Lemtrada® (alemtuzumab)

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Origination: 8/2015  
Last Review: 7/2020  
Next Review: 7/2021

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Lemtrada® (alemtuzumab) when it is determined to be medically necessary because the following criteria are met.

When Policy Topic is covered

The use of Lemtrada® (alemtuzumab) may be considered medically necessary when patient meets the following criteria:

1. **Multiple Sclerosis (MS), Initial Therapy (this includes patients who have started but not completed the first course of Lemtrada Therapy).** Approve in patients who meet all of the following criteria (a, b, c, and d):
   a) The patient is ≥ 17 years of age; AND
   b) The patient has a relapsing form of MS (relapsing forms of MS are RRMS, SPMS with relapses, and PRMS); AND
   c) The patient has had an inadequate response according to the prescribing physician to two of the following medications for MS: Avonex, Rebif, Betaseron, Extavia, Copaxone, Plegridy, Gilenya, Glatopa, Aubagio, Tecfidera, Tysabri, Ocrevus or Zinbryta; AND
   d) Lemtrada is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of MS.

Lemtrada is indicated for the treatment of patients with relapsing forms of MS. Due to its safety profile, Lemtrada should generally be reserved for patients who have had an inadequate response to two or more medications indicated for the treatment of MS. The safety and efficacy of Lemtrada in pediatric patients < 17 years of age have not been established. Lemtrada is administered by IV infusion over 4 hours for two treatment courses. The first course is 12 mg/day IV on 5 consecutive days and the second course is administered 12 months after the first treatment course. Many MS medications are available with established efficacy and a known safety profile.

Drug must be sourced from an approved specialty infusion provider.

When Policy Topic is not covered

The use of Lemtrada is considered investigational for all other indications. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Children with Multiple Sclerosis (MS) aged < 17 years.** The safety and effectiveness of Lemtrada in pediatric patients < 17 years of age have not been established. Use of Lemtrada is not recommended in pediatric patients due to the risk of autoimmunity, infusion reactions, and because it may increase the risk of malignancies (e.g., thyroid, melanoma, lymphoproliferative disorders, and lymphoma).

2. **Current Use of Lemtrada with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS).** Lemtrada should not be given in combination with other disease-modifying agents used for MS (e.g., Betaseron, Extavia, Rebif, Copaxone, Avonex, Plegridy, Gilenya,
Aubagio, Tecfidera, or Tysabri). Concomitant use of Lemtrada with immunosuppressive therapies could increase the risk of immunosuppression.¹

3. Human Immunodeficiency Virus (HIV) Infection (Patients With). Use of Lemtrada is contraindicated in patients who are infected with HIV because Lemtrada causes prolonged reductions of CD4+ lymphocyte counts.¹

4. Primary Progressive (Chronic Progressive) Multiple Sclerosis (MS). The safety and efficacy of Lemtrada have not been studied in patients with primary progressive (chronic progressive) MS. Lemtrada is indicated in patients with relapsing forms of MS.¹

Considerations
Lemtrada is a medical benefit, requiring prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service
Lemtrada, a CD52-directed cytolytic monoclonal antibody, is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS).¹ Due to its safety profile, use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more medications indicated for the treatment of MS. The recommended dose of Lemtrada is 12 mg/day given by intravenous (IV) infusion for two treatment courses. The first treatment course is 12 mg/day IV on 5 consecutive days (60 mg total dose) and the second treatment course is 12 mg/day IV on 3 consecutive days (36 mg total dose) given 12 months after the first treatment course. Infuse Lemtrada over 4 hours and administer the agent in a setting that has equipment and personnel to appropriately manage anaphylaxis or serious infusion reactions. Observe patients for infusion reactions during and for at least 2 hours after each Lemtrada infusion. Patients should complete any needed immunizations at least 6 weeks prior to initiating Lemtrada. Before Lemtrada treatment, determine whether patients have a history of varicella or have been vaccinated for varicella zoster virus (VZV). If not, test the patient for antibodies to VZV and consider vaccination for patients who are antibody-negative. It is recommended to premedicate patients with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to the first Lemtrada infusion and for the first 3 days of each treatment course. Administer antiviral prophylaxis for herpetic viral infections commencing on the first day of each treatment course and continue for a minimum of 2 months after Lemtrada therapy or until the CD4+ lymphocyte count is ≥ 200 cells per microliter. Two pivotal trials assessed the efficacy of Lemtrada in patients with relapsing-remitting MS (RRMS). One study involved patients who had at least one relapse while receiving interferon beta or glatiramer acetate therapy and the other study involved patients who were treatment naïve.¹⁻³ Lemtrada contains the same active ingredient found in Campath® (alemtuzumab injection for IV use), which is approved by the Food and Drug Administration (FDA) for the treatment of B-cell chronic lymphocytic leukemia.⁴

Risk Evaluation and Mitigation Strategy (REMS)
Lemtrada is available only through a restricted REMS program called the LEMTRADA REMS Program due to the risks of autoimmunity, infusion reactions, and malignancies.¹ Some program requirements include that prescribers must be certified with the program by enrolling and completing training. Also, patients must enroll in the program and comply with ongoing monitoring requirements. Pharmacies are required to be certified with the program and must only dispense Lemtrada to certified healthcare facilities that are authorized to receive Lemtrada. It is required that healthcare facilities enroll in the program and verify that patients are authorized before infusing Lemtrada. Healthcare facilities must have on-site access to equipment and personnel trained to manage infusion reactions.

