**09-J2000-27**

**Original Effective Date: 03/15/15**

**Reviewed: 10/11/23**

**Revised: 11/15/23**

# Subject: Alemtuzumab (Lemtrada™) IV

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**



## DESCRIPTION:

Alemtuzumab (Lemtrada) is U.S. Food and Drug Administration (FDA) approved for the treatment of relapsing forms of multiple sclerosis to include relapsing-remitting disease and active secondary progressive disease in adults. Due to the potential for serious adverse effects, it should be reserved for patients who have had an inadequate response to at least 2 drugs for the treatment of multiple sclerosis.

In two randomized trials, the rate of multiple sclerosis (MS) relapse was significantly reduced with alemtuzumab (rate of relapse, 22% and 35%) compared with interferon beta-1a (rate of relapse, 40% and 53%) in untreated (CARE-MS I; N=581) and previously treated (CARE-MS II; N=840) patients with relapsing-remitting MS. Alemtuzumab significantly improved the sustained accumulation of disability over 6 months compared with interferon beta-1a among previously treated patients (12.71% vs 21.13%); however, significance was not reached among previously untreated patients. In both studies alemtuzumab was associated with a higher incidence of serious infections, immune thrombocytopenia, autoimmunity, and thyroid papillary carcinoma, as well as a significantly higher incidence of herpes viral infections despite prophylaxis with acyclovir.

The FDA has required a Risk Evaluation and Mitigation Strategy for alemtuzumab.

## POSITION STATEMENT:

Initiation of alemtuzumab (Lemtrada) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with **ONE** of the following:
    a. Relapsing –remitting multiple sclerosis [RRMS]

b. Active secondary progressive MS [SPMS]

2. **ONE** of the following (a, b, or c) – documentation must be submitted:
    a. The patient has highly active MS disease activity and **BOTH** of the following:
        i. The patient has ≥ 2 relapses in the previous year
        ii. **ONE** of the following:
            1. The patient has ≥ 1 gadolinium enhancing lesion on MRI
            2. The patient has significant increase in T2 lesion load compared with a previous MRI
    b. The patient has been treated with at least 3 MS agents from different drug classes
    c. **BOTH** of the following (i and ii):
        i. **ONE** of the following (1,2, 3, or 4):
            1. The patient has tried and had an inadequate response to dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **OR** teriflunomide (generic)
            2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **OR** teriflunomide (generic)
            3. The patient has a FDA labeled contraindication to dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **AND** teriflunomide (generic)
            4. The prescriber has provided information in support of using the requested agent over dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), **AND** teriflunomide (generic)
        ii. **ONE** of the following (1,2,3, or 4):
            1. The patient has tried and had an inadequate response to **ONE** preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
            2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **ONE** preferred brand agent (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
            3. The patient has a FDA labeled contraindication to **ALL** preferred brand agents (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)
            4. The prescriber has provided information in support of using the requested agent over **ALL** preferred brand agents (Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, Zeposia)

3. Member has not previously been treated with alemtuzumab
4. Member has tested negative for HIV infection
5. Member will receive antiviral prophylaxis for at least 2 months from the start of each treatment course to prevent herpetic viral infection
6. Alemtuzumab is not administered in combination with **ANY** of the following:
    a. Cladribine (Mavenclad)
    b. Dimethyl fumarate (Tecfidera)
    c. Diroximel fumarate (Vumerity)
    d. Fingolimod (Gilenya, Tascenso ODT)
    e. Glatiramer acetate (Copaxone, Glatopa)
    f. Interferon beta-1a (Avonex, Rebif)
    g. Interferon beta-1b (Betaseron, Extavia)
    h. Mitoxantrone (Novantrone)
    i. Monomethyl fumarate (Bafiertam)
    j. Natalizumab (Tysabri)
    k. Ocrelizumab (Ocrevus)
    l. Ofatumumab (Kesimpta)
    m. Ozanimod (Zeposia)
    n. Peg-interferon beta-1a (Plegridy)
    o. Ponesimod (Ponvory)
    p. Rituximab (Rituxan or biosimilars)
    q. Siponimod (Mayzent)
    r. Teriflunomide (Aubagio)
    s. Ublituximab (Briumvi)
7. Dose does not exceed 12 mg/day

**Approval Duration**: 5 doses

Continuation of alemtuzumab (Lemtrada) **meets the definition of medical necessity** for RRMS or active SPMS when **ALL** of the following criteria are met:

1. The member was previously approved by Florida Blue or another healthplan OR the member previously met all indication-specific criteria for coverage
2. Member has demonstrated a beneficial response associated with alemtuzumab (i.e., reduction in relapses)
3. Member will receive antiviral prophylaxis for at least 2 months from the start of each treatment course to prevent herpetic viral infection

