POLICY: Multiple Sclerosis – Ocrevus (ocrelizumab injection for intravenous use – Biogen)

DATE REVIEWED: 11/13/2019

OVERVIEW

Ocrevus is a CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS) to include clinically isolated syndrome, relapsing remitting MS, and active secondary progressive MS in adults.[1] Ocrevus is also indicated for primary progressive MS in adults. Ocrevus is the only MS medication indicated for use in primary progressive MS.

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. Table 1 provides a comparison between relapsing MS and primary progressive MS.

Table 1. Relapsing MS vs. Primary Progressive MS.[2,5]

Characteristic	Relapsing MS	Primary Progressive MS
Percentage of the MS population	85% to 90%	10% to 15%
Clinical course	Recurrent subacute events of neurological dysfunction followed by complete or partial recovery.	Worsening of neurological dysfunction at disease onset with little or no recovery.
Age at onset	30 years of age	40 years of age
Gender	2:1 ratio of females to males	1:1 ratio of females to males

Table 1 (continued). Relapsing MS vs. Primary Progressive MS.[2,5]

Characteristic	Relapsing MS	Primary Progressive MS
Disability prognosis	Generally can occur after many years.	Rapid progression of disability.
Inflammation/brain lesions	There is less inflammation with primary progressive MS. Also, patients with primary progressive MS have fewer brain lesions vs. relapsing MS and the lesions tend to contain fewer inflammatory cells.	
Systems impacted	Patients with primary progressive MS have relatively more issues with ambulation compared to patients with relapsing forms of MS.	

MS – Multiple sclerosis.

Many disease-modifying MS agents are FDA-approved for use in patients with relapsing forms of MS.[2] Options include self-administered injectable agents (e.g., glatiramer acetate products, and interferon beta agents), oral agents (i.e., Tecfidera® [dimethyl fumarate delayed-release capsules], Gilenya® [fingolimod capsules], Mayzent® [siponimod tablets]), Aubagio® [teriflunomide tablets], Mavenclad® [cladribine tablets], Vumerity™ [diroximel fumarate delayed-release capsules]), and intravenously infused agents (i.e., Tysabri® [natalizumab injection for intravenous use], Lemtrada® [alemtuzumab injection for intravenous use], and mitoxantrone injection for intravenous use). No other therapies, besides Ocrevus, are FDA-approved for primary progressive MS.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Ocrevus. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Ocrevus as well as the monitoring required for adverse events and long-term efficacy, approval requires Ocrevus to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Multiple Sclerosis (MS), Relapsing Forms.** Approve for 1 year if the patients meets the following criteria (A, B, and C):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The patient has a relapsing form of multiple sclerosis (MS); AND
   - **C)** Ocrevus is prescribed by or in consultation with a physician who specializes in the treatment of multiple sclerosis (MS) and/or a neurologist.

   Dosing. Approve the following dosing regimens:
   - **A)** 300 mg by intravenous infusion, followed 2 weeks later by a second 300 mg intravenous infusion; OR
   - **B)** 600 mg by intravenous infusion once every 6 months.

2. **Multiple Sclerosis, Primary Progressive.** Approve for 1 year if the patients meets the following criteria (A and B):
   A) The patient is ≥ 18 years of age; AND
   B) Ocrevus is prescribed by or in consultation with a physician who specializes in the treatment of MS and/or a neurologist.

   Dosing. Approve the following dosing regimens:
   A) 300 mg by intravenous infusion, followed 2 weeks later by a second 300 mg intravenous infusion; OR
   B) 600 mg by intravenous infusion once every 6 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ocrevus 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. **1. Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS).** 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]), Plegridy® (peginterferon beta-1a injection), Copaxone®/Glatopa® (glatiramer acetate injection), glatiramer acetate injection, Gilenya® (fingolimod tablets), Aubagio® (teriflunomide tablets), Tecfidera® (dimethyl fumarate delayed-release capsules), Tysabri® (natalizumab injection for intravenous use), Mayzent® (siponimod tablets), Mavenclad® (cladribine tablets), Vumerity™ (diroximel fumarate delayed-release capsules), and Lemtrada® (alemtuzumab injection for intravenous use). The concomitant use of Ocrevus with other immune-modulating or immunosuppressive therapies is anticipated to increase the risk of immunosuppression.[1] Ocrevus is not indicated for use in combination with other MS disease-modifying therapies and the safety and efficacy have not been adequately established.

2. 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. Ocrevus® injection for intravenous infusion [prescribing information]. San Francisco, CA: Genentech, Inc (a Member of the Roche Group); July 2019.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated September 2019. Available at: https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf. Accessed on November 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.
5. Gajofatto A, Turatti M, Benedetti MD. Primary progressive multiple sclerosis: current therapeutic strategies and future perspectives. *Expert Rev Neurother*. 2017;17(4):393-406.

HISTORY

Type of Revision	Summary of Changes*	Date Reviewed
New policy	Not applicable.	10/31/2018
Annual revision	The following sections were removed from the Policy: duration of therapy and labs/diagnostics. The following criteria changes were made: 1. **Multiple Sclerosis, Relapsing Forms**: Criteria were revised such that the examples of relapsing forms of multiple sclerosis were removed. 2. **Conditions Not Recommended for Approval:** Regarding Concurrent Use with Other Disease-Modifying Agents for Multiple Sclerosis, the examples of glatiramer acetate injection, Vumerity, Mavenclad and Mayzent added. 3. **Dosing.** The labels of "initial" and "maintenance" were removed.	11/13/2019