Clinical Policy: Alemtuzumab (Lemtrada)
Reference Number: CP.PHAR.243
Effective Date: 08.01.16
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

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 two of the following at up to maximally indicated doses, 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®;
         *Prior authorization may be 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:
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
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Multiple Sclerosis (must meet all):
1. Currently receiving medication via Centene benefit 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:
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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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
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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aubagio® (teriflunomide)</td>
<td>7 mg or 14 mg PO QD</td>
<td>14 mg/day</td>
</tr>
<tr>
<td>Avonex®, Rebif® (interferon beta-1a)</td>
<td>Avonex: 30 mcg IM Q week</td>
<td>Avonex: 30 mcg/week</td>
</tr>
<tr>
<td></td>
<td>Rebif: 22 mcg or 44 mcg SC TIW</td>
<td>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® (interferon beta-1b)</td>
<td>250 mcg SC QOD</td>
<td>250 mg 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>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,</td>
<td>480 mg/day</td>
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<tr>
<td></td>
<td>followed by 240 mg PO BID</td>
<td></td>
</tr>
<tr>
<td>Mayzent® (siponimod)</td>
<td>All patients:</td>
<td>2 mg/day</td>
</tr>
<tr>
<td></td>
<td>Day 1 and 2: 0.25 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 3: 0.5 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 4: 0.75 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CYP2C9 genotypes *1/*1, *1/*2,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or *2/*2:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 5: 1.25 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 6 and onward: 2 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CYP2C9 genotypes *1/*3 or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*2/*3:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 5 and onward: 1 mg PO QD</td>
<td></td>
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</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®), diroximel fumarate (Vumery™), fingolimod (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus™), cladribine (Mavenclad®), and siponimod (Mayzent®).
Clinical Policy
Alemtuzumab

- 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>
</tr>
<tr>
<td></td>
<td>• Second course: 12 mg/day on 3 consecutive days 12 months after first course</td>
<td></td>
</tr>
<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

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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0202</td>
<td>Injection, alemtuzumab, 1 mg</td>
</tr>
</tbody>
</table>

Reviews, Revisions, and Approvals
Policy split from CP.PHAR.18 MS Treatments. Criteria: added max dosing, clarified monotherapy restriction, updated continuation criteria. Added information about REMS program.

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.16</td>
<td>08.16</td>
</tr>
</tbody>
</table>
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>Age requirement added; requirement for the trial and failure of at least 2 preferred regimens from different classes added.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Removed MRI requirement. Updated preferencing to require at least one of the highly effective DMTs on formulary (Tecfidera or Gilenya). Removed reasons to discontinue.</td>
<td>07.17</td>
<td>08.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: no significant changes; removed HIV contraindication; added HIM; references reviewed and updated.</td>
<td>01.05.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: 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>
<tr>
<td>RT4: updated policy with new indications.</td>
<td>11.14.19</td>
<td></td>
</tr>
<tr>
<td>RT4: updated criteria contents with new indication without additional data to consider: secondary progressive MS.</td>
<td>01.06.20</td>
<td></td>
</tr>
<tr>
<td>Updated re-directions per SDC and prior clinical guidance; added COM line of business (CP.CPA.325 retired); revised HIM-Medical Benefit to HIM line of business.</td>
<td>01.21.20</td>
<td></td>
</tr>
<tr>
<td>2Q 2020 annual review: no significant changes; clarified that only 1 treatment course may be approved per authorization; references reviewed and updated.</td>
<td>01.27.20</td>
<td>05.20</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. 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.

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members and/or submitting claims for payment for such services.

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.

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