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Section	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 19, 2019
Subject:	Mavenclad	**Page:**	1 of 7

Last Review Date: December 13, 2024

Mavenclad

Description

Mavenclad (cladribine)

Background
Mavenclad (cladribine) is a purine antimetabolite that is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. The exact mechanism of action in Multiple Sclerosis (MS) is unknown. It is thought that the cytotoxic effect and reduction in the number of circulating lymphocytes may result in a reduction of the damaging immune response seen in MS (1).

Regulatory Status
FDA-approved indication: Mavenclad is a purine antimetabolite indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults (1).

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 (1).

Limitations of Use: Mavenclad is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile (1).

Mavenclad has a boxed warning that it may increase the risk of malignancy. Mavenclad is contraindicated in patients with current malignancy. In patients with prior malignancy or with

increased risk of malignancy, they should be evaluated for the benefits and risks of the use of Mavenclad on an individual patient basis (1).

Mavenclad also carries a boxed warning regarding the risk of teratogenicity. Mavenclad is contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the potential for fetal harm (1).

Mavenclad is contraindicated in patients with: (1)

- 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)
- Women intending to breastfeed on a Mavenclad treatment day and for 10 days after the last dose

Before each Mavenclad treatment course, a complete blood count (CBC) with differential including lymphocyte count should be obtained. Lymphocytes must be within normal limits before initiating the first treatment course and lymphocytes must be at least 800 cells per microliter before initiating the second treatment course (1).

Vaccination of patients who are antibody-negative for varicella zoster virus is recommended prior to Mavenclad initiation (1).

A baseline (within 3 months) magnetic resonance imaging should be obtained prior to the first treatment course because of the risk of progressive multifocal leukoencephalopathy (PML) (1).

Mavenclad has not been administered concomitantly with antineoplastic, immunosuppressive or immune modulating therapies used for treatment of MS. Concomitant use of Mavenclad with any of these therapies would be expected to increase the risk of immunosuppression (1).

Due to the risk of liver injury, serum aminotransferase, alkaline phosphatase, and total bilirubin levels should be obtained (1).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting Mavenclad, because of a risk of

active vaccine infection. Avoid vaccination with live-attenuated or live vaccines during and after Mavenclad treatment while the patient's white blood cell counts are not within normal limits (1-2).

The recommended cumulative dosage of Mavenclad is 3.5 mg per kg body weight administered orally and divided into 2 yearly treatment courses (1.75 mg per kg per treatment course). 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 have not been studied (1).

The safety and effectiveness of Mavenclad in pediatric patients less than 18 years of age have not been established (1).

Related policies
Acthar Gel, Ampyra, Aubagio, Gilenya, Kesimpta, Lemtrada, Mayzent, MS Injectables, Ocrevus, Ponvory, Tecfidera, Tysabri, Zeposia

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Mavenclad may be considered **medically necessary** if the conditions indicated below are met.

Mavenclad may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including relapsing-remitting disease and active secondary progressive disease

AND ALL of the following:

1. Prescriber has reviewed baseline liver function tests (LFTs) and complete blood count (CBC) with differential including lymphocyte count
2. Female of reproductive potential: patient is not pregnant
3. Prescriber will advise females and males of reproductive potential to use effective contraception during Mavenclad dosing and for 6 months after the last dose in each treatment course
4. Prescriber agrees to delay the second treatment course until lymphocytes are greater than or equal to 800 cells per microliter
5. Patient **MUST** have tried **TWO** of the preferred MS medications (see Appendix 1) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

AND NONE of the following:

1. Diagnosis of clinically isolated syndrome (CIS)
2. Presence of current malignancy
3. HIV infection or active chronic infection (e.g., hepatitis or tuberculosis)
4. Concurrent use with other MS disease modifying agents
5. Given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

PA limit is 2 cycles per year, for a total of 4 cycles for 2 years.

Quantity

Dose of MAVENCLAD per Cycle by Patient Weight in Each Treatment Course	
Weight Range	**Dose in mg (Number of 10 mg Tablets)**

kg	First Cycle	Second Cycle	Total for 1 year
40* to less than 50	40 mg (4 tablets)	40 mg (4 tablets)	8 tablets
50 to less than 60	50 mg (5 tablets)	50 mg (5 tablets)	10 tablets
60 to less than 70	60 mg (6 tablets)	60 mg (6 tablets)	12 tablets
70 to less than 80	70 mg (7 tablets)	70 mg (7 tablets)	14 tablets
80 to less than 90	80 mg (8 tablets)	70 mg (7 tablets)	15 tablets
90 to less than 100	90 mg (9 tablets)	80 mg (8 tablets)	17 tablets
100 to less than 110	100 mg (10 tablets)	90 mg (9 tablets)	19 tablets
110 and above	100 mg (10 tablets)	100 mg (10 tablets)	20 tablets

*The use of MAVENCLAD in patients weighing less than 40 kg has not been investigated.

Duration 2 years

Prior – Approval *Renewal* Limits

None

Rationale

Summary

Mavenclad (cladribine) is a purine antimetabolite that is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. Although the exact mechanism of action in Multiple Sclerosis (MS) is unknown, it is thought that through this cytotoxic effect and by reducing the number of lymphocytes that are circulating in the bloodstream, this results in a reduction of the damaging immune response seen in MS (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Mavenclad while maintaining optimal therapeutic outcomes.

References

1. Mavenclad [package insert]. Rockland, MA: EMD Serono Inc.; May 2024.
2. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. Neurological Bulletin. 2010;2(1):17-21.

Policy History

Date	Action

April 2019	Addition to PA
June 2019	Annual review. Added requirement for prescriber to delay second treatment course until lymphocytes ≥ 800
September 2019	Annual review. Revised summary section and regulatory status per SME
March 2020	Annual review
September 2020	Annual review
December 2020	Annual review. Replaced the requirement that patient must t/f an alternate drug for MS with “patient must t/f generic Tecfidera: dimethyl fumarate and one of the other preferred MS medications”. Added Appendix 1 with a list of the preferred medications
June 2021	Annual review
October 2021	Added notation that PA limit is 2 cycles per year, for a total of 4 cycles for 2 years. Added column to the chart showing the total number of tablets approved per year
December 2021	Annual review
June 2022	Annual review
December 2022	Annual review and reference update. Changed policy number to 5.60.035.
January 2023	Per FEP, revised Medex requirement to t/f two preferred MS medications
March 2023	Annual review
June 2023	Annual review
December 2023	Annual review
June 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.

Appendix 1 - List of Preferred Multiple Sclerosis (MS) Medications

Medication Name	Route of Administration
dimethyl fumarate (generic Tecfidera)	Oral**
fingolimod (generic Gilenya)	Oral**
Mayzent	Oral**
teriflunomide (generic Aubagio)	Oral**
Zeposia	Oral**

****** indicates separate criteria will need to be met

Medication Name	Route of Administration
Avonex	Injectable
Betaseron	Injectable
glatiramer acetate (generic Copaxone)	Injectable
Glatopa	Injectable
Plegridy	Injectable
Rebif	Injectable