

Drug Policy

Policy:	Cladribine oral dosage forms	Annual Review Date: 02/19/2026 Last Revised Date: 02/19/2026
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OVERVIEW

Cladribine, 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 cladribine 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 cladribine is not recommended for use in patients with clinically isolated syndrome because of its safety profile.

POLICY STATEMENT

This policy involves the use of cladribine. Prior authorization is recommended for pharmacy benefit coverage of cladribine. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with cladribine as well as the monitoring required for adverse events and long-term efficacy, initial approval requires cladribine be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

- 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, c or d):
 - 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.

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- 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-xiyy intravenous infusion), Lemtrada (alemtuzumab intravenous infusion), Ocrevus (ocrelizumab intravenous infusion) or Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq subcutaneous injection); OR
- c) Patient has received cladribine in the past; OR
- d) According to the prescriber, the patient has highly-active or aggressive multiple sclerosis by meeting ONE of the following [(1), (2), (3), or (4)]:
 - (1) Patient has demonstrated rapidly advancing deterioration(s) in physical functioning*; OR
Note: Examples include loss of mobility or lower levels of ambulation and severe changes in strength or coordination.
 - (2) Disabling relapse(s) with suboptimal response to systemic corticosteroids*OR
 - (3) Magnetic resonance imaging (MRI) findings suggest highly active or aggressive multiple sclerosis*
OR
Note: Examples include new, enlarging, or a high burden of T2 lesions or gadolinium-enhancing lesions.
 - (4) Manifestations of multiple sclerosis-related cognitive impairment* 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 cladribine 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.

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Initial Approval/ Extended Approval.

A) *Initial Approval:* 365 days

B) *Extended Approval:* 365 days

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cladribine 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. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Clinically Isolated Syndrome.** Cladribine is not recommended for use in patients with clinically isolated syndrome due to its safety profile.
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 cladribine 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.

*Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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. 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.

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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

Medication	Mode of Administration
Aubagio® (teriflunomide tablets, generic)	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-xiiv intravenous infusion)	Intravenous infusion
Copaxone® (glatiramer acetate subcutaneous injection, generic)	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, generic)	Oral
Mayzent® (siponimod tablets)	Oral
Natalizumab Intravenous Products (Tysabri, biosimilar)	Intravenous infusion
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq subcutaneous injection)	Subcutaneous injection (not self-administered)
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
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral