Lemtrada® (Alemtuzumab)

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➲ Instructions for Use

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Community Plan Policy

- Lemtrada® (Alemtuzumab)

Application

UnitedHealthcare Commercial

This Medical Drug Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Drug Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

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

- Diagnosis of relapsing forms of multiple sclerosis (MS) (e.g., relapsing-remitting MS, active secondary-progressive MS); **and**
- **One** of the following:
  - **Treatment-naïve to alemtuzumab:**
    - Patient 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®)
      - Ocrelizumab (Ocrevus®)
      - Rituximab (Riabni™, Rituxan®, Ruxience®, & Truxima®)
      - Siponimod (Mayzent®)
      - Ozanimod (Zeposia®)
      - Ofatumumab (Kesimpta®)

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- Monomethyl fumarate (Bafiertam)
- Cladribine (Mavenclad)
- Ublituximab (Briumvi®)

and

- Patient has **not** been previously treated with alemtuzumab; **and**
- Patient is **not** receiving alemtuzumab in combination with another disease modifying agent for multiple sclerosis (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, teriflunomide, ocrelizumab, etc.); **and**
- Initial dosing is administered: 12 mg intravenously daily for 5 consecutive days; **and**
- Regimen is administered only once within 12 months; **and**
- Initial authorization is for no more than 12 months and no more than 5 doses

or

- **Treatment-experienced with alemtuzumab:**
  - Patient has previously received treatment with alemtuzumab; **and**
  - Documentation of positive clinical response to alemtuzumab therapy; **and**
  - Patient is **not** receiving alemtuzumab in combination with another disease modifying agent for multiple sclerosis (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, teriflunomide, ocrelizumab, etc.); **and**
  - Retreatment dosing is administered: 12 mg intravenously daily for 3 consecutive days; **and**
  - Regimen is administered only once within 12 months; **and**
  - Authorization is for no more than 12 months and no more than 3 doses

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
- Evans syndrome
- Autoimmune pancytopenia

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 and Guidelines may apply.

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

Diagnosis Code	Description
G35.A	Relapsing-remitting multiple sclerosis
G35.B0	Primary progressive multiple sclerosis, unspecified
G35.B1	Active primary progressive multiple sclerosis
G35.B2	Non-active primary progressive multiple sclerosis
G35.C0	Secondary progressive multiple sclerosis, unspecified
G35.C1	Active secondary progressive multiple sclerosis
G35.C2	Non-active secondary progressive multiple sclerosis
G35.D	Multiple sclerosis, unspecified

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

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binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Proven

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. 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. Of the 110 patients who received alemtuzumab retreatment, 77 (70.0%), 28 (25.5%), and 5 (4.5%) received a total of 1, 2, and 3 alemtuzumab retreatment courses, respectively, over years 3-5. 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). 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 β1A (SC INF-β-1a, 202 patients) 44 mcg, or alemtuzumab 12mg (426 patients), with baseline demographics, clinical characteristics and pre-study 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.

Professional Societies

In 2018, the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (AAN) published practice guideline recommendations for disease-modifying therapies (DMT) for adults with multiple sclerosis. Thirty recommendations were developed. The recommendations that specifically make reference to alemtuzumab (Lemtrada) are as follows:

- **Starting DMTs Recommendations**: Recommendation 14: Clinicians should prescribe alemtuzumab, fingolimod, or natalizumab for people with MS with highly active MS (Level B).
- **Switching DMTs Recommendations**: Recommendation 7 (Statement 7b): If a patient with MS develops a malignancy while using a DMT, clinicians should promptly discuss switching to an alternate DMT, especially for people with MS using azathioprine, methotrexate, mycophenolate, cyclophosphamide, fingolimod, teriflunomide, alemtuzumab, or dimethyl fumarate (Level B).

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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 µg 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.

A 2023 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

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.[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.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Lemtrada (alemtuzumab) is a CD52-directed cytolytic antibody indicated for the treatment of patients 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. 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 regard to the program may be found at: https://www.lemtradahcp.com/rems.

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

Effective September 4, 2012, Campath will no longer be available commercially, but will be provided through the Campath Distribution Program, managed by Clinigen, 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.clinigengroup.com/direct/en.

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Policy History/Revision Information

Date	Summary of Changes

04/01/2026	**Template Update**
	• Transferred content to shared policy template that applies to both UnitedHealthcare Commercial and Individual Exchange benefit plans
	• Added *Application* section to indicate this policy applies to:
	  ○ UnitedHealthcare Commercial benefit plans
	  ○ Individual Exchange benefit plans
	Supporting Information
	• Archived previous policy versions 2025D0023Y and IEXD0023.09

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

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UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies 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.

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