

LEMTRADA (ALEMTUZUMAB)

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Related Policies

- [Acquired Rare Disease Drug Therapy Exception Process](#)
- [Drug Coverage Guidelines](#)
- [Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting](#)

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General benefits package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes ¹
Precertification with Medical Director Review Required	Yes ¹
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Office, Outpatient ² , Home
Special Considerations	<p>¹Precertification with review by a Medical Director or their designee is required.</p> <p>²Participating hospitals are required to purchase Lemtrada (alemtuzumab) from the BriovaRx Specialty Pharmacy when the medication is administered in an outpatient hospital setting; refer to the policy titled Specialty Pharmacy for Certain Specialty Medications</p>

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

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, 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 policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Lemtrada (alemtuzumab) is proven and medically necessary for treatment of relapsing forms of multiple sclerosis when ALL of the following criteria are met:¹

- Diagnosis of relapsing forms of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses); **and**
- **One** of the following:
 - **Treatment-naïve to alemtuzumab:**
 - Member has history of failure following a trial for at least 4 weeks **or** history of intolerance to at least **two** of the following:
 - interferon β -1a (Avonex[®] or Rebif[®]))
 - interferon β -1b (Betaseron[®] or Extavia[®])
 - glatiramer acetate (Copaxone[®] or Glatopa[®])
 - dimethyl fumarate (Tecfidera[®])
 - teriflunomide (Aubagio[®])
 - fingolimod (Gilenya[®])
 - peginterferon beta-1a (Plegridy[™])
 - natalizumab (Tysabri[®])
 - daclizumab (Zinbryta[™])
 - ocrelizumab (Ocrevus[®])
 - and**
 - Member has **not** been previously treated with alemtuzumab; **and**
 - Member is **not** receiving alemtuzumab in combination with another disease modifying agent for multiple sclerosis (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, teriflunomide, etc.); **and**
 - Initial dosing is administered: 12 mg intravenously daily for 5 consecutive days; **and**
 - Regimen is administered only once within 12 months
 - or**
 - **Treatment-experienced with alemtuzumab:**
 - Member has previously received treatment with alemtuzumab; **and**
 - Member is **not** receiving alemtuzumab in combination with another disease modifying agent for multiple sclerosis (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, teriflunomide, etc.); **and**
 - Retreatment dosing is administered: 12 mg intravenously daily for 3 consecutive days; **and**
 - 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.

Alemtuzumab 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

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.¹ 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.² Additional details in regards to the program may be found at: <https://www.lemtradahcp.com/remis>.

Campath (alemtuzumab) is a CD52-directed cytolytic antibody indicated as a single agent for the treatment of B-cell chronic lymphocytic leukemia.³

Effective September 4th, 2012, Campath will no longer be available commercially, but will be provided through the Campath Distribution Program free of charge. In order to receive Campath, the healthcare provider is required to document and comply with certain requirements. Additional details about this program may be found at <https://www.campathproviderportal.com/>.⁴

BACKGROUND

Lemtrada is a recombinant humanized IgG1 kappa monoclonal antibody directed against the cell surface glycoprotein, CD52, present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following cell surface binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytotoxicity and complement-mediated lysis.

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 Code	Description
J0202	Injection, alemtuzumab, 1 mg (Lemtrada)

ICD-10 Diagnosis Code	Description
G35	Multiple sclerosis

CLINICAL EVIDENCE

Proven/Medically Necessary

Multiple Sclerosis

Havrdova et al., reported the findings from alemtuzumab-treated patients who completed the CARE-MS I and continued into the extension trial, where patients could receive additional alemtuzumab courses upon evidence of MS disease activity.⁴ Eligibility criteria for re-treatment were more than 1 protocol defined relapse or more than 2 new/enlarging T2 hyperintense and/or gadolinium (Gd)-enhancing brain or spinal cord lesions on MRI. Assessments included annualized relapse rate (ARR), 6-month confirmed disability worsening (CDW), 6-month confirmed disability improvement (CDI), no evidence of disease activity (NEDA), brain volume loss (BVL), and adverse events (AEs). Most alemtuzumab-treated patients (95.1%) completing CARE-MS I enrolled in the extension, and 68.5% received no additional alemtuzumab treatment. ARR remained low in years 3, 4, and 5 (0.19, 0.14, and 0.15, respectively). Over years 0–5, 79.7% were free of 6-month CDW; 33.4% achieved 6-month CDI. Most patients (61.7%, 60.2%, and 62.4%) had NEDA in years 3, 4, and 5. Median yearly BVL improved over years 2–4, remaining low in year 5 (years 1–5: 20.59%, 20.25%, 20.19%, 20.15%, and 20.20%). Exposure-adjusted incidence rates of most AEs declined in

the extension relative to the core study. Thyroid disorder incidences peaked at year 3 and subsequently declined. The authors concluded that based on the published data, alemtuzumab provides durable efficacy through 5 years in the absence of continuous treatment, with most patients not receiving additional courses.

