daclizumab (Zinbryta™)

Policy # 00540
Original Effective Date: 01/01/2017
Current Effective Date: 01/01/2017

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 daclizumab (Zinbryta™) for the treatment of relapsing forms of multiple sclerosis to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for daclizumab (Zinbryta) will be considered when the following criteria are met:
- Patient has a diagnosis of a relapsing form of multiple sclerosis; AND
- Patient is 18 years of age or older; AND
- Patient had an inadequate response to at least TWO disease modifying medications used to treat multiple sclerosis; AND
- Patient is NOT using Zinbryta in combination with other disease modifying medications used to treat multiple sclerosis

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 daclizumab (Zinbryta) when the patient selection criteria are not met to be investigational.*

Background/Overview
Zinbryta is an interleukin-2 (IL-2) receptor blocking antibody indicated for the treatment of adult patients with relapsing forms of multiple sclerosis. It is presumed that the effects of Zinbryta are due to the modulation of IL-2 mediated activation of lymphocytes through binding to CD25, a subunit of the high-affinity IL-2 receptor. The Food and Drug Administration (FDA) states that “because of its safety profile, the use of Zinbryta should generally be reserved for patients who have had an inadequate response to two or more drugs for the treatment of multiple sclerosis.” Zinbryta is dosed at 150 mg subcutaneously once monthly.

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. The most recent wave of disease modifying drugs included oral products such as Gilenya, Tecfidera, and Aubagio. Other disease modifying medications include Copaxone, Avonex, Rebif, Extavia, Betaseron, Plegridy, Tysabri, and Lemtrada. Zinbryta is the latest drug to be approved for the treatment of multiple sclerosis. However, due to its safety profile, the label does mention that Zinbryta should be used after an inadequate response to two other agents for multiple sclerosis.

**FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

Zinbryta was approved in May of 2016 and is an interleukin-2 (IL-2) receptor blocking antibody indicated for the treatment of adult patients with relapsing forms of multiple sclerosis.

**Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration 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 Zinbryta was demonstrated in two randomized, double-blind, controlled studies that both evaluated 150 mg of subcutaneous Zinbryta taken once every four weeks in patients with relapsing multiple sclerosis. The first study compared Zinbryta to 30 mcg weekly intramuscular doses of Avonex in 1,841 patients with relapsing multiple sclerosis. Treatment continued for up to 144 weeks until the last enrolled patient completed 96 weeks of treatment. The primary outcome of the first study was the annualized relapse rate. Zinbryta had a statistically significant effect on the annualized relapse rate and on the number of new or newly enlarging T2 hyperintense lesions. The annualized relapse rate was 0.216 in the Zinbryta group versus 0.393 in the Avonex group (p<0.0001). There was no statistically significant effect on 12 weeks confirmed disability progression.

The second study compared Zinbryta to placebo in 412 patients with relapsing forms of multiple sclerosis. Treatment duration was 52 weeks. The primary outcome measure of the second study was the annualized relapse rate at week 52. Zinbryta had a statistically significant effect on the annualized relapse rate, the proportion of patients relapse free, the number of new T1 Gd-enhancing lesions and the number of new or newly enlarging T2 hyperintense lesions. The annualized relapse rate was 0.211 in the Zinbryta group vs. 0.458 in the placebo group (p<0.0001).

**References**


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12/01/2016       Medical Policy Committee review
12/21/2016       Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date:  12/2017

*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. 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 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.

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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.