

PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis – Mavenclad Prior Authorization Policy

- Mavenclad® (cladribine tablets – EMD Serono)

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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.¹ 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.¹ 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.²⁻⁴ 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.²⁻⁴ Advances in the understanding of the MS disease process, as well as in MRI technology, spurred updated disease course descriptions in 2013,⁵ as well as in 2017.⁶ The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.²⁻⁶ 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 (or not active) disease, 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 September 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.

Safety

Mavenclad has a Boxed Warning regarding malignancies and the risk of teratogenicity.¹ 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); 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.

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Multiple Sclerosis.** Approve for 1 year if the patient meets ONE of the following (A or B):
 - A) **Initial Therapy.** Approve if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient has a relapsing form of multiple sclerosis; AND
Note: Examples of relapsing forms of multiple sclerosis include relapsing remitting disease and active secondary progressive disease.
 - ii. Patient meets ONE of the following (a, b, or c):
 - a) According to the prescriber, patient has experienced inadequate efficacy or significant intolerance to two disease-modifying agents used for multiple sclerosis; OR
Note: See [Appendix](#) for examples.
 - b) According to the prescriber, patient has experienced inadequate efficacy or significant intolerance to one of Kesimpta (ofatumumab subcutaneous injection), a natalizumab intravenous product (Tysabri, biosimilar), Briumvi (ublituximab-xiiy intravenous infusion), Lemtrada (alemtuzumab intravenous infusion), Ocrevus (ocrelizumab intravenous infusion) or Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq subcutaneous injection); OR
 - c) Patient has received Mavenclad in the past; AND
 - iii. The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; OR
 - B) **Patient is Currently Receiving Mavenclad for ≥ 1 Year.** Approve if the patient meets ALL of the following (i, ii, and iii):
 - i. Patient has a relapsing form of multiple sclerosis; AND
Note: Examples of relapsing forms of multiple sclerosis include relapsing remitting disease and active secondary progressive disease.
 - ii. Patient meets ONE of the following (a or b):
 - a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR

Note: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization or reduced worsening on the Expanded Disability State Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-3 (NEDA-3) or NEDA-4; improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Item MS Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and/or attenuation of brain volume loss.

- b) Patient experienced stabilization, slowed progression, or improvement in at least one symptom such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation; AND
- iii. The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Mavenclad is not recommended in the following situations:

1. **Clinically Isolated Syndrome.** Mavenclad is not recommended for use in patients with clinically isolated syndrome due to its safety profile.¹
2. **Current Use with Other Disease-Modifying Agents Used for Multiple Sclerosis.** These agents are not indicated for use in combination (See [Appendix](#) for examples). Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.
3. **Non-Relapsing Forms of Multiple Sclerosis.** The efficacy of Mavenclad has not been established in patients with multiple sclerosis with non-relapsing forms of the disease.¹
Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis.
4. 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. Mavenclad® tablets [prescribing information]. Rockland, MA: EMD Serono; May 2024.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. September 2019.
3. McGinley MP, Goldschmidt C, Rae-Grant AD. Diagnosis and treatment of multiple sclerosis. A review. *JAMA*. 2021;325(8):765-779.
4. No authors listed. Drugs for multiple sclerosis. *Med Lett Drugs Ther*. 2021;63(1620):42-48.
5. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*. 2014;83:278-286.
6. 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.

APPENDIX