4. Use is **NOT** in combination with any of the following:
    a. Cladribine (Mavenclad)
    b. Dimethyl fumarate (Tecfidera)
    c. Diroximel fumarate (Vumerity)
    d. Fingolimod (Gilenya, Tascenso ODT)
    e. Glatiramer acetate (Copaxone, Glatopa)
    f. Interferon beta-1a (Avonex, Rebif)
    g. Interferon beta-1b (Betaseron, Extavia)
    h. Mitoxantrone (Novantrone)
    i. Monomethyl fumarate (Bafiertam)
    j. Natalizumab (Tysabri)
    k. Ocrelizumab (Ocrevus)
    l. Ofatumumab (Kesimpta)
    m. Ozanimod (Zeposia)
    n. Peg-interferon beta-1a (Plegridy)
    o. Ponesimod (Ponvory)
    p. Rituximab (Rituxan or biosimilars)
    q. Siponimod (Mayzent)
    r. Teriflunomide (Aubagio)
    s. Ublituximab (Briumvi)
5. Member has not utilized any of the following agents since initiating treatment with alemtuzumab:
    a. Cladribine (Mavenclad)
    b. Dimethyl fumarate (Tecfidera)
    c. Diroximel fumarate (Vumerity)
    d. Fingolimod (Gilenya, Tascenso ODT)
    e. Glatiramer acetate (Copaxone, Glatopa)
    f. Interferon beta-1a (Avonex, Rebif)
    g. Interferon beta-1b (Betaseron, Extavia)
    h. Mitoxantrone (Novantrone)
    i. Monomethyl fumarate (Bafiertam)
    j. Natalizumab (Tysabri)
    k. Ocrelizumab (Ocrevus)

l. Ofatumumab (Kesimpta)
m. Ozanimod (Zeposia)
n. Peg-interferon beta-1a (Plegridy)
o. Ponesimod (Ponvory)
p. Rituximab (Rituxan or biosimilars)
q. Siponimod (Mayzent)
r. Teriflunomide (Aubagio)
s. Ublituximab (Briumvi)

6. **ONE** of the following:
    a. Member has received fewer than two treatment courses of alemtuzumab
    b. Member has received fewer than three treatment courses of alemtuzumab and experienced relapse, 2 or more new or enlarging T2 hyperintense lesions, or any new gadolinium-enhancing T1 brain or spinal cord lesions on MRI after the second course of treatment - documentation must be submitted
7. Member has not received alemtuzumab in the previous 12 months
8. Dose does not exceed 12 mg/day

**Approval Duration**: 3 doses

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

**FDA-approved**

- Administer by intravenous infusion over 4 hours for 2 or more treatment courses:
    - First course: 12 mg/day on 5 consecutive days
    - Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course
- Subsequent treatment courses of 12 mg per day on 3 consecutive days (36 mg total dose) may be administered, as needed, at least 12 months after the last dose of any prior treatment course
- Premedicate with corticosteroids prior to infusion for the first 3 days of each treatment course
- Administer antiviral agents for herpetic prophylaxis starting on the first day of dosing and continuing for a minimum of two months after completion of dosing or until CD4+ lymphocyte count is more than 200 cells per microliter, whichever occurs later
- Dilute prior to administration
- Baseline lab tests are required prior to treatment. See prescribing information.

**Drug Availability**

- Injection: 12 mg/1.2 mL (10 mg/mL) in a single-use vial

## PRECAUTIONS:

**Boxed Warning**

- Serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease may occur. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine counts at periodic intervals for 48 months after the last dose.
- Serious and life-threatening infusion reactions can occur. Administer in a setting with personnel and equipment to manage anaphylaxis or serious infusion reaction. Monitor for 2 hours after each infusion. Patients should be aware that serious infusion reactions can also occur after the 2 hour monitoring period.
- Serious and life-threatening stroke has been reported within 3 days of administration. Seek immediate medical attention if symptoms of stroke occur.
- May cause an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams.
- Available only through a restricted distribution program

**Contraindications**

- Infection with Human Immunodeficiency Virus

**Precautions/Warnings**

- Immune thrombocytopenia: Monitor complete blood counts with differential prior to initiation and monthly until 48 months after the last infusion.
- Glomerular nephropathies: Obtain serum creatinine levels, urinalysis with cell counts and urine protein to creatinine ratio prior to initiation of treatment. Monitor serum creatinine levels and urinalysis with cell counts at monthly intervals thereafter until 48 months after the last infusion.
- Thyroid Disorders: obtain thyroid function tests prior to initiation of treatment and every 3 months until 48 months after the last infusion
- Other Autoimmune Cytopenias: Monitor CBCs monthly until 48 months after the last infusion.
- Autoimmune Hepatitis: if signs of hepatic dysfunction occur, measure serum transaminases and total bilirubin and interrupt or discontinue treatment.
- Hemaphagocytic Lymphohistiocytosis: consider this diagnosis and evaluate patients immediately if they develop signs or symptoms of systemic inflammation.
- Adult Onset Still's Disease (AOSD): if AOSD develops, promptly evaluate and treat.
- Thrombotic Thrombocytopenic Purpura (TTP): Evaluate patients immediately if they develop TTP.

