Medicaid: 12 months

B. Acute or Chronic Graft-Versus-Host Disease (GVHD) (Off-label) (must meet all):

1. Diagnosis of acute or chronic GVHD;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Failure of prior systemic therapies (e.g. corticosteroids, immunosuppressants) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Prescribed in conjunction with systemic corticosteroids;
6. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use; (Prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. 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. If request is for a dose increase, request meets one of the following (a or b):*
   a. Dose does not exceed 12 mg per day for 3 consecutive days (36 mg total per treatment course).
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MS: multiple sclerosis
CD52: cluster of differentiation 52
CIS: clinically isolated syndrome

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Avonex®, Rebif®	Avonex: 30 mcg intramuscular once weekly Rebif: 22 mcg or 44 mcg subcutaneous three times weekly	Avonex: 30 mcg/week Rebif: 44 mcg three times weekly
Plegridy®	125 mcg subcutaneously or intramuscularly every 2 weeks	125 mcg/2 weeks
Betaseron®, Extavia®	250 mcg subcutaneously every other day	250 mg every other day
glatiramer acetate (Copaxone®, Glatopa®)	20 mg subcutaneously once daily or 40 mg subcutaneously three times weekly	20 mg/day or 40 mg three times weekly
Gilenya®	0.5 mg orally once daily once daily	0.5 mg/day
(dimethyl fumarate) Tecfidera®	120 mg orally twice daily for 7 days, followed by 240 mg orally twice daily	480 mg/day
Aubagio®	7 mg or 14 mg orally once daily	14 mg/day
Mayzent®	All patients: • Day 1 and 2: 0.25 mg orally once daily • Day 3: 0.5 mg orally once daily • Day 4: 0.75 mg orally once daily CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: • Day 5: 1.25 mg orally once daily • Day 6 and onward: 2 mg orally once daily CYP2C9 genotypes *1/*3 or *2/*3: • Day 5 and onward: 1 mg orally once daily	2 mg/day

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

APPENDIX C: Contraindications*/Boxed Warnings

- Contraindication(s):

  - Infection with human immunodeficiency virus;
  - Known hypersensitivity or anaphylactic reactions to alemtuzumab or any of the excipients in Lemtrada®;
  - Active infection.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - Autoimmune conditions (immune thrombocytopenia and anti-glomerular basement membrane disease), infusion reactions, stroke, and malignancies (thyroid cancer, melanoma, and lymphoproliferative disorders);
  - 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.

APPENDIX D: General Information

Disease-modifying therapies for MS include:

- Infusion therapies
  - Tysabri®
  - mitoxantrone
  - Ocrevus®
- Injectable therapies
  - glatiramer (Copaxone®, Glatopa®)
  - Avonex®, Rebif®
  - Betaseron®, Extavia®
  - Plegridy®
- Oral therapies
  - dimethyl fumarate (Tecfidera®)
  - Bafiertam™
  - Vumerity®
  - Aubagio®
  - Gileny®
  - Mayzent®
  - Zeposia®
  - cladribine (Mavenclad®)
  - dalfampridine (Ampyra®)

References

1. Lemtrada® Prescribing Information. Cambridge, MA: Genzyme Corporation; January 2022. Available at https://products.sanofi.us/lemtrada/lemtrada.pdf. Accessed February 03, 2022.
2. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. June 2019. Available at: https://ms-coalition.org/the-use-of-disease-modifying-therapies-in-multiple-sclerosis-updated/. Accessed February 03, 2022.
3. 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. Accessed February 03, 2022.

4. Alemtuzumab, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com . Accessed February 03, 2022.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/ . Accessed February 03, 2022.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Initial Approval criteria I.A.1 was updated to add a diagnosis. Initial approval criteria updated to trial and failure of at least 2 preferred disease modifying therapies, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced. 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. Approval duration was updated in initial and continued therapy approval to include Commercial and Medicaid plan. 5. Appendix B was updated to include 2 more drugs and directions for use updated to spell out. 6. Appendix D was updated to include 2 more drugs. 7. References were updated.	07/09/2020	09/14/2020
Policy was reviewed: 1. Dosing information was updated from "Intravenous infusion for 2 or more…" to Intravenous infusion over 4 hours for 2 or more…" 2. Dosing information's indication was updated to include "(relapsing-remitting disease and active secondary progressive disease)". 3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 4. Initial Approval Criteria I.A.4 was updated to include "(Avonex®,	07/12/2021	09/14/2021

Betaseron®, Copaxone®, Vumerity®, Bafiertam®, Kesimpta®)". 5. Appendix A was updated to include abbreviations for CD52, CIS. 6. Therapeutic Alternative verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 7. Appendix B was updated to remove " interferon beta-1a, peginterferon beta-1a, Interferon Beta-1b, fingolimod, teriflunomide, siponimod" generics as these were not available. 8. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 9. Appendix C was updated to include Contraindication(s) "Active infection". 10. Appendix D was updated to remove " Lemtrada®" as Disease-modifying therapies, and "natalizumab, ocrelizumab, interferon beta-1a, interferon beta-1b, peginterferon beta-1a, monomethyl fumarate, diroximel fumarate, teriflunomide, fingolimod, siponimod, ozanimod" as these were not available. 11. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.B: Updated to include Off Label criteria for Acute or Chronic Graft-Versus-Host Disease (GVHD). 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Continued Therapy Approval Criteria, II.A.5: Updated dosing criteria from	02/03/2022	04/18/2022

Dose does not exceed 12 mg per day for 3 consecutive days (36 mg total per treatment course) to If request is for a dose increase, request meets one of the following (a or b):* a. Dose does not exceed 12 mg per day for 3 consecutive days (36 mg total per treatment course). b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). *Prescribed regimen must be FDA-approved or recommended by NCCN. 4. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 5. Initial Approval Criteria, I.B.5: Updated to include “Prescribed in conjunction with systemic corticosteroids”. 6. Appendix C, Boxed Warnings: Updated boxed warning from Autoimmunity, infusion reactions, stroke, and malignancies to Autoimmune conditions (immune thrombocytopenia and anti-glomerular basement membrane disease), infusion reactions, stroke, and malignancies (thyroid cancer, melanoma, and lymphoproliferative disorders). 7. References were reviewed and updated.		