LEMTTRA (alemtuzumab)

Protocol: PHA010
Effective Date: August 1, 2017

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INSTRUCTIONS FOR USE

This protocol provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Evidence of Coverage (EOC)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this protocol. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Protocol. Other Protocols, Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Protocols, Policies and Guidelines as necessary. This protocol is provided for informational purposes. It does not constitute medical advice. This policy does not govern Medicare Group Retiree members.

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.

COMMERCIAL, MEDICARE & MEDICAID COVERAGE RATIONALE

Lemtrada (alemtuzumab) is medically necessary for treatment of relapsing-remitting multiple sclerosis when ALL of the following criteria are met:

1. Diagnosis of relapsing-remitting multiple sclerosis (RRMS)
   AND
2. One of the following:
   a. Treatment-naïve to alemtuzumab:
      1) Patient has history of failure following a trial for at least 4 weeks or history of intolerance or contraindication to two of the following:
         (a) interferon β-1a (Avonex® or Rebif®)
         (b) interferon β-1b (Betaseron® or Extavia®)
         (c) glatiramer acetate (Copaxone®)
         (d) dimethyl fumarate (Tecfidera®)
         (e) teriflunomide (Aubagio®)
(f) fingolimod (Gilenya®)
(g) peginterferon beta-1a (Plegridy™)
(h) natalizumab (Tysabri®)
(i) daclizumab (Zinbryta™)
(j) ocrelizumab (Ocrevus®)

AND

2) Patient has not been previously treated with alemtuzumab

AND

3) 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, etc)

AND

4) Initial dosing is administered: 12 mg intravenously daily for 5 consecutive days

AND

5) Regimen is administered only once within 12 months

OR

b. Treatment-experienced with alemtuzumab:

1) Patient has previously received treatment with alemtuzumab

AND

2) 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, etc)

AND

3) Retreatment dosing is administered: 12 mg intravenously daily for 3 consecutive days

AND

4) Regimen is administered only once within 12 months

Coverage of Lemtrada is limited to 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.

HPN will not provide coverage of Lemtrada for indications other than relapsing-remitting multiple sclerosis RRMS.

Alemtuzumab is not medically necessary for the treatment of:

1) Rheumatoid arthritis
2) Autoimmune neutropenia
3) Autoimmune hemolytic anemia
4) Pure red cell aplasia
5) Immune thrombocytopenic purpura
6) Evans syndrome
7) Autoimmune pancytopenia

Centers for Medicare and Medicaid Services (CMS)
Medicare does not have a National Coverage Determination (NCD) or a Local Coverage Determination (LCD) for Nevada for Lemtrada (alemtuzumab) Accessed June 2017.
In general, Medicare covers outpatient (Part B) drugs that are furnished “incident to” a physician’s service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf. Accessed June 2017.

For Medicare and Medicaid Determinations Related to States Outside of Nevada:
Please review Local Coverage Determinations that apply to other states outside of Nevada. http://www.cms.hhs.gov/mcd/search

Important Note: Please also review local carrier Web sites in addition to the Medicare Coverage database on the Centers for Medicare and Medicaid Services’ Website.

CLINICAL EVIDENCE

Medically Necessary
Multiple Sclerosis
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 β1A (SC INF-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 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.

**Not Medically Necessary**

**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). Accessed June 2017.

Campath (alemtuzumab) is a CD52-directed cytolytic 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). Accessed June 2017.

**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 Coverage Determination Guidelines may apply.

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<tr>
<th>ICD-10 Diagnosis Code</th>
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REFERENCES


PROTOCOL HISTORY/REVISION INFORMATION

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The foregoing Health Plan of Nevada/Sierra Health & Life Health Operations protocol has been adopted from an existing UnitedHealthcare policy that was researched, developed and approved by the UnitedHealthcare National Pharmacy & Therapeutics Committee.