Clinical Policy: Alemtuzumab (Lemtrada)
Reference Number: ERX.SPA.117
Effective Date: 10.01.16
Last Review Date: 05.19

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 of patients with relapsing forms of multiple sclerosis (MS).

Limitation(s) of use: 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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 MS;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. Failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
         a. Tysabri®, Tecfidera®, or Gilenya™ and any of the following: an interferon-beta agent (Betaseron® and Rebif® are preferred agents), glatiramer (Copaxone®, Glatopa®), Aubagio®;
         b. Two of the following: Tysabri, Tecfidera, Gilenya;
     *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: 12 months

   B. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. Multiple Sclerosis (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents;
B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
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 and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avonex®, Rebif® (interferon beta-1a)</td>
<td>Avonex: 30 mcg IM Q week Rebif: 22 mcg or 44 mcg SC TIW</td>
<td>Avonex: 30 mcg/week Rebif: 44 mcg TIW</td>
</tr>
<tr>
<td>Plegridy® (peginterferon beta-1a)</td>
<td>125 mcg SC Q2 weeks</td>
<td>125 mcg/2 weeks</td>
</tr>
<tr>
<td>Betaseron®, Extavia® (interferon beta-1b)</td>
<td>250 mcg SC QOD</td>
<td>250 mcg QOD</td>
</tr>
<tr>
<td>glatiramer acetate (Copaxone®, Glatopa®)</td>
<td>20 mg SC QD or 40 mg SC TIW</td>
<td>20 mg/day or 40 mg TIW</td>
</tr>
<tr>
<td>Aubagio® (teriflunomide)</td>
<td>7 mg or 14 mg PO QD</td>
<td>14 mg/day</td>
</tr>
<tr>
<td>Gilenya™ (fingolimod)</td>
<td>0.5 mg PO QD</td>
<td>0.5 mg/day</td>
</tr>
<tr>
<td>Tecfidera® (dimethyl fumarate)</td>
<td>120 mg PO BID for 7 days, followed by 240 mg PO BID</td>
<td>480 mg/day</td>
</tr>
<tr>
<td>Tysabri® (natalizumab)</td>
<td>300 mg IV every 4 weeks</td>
<td>300 mg/4 weeks</td>
</tr>
</tbody>
</table>

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

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®), fingolimod (Gilenya™), teriflunomide (Aubagio®),
alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocreliuzumab (Ocrevus™).

- 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

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

VI. Product Availability

Single-use vial: 12 mg/1.2 mL

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy split from USS.SPMN.36 Multiple Sclerosis (MS) Treatments and converted to new template. Removed all safety criteria, added max dosing, clarified monotherapy restriction, modified trial/failure criteria to require trial/failure of 2 agents from different classes, and updated continuation (second treatment course) criteria.</td>
<td>08.16</td>
<td>09.16</td>
</tr>
<tr>
<td>Converted to new template. Removed MRI requirement as it is a non-specific diagnostic test (plus, specialist involvement in care is required). Updated preferencing to require at least one of the highly effective DMTs on formulary (Tecfidera or Gilenya). Added PPMS as a diagnosis not covered.</td>
<td>06.17</td>
<td>08.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: No significant changes. Removed HIV contraindication per safety guidance endorsed by Medical Affairs. References reviewed and updated.</td>
<td>01.05.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: added Tysabri as a step-through option per its formulary status; for re-auth, removed restriction for a total of 2 treatment courses per updated FDA labeling which allows for 2 or more treatment courses; references reviewed and updated.</td>
<td>02.04.19</td>
<td>05.19</td>
</tr>
</tbody>
</table>

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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