Medication Policy Manual | **Policy No:** dru465

Topic: Zinbryta™, daclizumab | **Date of Origin:** August 12, 2016

Committee Approval Date: December 16, 2016 | **Next Review Date:** December 2017

Effective Date: January 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Daclizumab (Zinbryta) is a subcutaneously administered medication interleukin-2 receptor blocking antibody indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of daclizumab (Zinbryta) should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Policy/Criteria

I. Most contracts require prior authorization approval of daclizumab (Zinbryta) prior to coverage. Daclizumab (Zinbryta) may be considered medically necessary when criteria A and B below are met.

A. A definitive diagnosis of a relapsing form of multiple sclerosis (relapsing-remitting or secondary progressive multiple sclerosis) that has been established by a specialist in neurology or multiple sclerosis.

AND

B. There is clinical documentation that two of the following disease modifying therapies for multiple sclerosis , as specified in both criteria 1 and 2 below, were ineffective, contraindicated or not tolerated:

1. Dimethyl fumarate (Tecfidera) or fingolimod (Gilenya)

AND

2. Natalizumab (Tysabri). If natalizumab (Tysabri) is contraindicated due to a positive JC virus antibody, then at least one other disease modifying therapy must be ineffective, contraindicated or not tolerated (see Appendix A).

   Ineffectiveness is defined as meeting at least **two** of the following three criteria (a, b, or c) during treatment with one of these medications:

   a. The patient continues to have clinical relapses (at least one relapse within the past 12 months).

   b. The patient continues to have CNS lesion progression as measured by MRI.

   c. The patient continues to have worsening disability. Examples of worsening disability include, but are not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or an increase in EDSS score.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers daclizumab (Zinbryta) to be a self-administered medication.

B. When prior authorization is approved, daclizumab (Zinbryta) may be authorized in quantities of up to one 150 mg syringe per 28 days.

C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Daclizumab (Zinbryta) is considered not medically necessary when used at doses greater than 150 mg every 4 weeks.

IV. Daclizumab (Zinbryta) is considered investigational when used for all other conditions, including but not limited to:

A. Primary progressive MS

B. Prophylaxis of acute organ rejection

Position Statement

Summary

- Daclizumab (Zinbryta) is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis. Due to its safety profile, the use of daclizumab (Zinbryta) should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. [1]
- In clinical trials, daclizumab (Zinbryta) was shown to be superior to interferon beta-1a (Avonex) at reducing annualized relapse rate. Results for disability progression also favored daclizumab (Zinbryta) but were not statistically significant. [2]
- Daclizumab (Zinbryta) contains boxed warnings for hepatic injury, including autoimmune hepatitis, and other immune mediated disorders. Due to these safety concerns the use of daclizumab (Zinbryta) should generally be limited to patients who have failed at least two prior therapies. [1]
- The FDA approved dose of daclizumab (Zinbryta) is 150 mg subcutaneously once monthly. A higher dose of 300 mg monthly has been evaluated in clinical trials but was shown to have similar efficacy to 150 mg monthly. [1,3]
- Daclizumab (Zinbryta) has only been studied in relapsing forms MS. Use in other forms of MS, such as primary progressive MS, is considered investigational.
- The safety and efficacy of daclizumab (Zinbryta) in combination with other disease modifying therapies has not been established.

Clinical Efficacy

- One randomized, double-blind, controlled, phase 3 study (the DECIDE study) compared daclizumab (Zinbryta) with interferon beta-1a (Avonex) in patients with relapsing-remitting multiple sclerosis (RRMS).[2]
    * Daclizumab (Zinbryta) was superior to interferon beta-1a in reducing annualized relapse rate.
    * Results for slowing the progression of disability favored daclizumab (Zinbryta), but were not statistically significant.
- Daclizumab (Zinbryta) has not been directly compared to other disease-modifying therapies for MS.
- A second, phase 2b study (the SELECT study) compared daclizumab (Zinbryta) 150 mg or 300 mg monthly versus placebo. The results showed that both doses of daclizumab (Zinbryta) were superior to placebo for reducing annualized relapse rate, however there was no difference between the 150 mg and 300 mg doses of daclizumab (Zinbryta). [3]

Investigational Uses

- Daclizumab was previously approved as Zenapax, an intravenous product indicated for the prophylaxis of acute organ rejection in patients receiving renal transplants. While daclizumab is the active agent in both Zenapax and Zinbryta, the route of administration, frequency, and dosing differ.
- Daclizumab (Zinbryta) has only been studied for relapsing forms MS. The use in other forms of MS, such as primary progressive MS is considered investigational.

