HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MAVENCLAD safely and effectively. See full prescribing information for MAVENCLAD.

MAVENCLAD® (cladribine) tablets, for oral use
Initial U.S. Approval: 1993

WARNING: MALIGNANCIES and RISK OF TERATOGENICITY
See full prescribing information for complete boxed warning.

- **Malignancies**

MAVENCLAD may increase the risk of malignancy. MAVENCLAD is contraindicated in patients with current malignancy; evaluate the benefits and risks on an individual basis for patients with prior or increased risk of malignancy. (5.1)

- **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 risk of fetal harm. (5.2)

----------RECENT MAJOR CHANGES----------

Dosage and Administration (2.1)	9/2022
Warnings and Precautions (5.4)	9/2022

----------INDICATIONS AND USAGE----------

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. 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 *[see Warnings and Precautions (5)]*. (1)

Limitations of Use

MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile *[see Warnings and Precautions (5)]*. (1)

----------DOSAGE AND ADMINISTRATION----------

- Assessments are required prior to starting each MAVENCLAD treatment course. (2.1)
- Cumulative dosage of 3.5 mg/kg administered orally and divided into 2 treatment courses (1.75 mg/kg per treatment course). Each treatment course is divided into 2 treatment cycles. (2.2)
- MAVENCLAD is a cytotoxic drug. (2.4)
- Separate administration from any other oral drug by at least 3 hours. (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 10 mg (3)

----------CONTRAINDICATIONS----------

- Patients with current malignancy. (4)
- 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. (4, 8.3)
- HIV infection. (4)
- Active chronic infections (e.g., hepatitis or tuberculosis). (4)
- History of hypersensitivity to cladribine. (4, 5.8)
- Women intending to breastfeed on a MAVENCLAD treatment day and for 10 days after the last dose. (4, 8.2)

----------WARNINGS AND PRECAUTIONS----------

- Lymphopenia: Monitor lymphocyte counts before, during and after treatment. (5.3)
- Infections: Screen patients for latent infections; consider delaying treatment until infection is fully controlled. Vaccination of patients seronegative to varicella zoster virus (VZV) is recommended prior to treatment. Vaccination of patients seropositive to VZV with zoster vaccine recombinant, adjuvanted, is recommended prior to or during treatment. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections. (5.4)
- Hematologic toxicity: Monitor complete blood count before, during and after treatment. (5.5)
- Graft-versus-host-disease with blood transfusion: Irradiation of cellular blood components is recommended. (5.6)
- Liver injury: Obtain tests prior to treatment. Discontinue if clinically significant injury is suspected. (5.7)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence > 20%) are upper respiratory tract infection, headache, and lymphopenia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact EMD Serono at 1-800-283-8088 ext. 5563 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Immunosuppressive drugs: Consider overlapping effects on immune system, when used sequentially. Concomitant use not recommended. (7.1)
- Hematotoxic drugs: Monitor patients for additive effects on the hematological profile. (7.3)
- Antiviral and antiretroviral drugs: Avoid concomitant use. (7.4)
- BCRP or ENT/CNT inhibitors: May alter bioavailability of cladribine. Avoid concomitant use. (7.5)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 9/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: MALIGNANCIES AND RISK OF TERATOGENICITY

- **Malignancies**

Treatment with MAVENCLAD 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, evaluate the benefits and risks of the use of MAVENCLAD on an individual patient basis. Follow standard cancer screening guidelines in patients treated with MAVENCLAD *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

- **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. Malformations and embryolethality occurred in animals. Exclude pregnancy before the start of treatment with MAVENCLAD in females of reproductive potential. 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. Stop MAVENCLAD if the patient becomes pregnant *[see Contraindications (4), Warnings and Precautions (5.2), and Use in Specific Populations (8.1, 8.3)]*.

1 INDICATIONS AND USAGE

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 *[see Warnings and Precautions (5)]*.

Limitations of Use

MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile *[see Warnings and Precautions (5)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Assessments Prior to Starting Each MAVENCLAD Treatment Course

Cancer Screening

Follow standard cancer screening guidelines because of the risk of malignancies *[see Boxed Warning and Warnings and Precautions (5.1)]*.

Pregnancy

Exclude pregnancy prior to treatment with MAVENCLAD in females of reproductive potential *[see Contraindications (4), Warnings and Precautions (5.2), and Use in Specific Populations (8.1, 8.3)]*.

Complete Blood Count (CBC)

Obtain a CBC with differential including lymphocyte count *[see Dosage and Administration (2.5) and Warnings and Precautions (5.3)]*. Lymphocytes must be:

- within normal limits before initiating the first treatment course
- at least 800 cells per microliter before initiating the second treatment course

If necessary, delay the second treatment course for up to 6 months to allow for recovery of lymphocytes to at least 800 cells per microliter. If this recovery takes more than 6 months, the patient should not receive further treatment with MAVENCLAD.

Infections *[see Warnings and Precautions (5.4)]*

- Exclude HIV infection.
- Perform tuberculosis screening.
- Screen for hepatitis B and C.
- Evaluate for acute infection. Consider a delay in MAVENCLAD treatment until any acute infection is fully controlled.
- Vaccination of patients who are seronegative for VZV is recommended prior to initiation of MAVENCLAD.
- Vaccination of patients who are seropositive to VZV is recommended with zoster vaccine recombinant, adjuvanted. Patients may be administered zoster vaccine recombinant, adjuvanted at any time prior to or during the year 1 or year 2 course of MAVENCLAD treatment. These patients may also be administered the vaccine if their lymphocyte counts are ≤ 500 cells per microliter.
- Administer all immunizations (except as noted for VZV) according to immunization guidelines prior to starting MAVENCLAD. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting MAVENCLAD.
- Obtain a baseline (within 3 months) magnetic resonance imaging prior to the first treatment course because of the risk of progressive multifocal leukoencephalopathy (PML).

Liver Injury

Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels *[see Warnings and Precautions (5.7)]*.

2.2 Recommended Dosage

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) (see Table 1). Each treatment course is divided into 2 treatment cycles:

Administration of First Treatment Course

- First Course/First Cycle: start any time.
- First Course/Second Cycle: administer 23 to 27 days after the last dose of First Course/First Cycle.

Administration of Second Treatment Course

- Second Course/First Cycle: administer at least 43 weeks after the last dose of First Course/Second Cycle.
- Second Course/Second Cycle: administer 23 to 27 days after the last dose of Second Course/First Cycle.

Table 1 Dose of MAVENCLAD per Cycle by Patient Weight in Each Treatment Course

Weight Range	**Dose in mg (Number of 10 mg Tablets) per Cycle**	
kg	First Cycle	Second Cycle
40* to less than 50	40 mg (4 tablets)	40 mg (4 tablets)
50 to less than 60	50 mg (5 tablets)	50 mg (5 tablets)
60 to less than 70	60 mg (6 tablets)	60 mg (6 tablets)
70 to less than 80	70 mg (7 tablets)	70 mg (7 tablets)
80 to less than 90	80 mg (8 tablets)	70 mg (7 tablets)
90 to less than 100	90 mg (9 tablets)	80 mg (8 tablets)
100 to less than 110	100 mg (10 tablets)	90 mg (9 tablets)
110 and above	100 mg (10 tablets)	100 mg (10 tablets)

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

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