Clinical Policy: Cladribine (Mavenclad)

Reference Number: CP.CPA.342
Effective Date: 05.14.19
Last Review Date: 08.19
Line of Business: Commercial

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 (RRMS), and failure of two of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: Aubagio®, Tecfidera®, Gilenya™, Avonex®, Betaseron®, Plegridy®, glatiramer®, Copaxone®, Glatopa®, or Rebif®;*
      **Prior authorization is required for all disease modifying therapies for MS.*
   b. Secondary progressive MS (SPMS);
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: 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Multiple Sclerosis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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: 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

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 or evidence of coverage documents.

B. CIS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIS: clinically isolated syndrome
FDA: Food and Drug Administration
MS: multiple sclerosis
RRMS: relapsing-remitting multiple sclerosis
SPMS: secondary progressive 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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
Aubagio® (teriflunomide)	7 mg or 14 mg PO QD	14 mg/day
Gilenya™ (fingolimod)	0.5 mg PO QD	0.5 mg/day
Tecfidera® (dimethyl fumarate)	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: Disease-Modifying Therapies for Multiple Sclerosis
Glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus™), siponimod (Mayzent®), Zinbryta® (daclizumab).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RRMS and SPMS	*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.	2 tablets/day, 10 tablets/cycle, 2 cycles/course/year, 2 courses total

Indication	Dosing Regimen	Maximum Dose
	• 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 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) Complete pre-treatment assessment. o First CYCLE: start any time o Second CYCLE: start 23 to 27 days after last dose of first cycle. • COURSE TWO (year two) Complete pre-treatment assessment. 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)	

Indication	Dosing Regimen	Maximum Dose

	• 100 to less than 110 kg
	  ○ 100 mg (10 tablets) (cycle 1)
	  ○ 90 mg (9 tablets) (cycle 2)
	• 110 kg and above
	  ○ 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.; March 2019. Available at https://www.emdserono.com/content/dam/web/corporate/non-images/country-specifics/us/pi/mavenclad-pi.pdf. Accessed April 15, 2019.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/.
3. 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.
4. Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review 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;90:789-800. doi:10.1212/WNL.0000000000005345.
5. Costello K, Kalb R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. Revised September 2018. Available at http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed April 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.14.19	08.19

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.

©2019 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.