Effective Date **1/1/2024**
Next Review Date… **1/1/2025**
Coverage Policy Number **IP0261**

Cladribine

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for cladribine (**Mavenclad®**).

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Cladribine (Mavenclad) is considered medically necessary when the following is met:

Multiple Sclerosis. Individual meets **ALL** of the following criteria:
A. Documented diagnosis of **ONE** of the following relapsing forms of Multiple Sclerosis:
i. Active Secondary Progressive Multiple Sclerosis (SPMS) (for example, SPMS with a documented relapse)

ii. Relapsing-Remitting Multiple Sclerosis (RRMS)

B. Preferred Product Step Therapy Criteria is met, refer to below table(s)

Employer Group Drug Lists:

Product	Criteria
Mavenclad (cladribine)	**ONE** of the following: 1. Documentation of failure or intolerance to **ONE** of the following: A. dimethyl fumarate (generic for Tecfidera) [may require prior authorization] B. fingolimod (generic for Gilenya) [may require prior authorization] 2. Documented contraindication to **BOTH** of the following: A. dimethyl fumarate (generic for Tecfidera) [may require prior authorization] B. fingolimod (generic for Gilenya) [may require prior authorization] 3. Currently receiving Mavenclad

Individual and Family Plan Preferred Alternatives:

Product	Criteria
Mavenclad (cladribine)	**ONE** of the following: 1. Documentation of failure, contraindication, or intolerance to dimethyl fumarate (generic for Tecfidera) [may require prior authorization] 2. Currently receiving Mavenclad

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of cladribine (Mavenclad) is considered medically necessary for Multiple Sclerosis when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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 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]

Background

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, spurned 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 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 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); 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.

Appendix

Medication	Mode of Administration
Aubagio® (teriflunomide tablets)	Oral

Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Briumvi™ (ublituximab-xiiy intravenous infusion)	Intravenous infusion
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)
Extavia® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Gilenya® (fingolimod capsules, generic)	Oral
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)
Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion
Mavenclad® (cladribine tablets)	Oral
Mayzent® (siponimod tablets)	Oral
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Plegridy® (peginterferon beta-1a subcutaneous or intramuscular injection)	Injection (self-administered)
Ponvory™ (ponesimod tablets)	Oral
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)
Tascenso ODT™ (fingolimod orally disintegrating tablets)	Oral
Tecfidera® (dimethyl fumarate delayed-release capsules, generic)	Oral
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral

References

1. Mavenclad® tablets [prescribing information]. Rockland, MA: EMD Serono; September 2022.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. September 2019. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed on October 22, 2022.
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.