

## PRIOR AUTHORIZATION POLICY

**POLICY:** Multiple Sclerosis – Mavenclad® (cladribine tablets – EMD Serono)

**TAC APPROVAL DATE:** 07/17/2019

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### OVERVIEW

Mavenclad, a purine antimetabolite, is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing remitting disease, and active secondary progressive disease, in adults.<sup>1,2</sup> Due to its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug for the treatment of MS.<sup>1</sup> A limitation of use is that Mavenclad is not recommended for use in patients with clinically isolated syndrome because of its safety profile.

### 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.<sup>2</sup> 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, spurred updated disease course descriptions in 2013,<sup>3</sup> as well as in 2017.<sup>4</sup> The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.<sup>2-4</sup> 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.

### Safety

Mavenclad has a Boxed Warning regarding malignancies and the risk of teratogenicity.<sup>1</sup> Mavenclad may increase the risk of malignancy. Also, Mavenclad is a cytotoxic drug. Special handling instructions and disposal procedures should be followed. There are several contraindications associated with the use of Mavenclad including: patients with current malignancy; pregnant women, women and men of reproductive potential who do not plan to use effective contraception during Mavenclad dosing and for 6 months after the last dose in each treatment course; human immunodeficiency virus (HIV); active chronic infection (e.g., hepatitis or tuberculosis); history of

hypersensitivity to cladribine; and women intending to breastfeed on a treatment day in which Mavenclad is administered and for 10 days after the last dose. Warnings and Precautions for Mavenclad include lymphopenia, infections, hematologic toxicity, graft-versus-host disease with blood transfusion, and liver injury.

### **Guidelines**

In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.<sup>2</sup> 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 Mavenclad. All approvals are provided for the duration cited below.

**Automation:** None.

### **RECOMMENDED AUTHORIZATION CRITERIA**

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

#### **FDA-Approved Indications**

1. **Multiple Sclerosis.** Approve for 1 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 agent is prescribed by or in consultation with a neurologist or a physician that specializes in the treatment of multiple sclerosis.

#### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Mavenclad 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. **Clinically Isolated Syndrome.** Mavenclad is not recommended for use in patients with clinically isolated syndrome due to its safety profile.<sup>1</sup>
2. **Non-Relapsing Forms of Multiple Sclerosis (MS).** Note: An example of a non-relapsing form of MS is primary progressive MS. The efficacy of Mavenclad has not been established in patients with MS with non-relapsing forms of the disease.<sup>1</sup>
3. **Current Use with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS).** Note: Examples of disease modifying agents used for multiple sclerosis include Avonex<sup>®</sup> (interferon beta 1a injection [intramuscular]), Betaseron<sup>®</sup>/Extavia<sup>®</sup> (interferon beta-1b injection), Rebif<sup>®</sup> (interferon beta-1a injection [subcutaneous]), Copaxone<sup>®</sup>/Glatopa<sup>®</sup> (glatiramer acetate injection), Plegridy<sup>®</sup> (peginterferon beta-1a injection), Aubagio<sup>®</sup> (teriflunomide tablets), Gilenya<sup>®</sup> (fingolimod tablets), Mayzent<sup>®</sup> (siponimod tablets), Tecfidera<sup>®</sup> (dimethyl fumarate delayed-

release capsules), Ocrevus® (ocrelizumab injection for intravenous use), Tysabri® (natalizumab injection for intravenous infusion), and Lemtrada® (alemtuzumab injection for intravenous use).<sup>2</sup> 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.

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

## REFERENCES

- Mavenclad® tablets [prescribing information]. Rockland, MA: EMD Serono; March 2019.
- 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/MS\\_CDMTPaper\\_062019.pdf](http://ms-coalition.org/wp-content/uploads/2019/06/MS_CDMTPaper_062019.pdf). Accessed on July 7, 2019.
- Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
- 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
New policy	--	04/01/2019
Selected revision	The criterion that required a patient to have tried at least one other disease-modifying agent for multiple sclerosis and to have had an inadequate response to this therapy according to the prescribing physician was removed.	06/12/2019
Early annual revision	The following criteria changes were made. <ol style="list-style-type: none"> <li><b>Multiple Sclerosis:</b> The criterion that required that the patient has a relapsing form of MS was revised to remove the phrase that state “to include relapsing remitting MS or active secondary progressive MS forms”.</li> <li><b>Conditions Not Recommended for Approval:</b> For Patients with Non-Relapsing Forms of MS, the example of primary progressive MS is now listed as a note. Regarding Use with Other Disease-Modifying Agents for MS, the examples are now listed as a note.</li> </ol>	07/17/2019

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