Clinical Policy: Cladribine (Mavenclad)

Reference Number: CP.PHAR.422
Effective Date: 09.01.19
Last Review Date: 05.25
Line of Business: Commercial, HIM, 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.

It is the policy of health plans affiliated with Centene Corporation® 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 all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (i, ii, iii, and iv):*
      i. **Dimethyl fumarate** (generic Tecfidera®);
      ii. **Teriflunomide** (generic Aubagio®);
      iii. **Fingolimod** (Gilenya®);
      iv. An **interferon-beta agent** (Avonex®, Betaseron®/Extavia®†, Rebif®, or Plegridy®) or **glatiramer** (Copaxone®, Glatopa®);

      **Prior authorization may be required for all disease modifying therapies for MS*
      †Betaseron is the preferred interferon beta-1b product for the Commercial and HIM lines of business
   b. Secondary progressive 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 for MS *(see Appendix D)*;
5. Dose does not exceed any of the following:
   a. 2 tablets per day;
   b. 10 tablets per cycle;
   c. 2 cycles per course;
   d. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations *(refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. 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:
   a. 2 tablets per day;
   b. 10 tablets per cycle;
   c. 2 cycles per course;
   d. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. CIS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIS: clinically isolated syndrome
MS: multiple sclerosis
FDA: Food and Drug Administration

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
teriflunomide (Aubagio®)	7 mg or 14 mg PO QD	14 mg/day
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
fingolimod (Gilenya®)	0.5 mg PO QD	0.5 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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®, Tascenso ODT™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®, and biosimilar Tyruko®), ocrelizumab (Ocrevus®), ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo™), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ponesimod (Ponvory™), ublituximab-xiiy (Briumvi™), and ofatumumab (Kesimpta®).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Relapsing MS	*DOSAGE ADMINISTRATION OVERVIEW* • Cumulative dosage of 3.5 mg/kg PO divided into 2 yearly treatment COURSES (1.75 mg/kg per treatment course). • Each treatment COURSE is divided into 2 treatment CYCLES. • See dosage chart in package insert and below for number of tablets per CYCLE based on body weight in kg. • Administer the CYCLE dosage as 1 or 2 tablets once daily over 4 or 5 consecutive days. Do not	2 tablets/day, 10 tablets/cycle, 2 cycles/course/year, 2 courses total

Indication	Dosing Regimen	Maximum Dose
	administer more than 2 tablets daily. Separate administration from any other oral drug by at least 3 hours. • 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. *COURSES AND CYCLES* • COURSE ONE (year one) o First CYCLE: start any time. o Second CYCLE: start 23 to 27 days after last dose of first cycle. • COURSE TWO (year two) o First CYCLE: start at least 43 weeks after last dose of first course's second cycle. o Second CYCLE: start 23 to 27 days after the last dose of second course's first cycle. *WEIGHT RANGE (KG): # OF TABLETS - FIRST AND SECOND CYCLES* • 40* to less than 50 kg o 40 mg (4 tablets) (cycles 1 and 2) • 50 to less than 60 kg o 50 mg (5 tablets) (cycles 1 and 2) • 60 to less than 70 kg o 60 mg (6 tablets) (cycles 1 and 2) • 70 to less than 80 kg o 70 mg (7 tablets) (cycles 1 and 2) • 80 to less than 90 kg o 80 mg (8 tablets) (cycle 1) o 70 mg (7 tablets) (cycle 2) • 90 to less than 100 kg o 90 mg (9 tablets) (cycle 1) o 80 mg (8 tablets) (cycle 2) • 100 to less than 110 kg o 100 mg (10 tablets) (cycle 1) o 90 mg (9 tablets) (cycle 2) • 110 kg and above o 100 mg (10 tablets) (cycles 1 and 2) *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.; May 2024. Available at: https://www.mavenclad.com. Accessed January 24, 2025.
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. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/898. Reaffirmed on October 19, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	02.08.21	05.21
2Q 2022 annual review: no significant changes; added legacy WellCare line of business (WCG.CP.PHAR.422 to be retired); clarified interferon-beta product redirections for each line of business per SDC; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.23.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.31.23	05.23
Per August SDC, added generic references to Aubagio and Gilenya redirections.	08.22.23	11.23
2Q 2024 annual review: no significant changes; references reviewed and updated.	01.30.24	05.24
2Q 2025 annual review: per competitor analysis, removed requirements for documentation of baseline relapses/expanded disability status score and specific measures of positive response; per SDC, removed notation that Extavia is the preferred interferon beta-1b product for the Medicaid line of business as it is no longer available on market; references reviewed and updated.	02.12.25	05.25

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.