- Autoimmune Encephalitis (AIE): Evaluate patients if they develop signs and symptoms suggestive of AIE, such as subacute onset of memory impairment, altered mental status, psychiatric symptoms, neurological findings, and seizures.
- Acquired Hemophilia A: Obtain a coagulopathy panel including aPTT in patients who present with signs such as spontaneous subcutaneous hematomas, extensive bruising, hematuria, epistaxis, or gastrointestinal or other types of bleeding.
- Infections: Consider delaying initiation in patients with active infections until the infection is fully controlled. Fatal infections have occurred.
- Progressive Multifocal Leukoencephalopathy (PML): Withhold at the first sign or symptom suggestive of PML.
- Acute Acalculous Cholecystitis: increase risk with treatment.
- Pneumonitis: Cases of hypersensitivity pneumonitis and pneumonitis with fibrosis may occur
- Do not administer live viral vaccines following a course of treatment

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding

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|---|---|
| J0202 | Injection, alemtuzumab, 1 mg |

Do **NOT** use code J9010 (injection, alemtuzumab, 10 mg). This is a retired code for Campath.

### ICD-10 Diagnosis Codes That Support Medical Necessity

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|---|---|
| G35 | Multiple sclerosis |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

## DEFINITIONS:

**Clinically isolated syndrome (CIS):** the first clinical presentation of disease that shows characteristics of inflammatory demyelination that could be MS but has yet to fulfill criteria of dissemination in time.

**Primary-progressive multiple sclerosis (PPMS):** Steadily progressive course from onset; occurs in 10-15% of patients with MS.

**Relapsing-remitting multiple sclerosis (RRMS):** Characterized by acute attacks followed by periods of remission; primary form of MS that occurs in approximately 85% of patients.

**Secondary-progressive multiple sclerosis (SPMS):** An initial period of RRMS, followed by a steadily progressive course, with acute relapses (active disease) or without acute relapses (not active disease); 75-85% of patients diagnosed with RRMS will transition to SPMS.

## RELATED GUIDELINES:

**Cladribine (Mavenclad), 09-J3000-34**
**Dimethyl Fumarate (Tecfidera), Diroximel fumarate (Vumerity), and Monomethyl fumarate (Bafiertam), 09-J1000-96**
**Fingolimod (Gilenya), 09-J1000-30**
**Multiple Sclerosis Self Injectable Therapy, 09-J1000-39**
**Natalizumab (Tysabri) IV, 09-J0000-73**
**Ocrelizumab (Ocrevus), 09-J2000-78**
**Ofatumumab (Kesimpta), 09-J3000-84**
**Ozanimod (Zeposia), 09-J3000-70**
**Siponimod (Mayzent), 09-J3000-35**
**Teriflunomide (Aubagio), 09-J1000-82**

## OTHER:

None

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## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/11/23.

## GUIDELINE UPDATE INFORMATION:

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|---|---|
| 03/15/15 | New Medical Coverage Guideline. |
| 10/01/15 | Revision to guideline consisting of HCPCS code update. |
| 10/15/15 | Review and revision to guideline; consisting of updating position statement. |
| 01/01/16 | Annual HCPCS coding update: added code J0202 and deleted codes C9399 and C9979. |
| 01/01/17 | Review and revision to guideline; consisting of updating position statement, precautions and references. |
| 10/15/17 | Review and revision to guideline; consisting of updating position statement and references. |
| 12/15/18 | Review and revision to guideline; consisting of updating position statement and references. |
| 01/15/19 | Revision to guideline; consisting of updating position statement and references. |

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| 11/15/19 | Review and revision to guideline; consisting of updating position statement and references. |
| 01/15/20 | Revision to guideline; consisting of updating the position statement and references. |
| 07/01/20 | Revision to guideline; consisting of updating position statement. |
| 10/01/20 | Revision to guideline; consisting of updating position statement. |
| 03/15/20 | Revision to guideline; consisting of updating position statement. |
| 10/15/22 | Review and revision to guideline; consisting of updating documentation requirements of prior therapy and subsequent doses. Updated medications not to be used in combination, warnings, and references. |
| 05/15/23 | Review and revision to guideline; consisting of updating step requirements. Updated medications not to be used in combination. |
| 11/15/23 | Review and revision to guideline; consisting of updating the position statement to include Glatopa. |