Rationale
Multiple Sclerosis (MS)
MS is a chronic disabling disease of the central nervous system (CNS) characterized by inflammation, demyelination, and degenerative changes. Patients experience relapses followed by remission of neurological symptoms. MS lesions occur in many different parts of the CNS and the symptoms and clinical course of the disease are highly variable. Some common signs and symptoms of the disease include vision problems (e.g., nystagmus), ambulation problems, pain, fatigue, spasticity, cognitive dysfunction, depression, ataxia, sensory loss, bladder disturbances, bowel dysfunction, dizziness, and vertigo. In general, patients with MS may have diminished ratings on vitality and physical functions. Most people with MS are diagnosed between the ages of 20 and 50 years, but MS can manifest in young children and older adults. Approximately 450,000 people are living with MS in the US. Women are impacted 2 to 3 times more commonly than men, and MS is more predominant in Caucasians compared with other racial groups.

Four different clinical courses of MS have been delineated. A relapse is defined as the development of new or recurring symptoms lasting at least 24 hours and separated from a previous attack by at least one month. RRMS is characterized by acute attacks usually followed by almost complete recovery with limited progression. Disease progression is minimal between attacks. Approximately 85% of people are initially diagnosed with RRMS. Secondary progressive MS (SPMS) begins as a relapsing-remitting course but the disease transitions in many patients to a steadily progressive form with increased loss of function. Of the 85% of patients who initially have RRMS, more than 50% of patients will develop to SPMS within 10 years and 90% of patients within 25 years. Primary-progressive MS (PPMS) is noted by a steady decline in function from the onset without noted relapses. Around 10% of patients are diagnosed with primary-progressive. Progressive-relapsing MS (PRMS) starts with disease progression at onset with occasional acute relapses and continued disease progression. Only a small minority of patients (< 5%) have PRMS. About 10% of the MS population has a benign disease course, which is generally determined retrospectively. Among those with relapsing forms of MS, the severity, duration, and frequency of relapses vary widely among patients. The Expanded Disability Scale Score (EDSS) is the scale most often used to assess neurologic disability and evaluates cerebellar, pyramidal, brainstem, sensory, bowel, bladder, visual, and mental functional systems on a scale that ranges from 0 (normal neurologic examination) to 10 (death due to MS). Magnetic resonance imaging (MRI) evaluations are used to assess current MS disease activity, as well as to monitor for permanent neurologic damage.

Other Disease-Modifying Drug Therapies for Multiple Sclerosis

Interferon beta therapies indicated for use in relapsing forms of MS include Avonex® (interferon beta-1a for intramuscular [IM] injection),7 Rebif® (interferon beta1-a for subcutaneous [SC] injection),8 and Betaseron®/Extavia® (interferon beta-1b for SC injection).9-10 Dosing of these products is IM once weekly (QW), SC three times weekly (TIW), and SC every other day, respectively. Plegridy™ (peginterferon beta-1a injection) is a pegylated interferon beta-1a product that is also indicated for the treatment of relapsing forms of MS and is dosed SC every 14 days.11 Another self-injectable MS therapy is Copaxone® (glatiramer acetate injection for SC use), which can be dosed SC either once daily (QD) or TIW.12 Although some differences in efficacy have been observed in clinical trials among the interferon beta products, in general, these self-injectable MS therapies appear to reduce the annualized relapse rate (ARR) by approximately one-third.13 Copaxone and several interferon beta products have been available for over 20 years with established efficacy and known safety. Oral therapies indicated in relapsing forms of MS include Aubagio® (teriflunomide tablets),14 Gilenya™ ( fingolimod capsules),15 and Tecfidera™ (dimethyl fumarate delayed-release capsules).16 Compared with placebo, these agents lead to reductions in the ARR of approximately 31% with Aubagio, 54% with Gilenya, and 44% to 53% with Tecfidera.6 Therapies administered by IV infusion include Tysabri® (natalizumab for IV infusion)17 and mitoxantrone injection,18 which are administered once every four weeks (over 1 hour), and once every 3 months (over 5 to 15 minutes), respectively. These therapies have also demonstrated benefits in patients with MS with the effect of ARR being reduced by approximately 67%.6,19 However, Tysabri must be used cautiously due to the risk of progressive multifocal leukoencephalopathy (PML).17 Due to toxicities (e.g., cardiotoxicity, increased risk of
developing secondary acute myeloid leukemia) the role of mitoxantrone is limited to a carefully selected patient population who have not responded to other therapies.\textsuperscript{19}

References

10. Extavia\textsuperscript{®} [prescribing information]. East Hanover, NJ: Novartis: March 2012.
14. Aubagio\textsuperscript{®} [prescribing information]. Cambridge, MA: Genzyme (a Sanofi Corporation); October 2014.
15. Gilenya\textsuperscript{®} [prescribing information]. East Hanover, NJ: Novartis; April 2014.
17. Tysabri\textsuperscript{®} injection [prescribing information]. South San Francisco, CA: Elan Pharmaceuticals, Inc.; (manufactured by Biogen Idec Inc); December 2013.

Billing Coding/Physician Documentation Information

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Additional Policy Key Words

Policy Number: 5.02.517

Policy Implementation/Update Information

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<tr>
<td>08/2015</td>
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<td>08/2016</td>
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<td>05/2017</td>
<td>Added specialty infusion provider requirement</td>
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<td>07/2018</td>
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