- Daclizumab (Zinbryta) has not been studied concomitantly with any other disease modifying therapy for MS.

Safety [1]

- Daclizumab (Zinbryta) has boxed warnings for the following:
    - * Hepatic Injury Including Autoimmune Hepatitis
        - Daclizumab (Zinbryta) can cause severe liver injury including life-threatening events, liver failure, and autoimmune hepatitis. Transaminase and bilirubin levels should be obtained before initiation. Transaminase and bilirubin levels should be monitored and evaluated monthly and up to 6 months after the last dose. Daclizumab (Zinbryta) is contraindicated in patients with pre-existing hepatic disease or hepatic impairment.
    - * Other Immune-Mediated Disorders, including skin reactions, lymphadenopathy, non-infectious colitis, and other immune-mediated disorders.
- Daclizumab (Zinbryta) also contains warnings for hypersensitivity reactions, infections, and depression and suicide.
- Due to its significant safety concerns a FDA Risk Evaluation and Mitigation Strategy (REMS) program limits the availability of daclizumab (Zinbryta) to certified prescribers, healthcare facilities, and specialty pharmacies.

Appendix A: FDA-approved Disease-Modifying Agents Used in the Treatment of Multiple Sclerosis (MS)
alemtuzumab (Lemtrada®)
daclizumab (Zinbryta™)
dimethyl fumarate (Tecfidera®)
fingolimod (Gilenya®)
glatiramer acetate (Copaxone®)
interferon beta-1a (Avonex®, Rebif®)
interferon beta-1b (Betaseron®, Extavia®)
mitoxantrone (Novantrone®)
natalizumab (Tysabri®)
peginterferon beta-1a (Plegridy®)
teriflunomide (Aubagio®)

Cross References
Aubagio®, teriflunomide, Medication Policy Manual, Policy No. dru283
Copaxone®, glatiramer acetate, Medication Manual, Policy No. 412
Gilenya®, fingolimod, Medication Policy Manual, Policy No. dru229
Lemtrada®, alemtuzumab, Medication Policy Manual, Policy No. dru381
Non-Preferred interferon beta products for MS, Medication Manual, Policy No. 108
Preferred interferon beta products for MS, Medication Manual, Policy No. 000
Ocrevus®, ocrelizumab, Medication Manual, Policy No. 000
Rituxan®, rituximab, Medication Policy Manual, Policy No. dru214
Tecfidera®, dimethyl fumarate, Medication Policy Manual, Policy No. dru299
Tysabri®, natalizumab, Medication Policy Manual, Policy No. dru111

References

1. Zinbryta™ [Prescribing Information]. Cambridge, MA/North Chicago, IL: Biogen and AbbVie Inc.; May 2016.
2. Kappos, L, Wiendl, H, Selmaj, K, et al. Daclizumab HYP versus Interferon Beta-1a in Relapsing Multiple Sclerosis. *The New England journal of medicine*. 2015 Oct 8;373(15):1418-28. PMID: 26444729
3. Gold, R, Giovannoni, G, Selmaj, K, et al. Daclizumab high-yield process in relapsing-remitting multiple sclerosis (SELECT): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2013 Jun 22;381(9884):2167-75. PMID: 23562009

Revision History

Revision Date	Revision Summary
12/16/2016	• Removed requirement that Zinbryta is prescribed by or in conjunction with a specialist in MS or neurology due to redundancy with diagnostic criteria • Revised step therapy criteria
08/12/2016	New policy