# Clinical Policy: Cladribine (Mavenclad)

Reference Number: IL.ERX.SPA.335
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Illinois Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Cladribine (Mavenclad®) is a cytotoxic purine antimetabolite.

**FDA Approved Indication(s)**
Mavenclad is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults.

Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS.

Limitation(s) of use: Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Mavenclad is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Multiple Sclerosis** (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Relapsing-remitting MS, and failure of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: dimethyl fumarate (*Tecfidera® brand is preferred*) and any of the following: an interferon-beta agent *(Betaseron® and Rebif® are preferred agents)* or glatiramer *(Copaxone® 20 mg is preferred*);*
      **Prior authorization is required for all disease modifying therapies for MS*
   b. Secondary progressive disease MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Mavenclad is not prescribed concurrently with other disease modifying therapies *(see Appendix D)*;
5. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
6. Dose does not exceed any of the following: 2 tablets per day, 10 tablets per cycle, 2 cycles per course, 1 course per year.

**Approval duration: 12 months - up to 1 course *(2 courses lifetime total)***

**B. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## II. Continued Therapy

**A. Multiple Sclerosis** (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Member has not had an increase in the number of relapses per year compared to baseline;
   b. Member has not had ≥ 2 new MRI-detected lesions;
   c. Member has not had an increase in EDSS score from baseline;
   d. Medical justification supports that member is responding positively to therapy;
3. Mavenclad is not prescribed concurrently with other disease modifying therapies for MS *(see Appendix D)*;
4. Dose does not exceed any of the following: 2 tablets per day, 10 tablets per cycle, 2 cycles per course, 1 course per year.

**Approval duration: 12 months - up to 1 course *(2 courses lifetime total)***

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

**B.** CIS.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

CIS: clinically isolated syndrome
EDSS: expanded disability status scale
FDA: Food and Drug Administration
MS: multiple sclerosis

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Rebif® (interferon beta-1a) | 22 mcg or 44 mcg SC TIW | 44 mcg TIW |
| Betaseron® (interferon beta-1b) | 250 mcg SC QOD | 250 mg QOD |
| glatiramer acetate (Copaxone®) | 20 mg SC QD or 40 mg SC TIW | 20 mg/day or 40 mg TIW |
| dimethyl fumarate (Tecfidera®) | 120 mg PO BID for 7 days, followed by 240 mg PO BID | 480 mg/day |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Patients with current malignancy
  - Pregnant women, and 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
  - HIV infection

- Active chronic infections (e.g., hepatitis or tuberculosis)
- History of hypersensitivity to cladribine
- Women intending to breastfeed on a Mavenclad treatment day and for 10 days after the last dose

- Boxed warning(s):
  - Malignancies
  - Risk of teratogenicity

*Appendix D: General Information*

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ofatumumab (Kesimpta®).

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| RRMS and SPMS | *DOSAGE ADMINISTRATION OVERVIEW*<br>• Cumulative dosage of 3.5 mg/kg PO divided into 2 yearly treatment COURSES (1.75 mg/kg per treatment course).<br>• Each treatment COURSE is divided into 2 treatment CYCLES.<br>• See dosage chart in package insert and below for number of tablets per CYCLE based on body weight in kg.<br>• Administer the CYCLE dosage as 1 or 2 tablets once daily over 4 or 5 consecutive days. Do not administer more than 2 tablets daily. Separate administration from any other oral drug by at least 3 hours.<br>• Following the administration of 2 treatment COURSES, do not administer additional Mavenclad treatment during the next 2 years. Treatment during these 2 years may further increase the risk of malignancy. The safety and efficacy of reinitiating Mavenclad more than 2 years after completing 2 treatment courses has not been studied.<br>*COURSES AND CYCLES*<br>• COURSE ONE (year one)<br>  ○ First CYCLE: start any time<br>  ○ Second CYCLE: start 23 to 27 days after last dose of first cycle.<br>• COURSE TWO (year two)<br>  ○ First CYCLE: start at least 43 weeks after last dose of first course's second cycle.<br>  ○ Second CYCLE: start 23 to 27 days after the last dose of second course's first cycle.<br>*WEIGHT RANGE (KG): # OF TABLETS - FIRST AND SECOND CYCLES*<br>• 40* to less than 50 kg<br>  ○ 40 mg (4 tablets) (cycles 1 and 2)<br>• 50 to less than 60 kg<br>  ○ 50 mg (5 tablets) (cycles 1 and 2)<br>• 60 to less than 70 kg<br>  ○ 60 mg (6 tablets) (cycles 1 and 2) | 2 tablets/day,<br>10 tablets/cycle,<br>2 cycles/course/year,<br>2 courses total |

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| | • 70 to less than 80 kg<br>  ○ 70 mg (7 tablets) (cycles 1 and 2)<br>• 80 to less than 90 kg<br>  ○ 80 mg (8 tablets) (cycle 1)<br>  ○ 70 mg (7 tablets) (cycle 2)<br>• 90 to less than 100 kg<br>  ○ 90 mg (9 tablets) (cycle 1)<br>  ○ 80 mg (8 tablets) (cycle 2)<br>• 100 to less than 110 kg<br>  ○ 100 mg (10 tablets) (cycle 1)<br>  ○ 90 mg (9 tablets) (cycle 2)<br>• 110 kg and above<br>  ○ 100 mg (10 tablets) (cycles 1 and 2)<br>*The use of Mavenclad in patients weighing less than 40 kg has not been investigated. | |

## VI. Product Availability

Tablet: 10 mg

## VII. References

1. Mavenclad Prescribing Information. Rockland, MD: EMD Serono, Inc.; April 2019. Available at https://www.mavenclad.com. Accessed February 8, 2021.
2. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology, 2018;90:777-788. doi:10.1212/WNL.0000000000005347.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created. | 04.19.21 | 05.21 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.