RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	alemtuzumab
Policy Number:	RxA.202
Drug(s) Applied:	Lemtrada®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
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 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Alemtuzumab (Lemtrada®)	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 at least 12 months after any prior course	See regimen

Dosage Forms

- Single-use vial: 12 mg/1.2 mL

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.

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, 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. 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

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously 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. Dose does not exceed 12 mg per day for 3 consecutive days (36 mg total per treatment course).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MS: multiple sclerosis

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® (interferon beta-1a)	*Avonex*: 30 mcg IM once weekly *Rebif*: 22 mcg or 44 mcg SC three	*Avonex*: 30 mcg/week *Rebif*: 44 mcg three times

	times weekly	weekly
Plegridy® (peginterferon beta-1a)	125 mcg SC every 2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC every other day	250 mg every other day
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC once daily or 40 mg SC three times weekly	20 mg/day or 40 mg three times weekly
Gilenya® (fingolimod)	0.5 mg PO once daily	0.5 mg/day
Tecfidera® (dimethyl fumarate)	120 mg PO twice daily for 7 days, followed by 240 mg PO twice daily	480 mg/day
Aubagio® (teriflunomide)	7 mg or 14 mg PO once daily	14 mg/day
Mayzent® (siponimod)	All patients: • Day 1 and 2: 0.25 mg PO once daily • Day 3: 0.5 mg PO once daily • Day 4: 0.75 mg PO once daily CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: • Day 5: 1.25 mg PO once daily • Day 6 and onward: 2 mg PO once daily CYP2C9 genotypes *1/*3 or *2/*3: • Day 5 and onward: 1 mg PO once daily	2 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):
  - Infection with human immunodeficiency virus

- Boxed Warning(s):
  - Autoimmunity, infusion reactions, stroke, and malignancies

- 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
  - natalizumab (Tysabri®)
  - mitoxantrone
  - ocrelizumab (Ocrevus™)
  - alemtuzumab (Lemtrada®)
- Injectable therapies
  - glatiramer (Copaxone®, Glatopa®)
  - interferon beta-1a (Avonex®, Rebif®)
  - interferon beta-1b (Betaseron®, Extavia®)
  - peginterferon beta-1a (Plegridy®)
- Oral therapies
  - dimethyl fumarate (Tecfidera®)
  - monomethyl fumarate (Bafiertam™)
  - diroximel fumarate (Vumerity®)
  - teriflunomide (Aubagio®)
  - fingolimod (Gilenya™)
  - siponimod (Mayzent®)
  - ozanimod (Zeposia®)
  - cladribine (Mavenclad®)
  - dalfampridine (Ampyra®)
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- 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.

References

1. Lemtrada Prescribing Information. Cambridge, MA: Genzyme Corporation; May 2020. Available at http://www.lemtrada.com. Accessed June 19, 2020.
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. March 2017. Accessed June 19, 2020.
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.

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