alemtuzumab (Lemtrada®)

Policy # 00448
Original Effective Date: 01/21/2015
Current Effective Date: 02/08/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider alemtuzumab (Lemtrada®)‡ for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for alemtuzumab (Lemtrada) will be considered when the following criteria are met:

- Patient has a diagnosis of a relapsing form of multiple sclerosis (i.e., relapsing remitting or active secondary progressive disease); AND
- Patient is 17 years of age or older; AND
- Patient has had an inadequate response to 2 disease modifying medications used to treat multiple sclerosis; AND
- Patient is NOT using Lemtrada in combination with other disease modifying medications used to treat multiple sclerosis; AND
- The requested dose does not exceed 60 mg total dose for the first treatment course and 36 mg total dose for subsequent courses (which are to be given no sooner than 12 months after the prior course).

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of alemtuzumab (Lemtrada) when patient selection criteria are not met to be **investigational.***

Background/Overview

Lemtrada is a CD52-directed cytolytic monoclonal antibody. The antibody binds to CD52, which is a cell surface antigen present on T and B lymphocytes, natural killer cells, monocytes, and macrophages. Following binding to T and B lymphocytes, Lemtrada results in antibody dependent cellular cytolysis and compliment mediated lysis. Lemtrada is dosed at 12 mg/day for 5 consecutive days and 12 mg/day for 3 consecutive days 12 months after the first treatment course. Following the second 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 courses. The Lemtrada label contains several black box warnings of autoimmunity, infusion reactions, stroke, and malignancies possible with Lemtrada administration. Because of these risks, Lemtrada is only available through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) program.

Multiple Sclerosis

Multiple sclerosis is believed to have an immunologic mechanism that is characterized by demyelination in the brain and spinal cord. This is often expressed by symptoms such as visual and oculomotor abnormalities, weakness, urinary dysfunction, and mild cognitive impairment. Often patients will experience remissions and exacerbations. Treatment can include corticosteroids for acute exacerbations and immunomodulatory (disease modifying) drugs to prevent exacerbations. Disease modifying drugs include oral products such as Gilenya®‡, Mayzent®‡, Tecfidera®‡, and Aubagio®‡; subcutaneous and intramuscular injectable products such as Copaxone®‡, Avonex®‡, Rebif®‡, Extavia®‡, Betaseron®‡, and Plegridy®‡; and intravenous infusions such as Ocrevus®‡, Tysabri®‡, Mavenclad®‡, and Lemtrada. The placement of Lemtrada in the treatment of multiple sclerosis is still evolving. However, due to its safety profile, the label does mention that Lemtrada should be used after an inadequate response to two other agents for multiple sclerosis.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Lemtrada was approved in November of 2014 for the treatment of patients with relapsing forms of multiple sclerosis. The ingredient, alemtuzumab, was previously approved under the brand name Campath to treat cancer. Campath has since been pulled from the market, however it is available directly from the manufacturer. In October 2019, the indication of relapsing forms of multiple sclerosis was clarified to include only active secondary progressive disease and relapsing-remitting disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Lemtrada was demonstrated in 2 studies (Study 1 and Study 2) that evaluated Lemtrada 12 mg in patients with relapsing remitting multiple sclerosis. Lemtrada was administered by IV infusion once daily over a 5 day course, then once daily over a 3 day course. Study 1 was a randomized, open label, active comparator study over a 2 year period in patients with relapsing remitting multiple sclerosis. The active comparator arm was interferon beta-1a 44 mcg given subcutaneously three times per week. Clinical outcomes measured were the annualized relapse rate (ARR) over 2 years and the time to confirmed disability progression. The ARR was significantly lower in the Lemtrada group as compared to the interferon group (0.26 vs. 0.52, $p<0.0001$). The proportion of patients with disability progression at year 2 was also statistically lower in the Lemtrada group (13% vs. 21%), $p=0.0084$). The change in T2 lesion volume from baseline was not statistically significant between the two groups. The setup of Study 2 was similar to that of Study 1. The ARR was significantly lower in the Lemtrada group (0.18 vs. 0.39, $p<0.0001$). There was no significant difference between the treatment groups for the time to confirmed disability progression and for the primary MRI endpoint.

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References

1. Lemtrada [package insert]. Genzyme Corporation. Cambridge, Massachusetts. Updated October 2019.

Policy History

Original Effective Date: 01/21/2015
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01/08/2015	Medical Policy Committee review
01/21/2015	Medical Policy Implementation Committee approval. New policy.
01/07/2016	Medical Policy Committee review
01/22/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
01/05/2017	Medical Policy Committee review
01/18/2017	Medical Policy Implementation Committee approval. No change to coverage.
01/04/2018	Medical Policy Committee review
01/17/2018	Medical Policy Implementation Committee approval. No change to coverage
01/10/2019	Medical Policy Committee review
01/23/2019	Medical Policy Implementation Committee approval. Added coverage for third and subsequent courses based on updated label. Updated background information to include up to date information.
01/03/2020	Medical Policy Committee review
01/08/2020	Medical Policy Implementation Committee approval. Added new disease modifying therapies into background information and updated indication to include the FDA clarification of the definition of relapsing disease.
01/07/2021	Medical Policy Committee review
01/13/2021	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 01/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of

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descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0202, J3590
ICD-10 Diagnosis	G35

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.