VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis – Rebif® (interferon beta-1a injection for subcutaneous use – EMD Serono)

TAC REVIEW DATE: 07/17/2019

OVERVIEW

Rebif is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to include clinically isolated syndrome, relapsing remising disease, and active secondary progressive disease in adults. The recommended dosing for this indication is 22 mcg or 44 mcg subcutaneously (SC) three times per week (TIW). The dose may be titrated.[1]

Disease Overview

MS is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system (CNS) that impacts almost 1,000,000 people in the US.[2] The condition is marked by inflammation and demyelination, as well as degenerative alterations. Patients usually experience relapses and remissions in their neurological symptoms. For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults. The MS disease course is heterogeneous but has some patterns. Approximately 85% to 90% of patients have a relapsing pattern at onset. However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS). Around 10% to 15% of patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity. Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age) and the distribution is equivalent among the two genders. Advances in the understanding of the MS disease process, as well as in MRI technology, spurned updated disease course descriptions in 2013,[3] as well as in 2017.[4] The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.[2-4] Clinically isolated syndrome is now more recognized among the course descriptions of MS. It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be MS but has yet to fulfill diagnostic criteria. It is notable that the other MS designations can be further characterized considering whether patients have active disease (or not active), as well as if disease is worsening or stable. Disability in MS is commonly graded on the deterioration of mobility per the Expanded Disability Status Scale (EDSS) an ordinal scale that ranges from 0 to 10, with higher scores indicating greater disability.

Guidelines

In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.[2] Many options from various disease classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Rebif. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rebif as well as the monitoring required for adverse events and long-term efficacy, approval requires Rebif to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rebif is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Multiple Sclerosis (MS).** Approve for 3 year if the patient meets the following criteria (A and B):
   - **A)** The patient has a relapsing form of multiple sclerosis (MS); AND
   - **B)** The medication is prescribed by or after consultation with a neurologist or a physician who specializes in the treatment of MS.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Rebif has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Non-Relapsing Forms of Multiple Sclerosis.** Note: An example of a non-relapsing form of multiple sclerosis (MS) is primary progressive MS. The efficacy of Rebif has not been established in patients with MS with non-relapsing forms of MS.[1]

2. **Concurrent Use with Other Disease-Modifying Agents used for Multiple Sclerosis.** Note: Examples of disease modifying agents used for multiple sclerosis include Avonex® (interferon beta-1a injection [intramuscular]), Betaseron®/Extavia® (interferon beta-1b injection), Rebif® (interferon beta-1a injection [subcutaneous]), Copaxone®/Glatopa® (glatiramer acetate injection), Plegridy® (peginterferon beta-1a injection), Aubagio® (teriflunomide tablets), Gilenya® (fingolimod tablets), Mavenclad® (cladribine tablets), Mayzent® (siponimod tablets), Tecfidera® (dimethyl fumarate delayed-release capsules), Ocrevus® (ocrelizumab injection for intravenous use), Tysabri® (natalizumab injection for intravenous infusion), and Lemtrada® (alemtuzumab injection for intravenous use).[2] These agents are not indicated for use in combination. Additional data are required to determine if use of disease-modifying MS agents in combination is safe provides added efficacy.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rebif® injection for subcutaneous use [prescribing information]. Rockland, MD: EMD Serono; July 2019.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated June 2019. Available at: http://ms-coalition.org/wp-content/uploads/2019/06/MSC_DMTPaper_062019.pdf. Accessed on July 7, 2019.
3. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
4. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*. 2018;17(2):162-173.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Under the "Conditions Not Recommended for Approval" section, added Ocrevus to the list of disease-modifying agents used for MS in which concurrent use with Rebif is not recommended.	08/02/2017
Annual revision	Zinbryta was removed from the market. Therefore, Zinbryta was deleted from the list of medications in which Rebif should not be used with concomitantly.	08/15/2018
Annual revision	The following criteria changes were made. **1. Multiple Sclerosis:** The criteria was changed to require that the patient has a relapsing form of MS. The criteria previously required the patient have a diagnosis of MS or has experienced an attack and is at risk of MS. **2. Conditions Not Recommended for Approval:** The condition of Non-Relapsing Forms of MS were added as an exclusion. A note is provided that an example of a non-relapsing form of MS is primary progressive MS disease. Regarding Use with Other Disease-Modifying Agents for MS, the examples are now listed as a note with Mavenclad and Mayzent added.	07/17/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; MS – Multiple sclerosis.