The services described in Oxford policies are subject to the terms, conditions and limitations of the Member's contract or certificate. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage enrollees. Oxford reserves the right, in its sole discretion, to modify policies as necessary without prior written notice unless otherwise required by Oxford's administrative procedures or applicable state law. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

Certain policies may not be applicable to Self-Funded Members and certain insured products. Refer to the Member's plan of benefits or Certificate of Coverage to determine whether coverage is provided or if there are any exclusions or benefit limitations applicable to any of these policies. If there is a difference between any policy and the Member's plan of benefits or Certificate of Coverage, the plan of benefits or Certificate of Coverage will govern.

**CONDITIONS OF COVERAGE**

<table>
<thead>
<tr>
<th>Benefit Type</th>
<th>Referral Required</th>
<th>Authorization Required</th>
<th>Precertification with Medical Director Review Required</th>
<th>Applicable Site(s) of Service</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>General benefits package</td>
<td>No</td>
<td>Yes’</td>
<td>Yes’</td>
<td>Office, Outpatient, Home</td>
<td>'Precertification with review by a Medical Director or their designee is required.</td>
</tr>
</tbody>
</table>

This policy applies to Oxford Commercial plan membership.
COVERAGE RATIONALE

Lemtrada (alemtuzumab) is proven and medically necessary for treatment of relapsing-remitting multiple sclerosis when all of the following criteria are met:\(^1\)

A. Diagnosis of relapsing-remitting multiple sclerosis (RRMS); and

B. One of the following:

1. **Treatment - naïve to alemtuzumab:**
   a. Member has history of failure following a trial for at least 4 weeks or history of intolerance or contraindication to two of the following:
      - interferon β-1a (Avonex\textsuperscript{®} or Rebif\textsuperscript{®})
      - interferon β-1b (Betaseron\textsuperscript{®} or Extavia\textsuperscript{®})
      - glatiramer acetate (Copaxone\textsuperscript{®})
      - dimethyl fumarate (Tecfidera\textsuperscript{®})
      - teriflunomide (Aubagio\textsuperscript{®})
      - fingolimod (Gilenya\textsuperscript{®})
      - peginterferon beta-1a (Plegridy™)
      and
   b. Member has not been previously treated with alemtuzumab; and
   c. Member is not receiving alemtuzumab in combination with another disease modifying agent (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, or teriflunomide); and
   d. Initial dosing is administered: 12 mg intravenously daily for 5 consecutive days; and
   e. Regimen is administered only once within 12 months

2. **Treatment-experienced with alemtuzumab:**
   a. Member has previously received treatment with alemtuzumab; and
   b. Member is not receiving alemtuzumab in combination with another disease modifying agent (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, or teriflunomide); and
   c. Retreatment dosing is administered: 12 mg intravenously daily for 3 consecutive days; and
   d. Regimen is administered only once within 12 months

Coverage of Lemtrada is limited up to two treatment courses (5 day initial and 3 day end course). Requests for additional doses/courses beyond two courses will not be approved.

**Alemteuzumab is unproven and not medically necessary for the treatment of:**
- Rheumatoid arthritis
- Autoimmune neutropenia
- Autoimmune hemolytic anemia
- Pure red cell aplasia
- Immune thrombocytopenic purpura
- Evan's syndrome
- Autoimmune pancytopenia

**BENEFIT CONSIDERATIONS**

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria. Coverage for an otherwise unproven service for the treatment of serious rare
diseases may occur when certain conditions are met. Please see policy titled [Acquired Rare Disease Drug Therapy Exception Process](#).

**Essential Health Benefits for Individual and Small Group**

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs (such as maternity benefits), the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this guideline, it is important to refer to the member specific benefit plan document to determine benefit coverage.

**CLINICAL EVIDENCE**

**Proven/Medically Necessary Uses**

**Multiple Sclerosis**

Lemtrada (alemtuzumab) is indicated for the treatment of patients with relapsing forms of multiple sclerosis. Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response two or more drugs for the treatment of multiple sclerosis.

**Unproven/Not Medically Necessary Uses**

**Miscellaneous**

Alemtuzumab has been used in the treatment of other conditions including rheumatoid arthritis, autoimmune neutropenia, autoimmune hemolytic anemia, pure red cell aplasia, immune thrombocytopenic purpura, Evans syndrome, and autoimmune pancytopenia. While a beneficial effect of alemtuzumab has been reported in some of these conditions, none of them have been studied in large, controlled clinical trials or studies were discontinued before completion due to alemtuzumab associated toxicity.

**U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Lemtrada (alemtuzumab) is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). 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. Because of the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada is available only through restricted distribution under a Risk Evaluation and Mitigation Strategy (REMS) Program. Additional details in regards to the program may be found at: [https://www.lemtradahcp.com/rem](https://www.lemtradahcp.com/rem).

Campath (alemtuzumab) is a CD52-directed cytolitic antibody indicated as a single agent for the treatment of B-cell chronic lymphocytic leukemia.

Effective September 4th, 2012, Campath will no longer be available commercially, but will be provided through the Campath Distribution Program free of charge. Additional details about this program may be found at [www.campath.com](http://www.campath.com).

**APPLICABLE CODES**

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that
may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0202</td>
<td>Injection, alemtuzumab, 1 mg (Lemtrada)</td>
</tr>
</tbody>
</table>

ICD-9 Diagnosis Codes (Discontinued 10/01/15)
The following list of codes is provided for reference purposes only. Effective October 1, 2015, the Centers for Medicare & Medicaid Services (CMS) implemented ICD-10-CM (diagnoses) and ICD-10-PCS (inpatient procedures), replacing the ICD-9-CM diagnosis and procedure code sets. ICD-9 codes will not be accepted for services provided on or after October 1, 2015.

<table>
<thead>
<tr>
<th>ICD-9 Code (Discontinued 10/01/15)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>340</td>
<td>Multiple sclerosis</td>
</tr>
</tbody>
</table>

ICD-10 Codes
ICD-10-CM (diagnoses) and ICD-10-PCS (inpatient procedures) must be used to report services provided on or after October 1, 2015. ICD-10 codes will not be accepted for services provided prior to October 1, 2015.

<table>
<thead>
<tr>
<th>ICD-10 Diagnosis Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G35</td>
<td>Multiple sclerosis</td>
</tr>
</tbody>
</table>

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee [2016D0023N]


POLICY HISTORY/REVISION INFORMATION

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/01/2016</td>
<td>• Changed policy title; previously titled Alemtuzumab</td>
</tr>
</tbody>
</table>
- Removed reference link to policy titled Injectable Chemotherapy Drugs: Application of NCCN Clinical Practice Guidelines
- Revised coverage rationale; removed coverage criteria for Campath
- Updated benefit considerations; added language for Essential Health Benefits for Individual and Small Group plans to indicate:
  - For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs")
  - Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs; however, if such plans choose to provide coverage for benefits which are deemed EHBs (such as maternity benefits), the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans
  - The determination of which benefits constitute EHBs is made on a state by state basis; as such, when using this guideline, it is important to refer to the member specific benefit plan document to determine benefit coverage
- Updated list of applicable ICD-9 codes; removed notation indicating the listed codes are used post-transplant in the absence of complications
- Updated supporting information to reflect the most current clinical evidence, FDA information, and references
- Archived previous policy version PHARMACY 186.11 T2