Giovannoni et al., reported additional prespecified and post hoc disability outcomes from the CARE-MS II trial that included the Expanded Disability Status Scale (EDSS), Multiple Sclerosis Functional Composite (MSFC), and Sloan low-contrast letter acuity (SLCLA).^{11,12} These outcomes focused on the improvement of preexisting disability, in addition to slowing of disability accumulation. From the CARE-MS II trial, patients were randomized to either receive subcutaneous interferon β 1A (SC IFN- β -1a, 202 patients) 44 mcg, or alemtuzumab 12mg (426 patients), with baseline demographics, clinical characteristics and prestudy relapse rates equivalent between groups. Alemtuzumab-treated patients were more likely than SC IFN-b-1a-treated patients to show improvement in EDSS scores ($p < 0.0001$) on all 7 functional systems. Significantly more alemtuzumab patients demonstrated 6-month confirmed disability improvement (28.8% vs. 12.9%, $p = 0.0003$). The likelihood of improved vs stable/worsening MSFC scores was greater with alemtuzumab than SC IFN-b-1a ($p = 0.0300$); improvement in MSFC scores with alemtuzumab was primarily driven by the upper limb coordination and dexterity domain. Alemtuzumab-treated patients had more favorable changes from baseline in SLCLA (2.5% contrast) scores ($p = 0.0014$) and MSFC + SLCLA composite scores ($p = 0.0097$) than SC IFN-b-1a-treated patients. The authors concluded that in patients with RRMS and inadequate response to prior disease-modifying therapies, alemtuzumab provides greater benefits than SC IFN-b-1a across several disability outcomes, reflecting improvement of preexisting disabilities, and that alemtuzumab modifies disability measures favorably compared with SC IFN-b-1a.

Technology Assessments

A 2017 Cochrane review was published to compare the efficacy, tolerability and safety of alemtuzumab versus interferon beta 1a in the treatment of people with RRMS to prevent disease activity. The review included three trials involving 1694 participants. All trials compared alemtuzumab 12 mg per day or 24 mg per day versus IFN beta 1a for treating RRMS. The authors concluded that there is low- to moderate-quality evidence that annual intravenous cycles of alemtuzumab at a dose of 12 mg per day or 24 mg per day reduces the proportion of participants with relapses, disease progression, change of EDSS score and developing new T2 lesions on MRI over 24 to 36 months in comparison with subcutaneous IFN beta-1a 44 μ g three times per week. Alemtuzumab appeared to be relatively well tolerated. The most frequently reported adverse events were infusion-associated reactions, infections and autoimmune events. The use of alemtuzumab requires careful monitoring so that potentially serious adverse effects can be treated early and effectively.¹⁴

A 2016 Cochrane review was published to assess the safety and effectiveness of alemtuzumab used alone or associated with other treatments to decrease disease activity in patients with any form of MS. The review evaluated three studies with 1713 participants. The authors concluded that in patients with relapsing-remitting MS, alemtuzumab 12 mg was better than subcutaneous interferon beta-1a for the following outcomes assessed at 24 months: relapse-free survival, sustained disease progression-free survival, number of participants with at least one adverse event and number of participants with new or enlarging T2-hyperintense lesions on MRI. The quality of the evidence for these results was low to moderate. Alemtuzumab 24 mg seemed to be better than subcutaneous interferon beta-1a for relapse-free survival and sustained disease progression-free survival, at 36 months. More randomized clinical trials are needed to evaluate the effects of alemtuzumab on other forms of MS and compared with other therapeutic options. These new studies should assess additional relevant outcomes such as the rate of participants free of clinical disease activity, quality of life, fatigue and adverse events (individual rates, serious adverse events and long-term adverse events). Moreover, these new studies should evaluate other doses and durations of alemtuzumab course.

Unproven/Not Medically Necessary

Miscellaneous

Alemtuzumab has been used in the treatment of other conditions including rheumatoid arthritis,⁵⁻⁶ autoimmune neutropenia,⁷ autoimmune hemolytic anemia,⁸⁻⁹ pure red cell aplasia,^{7,10} immune thrombocytopenic purpura,⁷⁻⁸ Evans syndrome,⁷ and autoimmune pancytopenia.⁷ 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.

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. [2018D0023P]

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
10/01/2018	<ul style="list-style-type: none"> • Updated list of related policies; added reference link to the policy titled <i>Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting</i> • Revised conditions of coverage/special considerations; added language to indicate: <ul style="list-style-type: none"> ○ Participating hospitals are required to purchase Lemtrada (alemtuzumab) from the BrioVaRx Specialty Pharmacy when the medication is administered in an outpatient hospital setting; refer to the policy titled Specialty Pharmacy for Certain Specialty Medications Administered in an Outpatient Hospital Setting for additional information • Archived previous policy version PHARMACY 186.15 T2