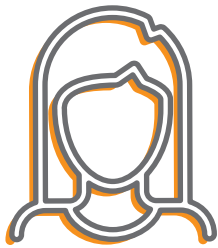


A female patient who cannot adhere to her previous oral treatment due to side effects^{1*}



40-year-old female



Discontinued an oral therapy due to side effects



JCV positive

Contributed by an MS Specialist

Duke University School of Medicine, Durham, North Carolina

*This case is based on a single patient and may not be fully representative of the overall patient population.

To protect patient privacy, patient details have been modified.

**EMD
SERONO**

A female MS patient who was unable to tolerate existing treatment¹

Disease and treatment history

- Diagnosed with relapsing MS in 2012; started an injectable DMT and continued for 1 year before discontinuing due to injection-site reactions
- Started a daily oral therapy in 2013; continued on and off until 2017; discontinued due to side effects
- No DMT since late 2017

Recent disease activity (as of May 2019)

- Relapses: no discernible relapse
- MRI: several areas of T2 hyperintensity seen in both brain and cervical cord without abnormal enhancement; stable from 2017–2019
- Disability progression: gradual progression of right upper extremity symptoms (right-hand dominant); EDSS score not available

Treatment plan

- Treatment concerns: JCV positive; family history of cardiovascular problems
- Completed pre-screening assessments
- Started treatment with MAVENCLAD in July 2019

Treatment follow-up and outcomes

- Routine labs at next visit (month 3)
- Follow-up MRI of brain and cervical spine (month 7)

Factors the healthcare provider considered

- Patient unable to tolerate multiple DMTs
- Patient's desire to be on active treatment again due to lesion burden and distribution, and wants to start an oral DMT
- JCV status and cardiovascular history

DMT: disease-modifying therapy; EDSS: Expanded Disability Status Scale; JCV: John Cunningham virus.

INDICATION

MAVENCLAD® (cladribine) tablets 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.

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

IMPORTANT SAFETY INFORMATION

WARNING: MALIGNANCIES and RISK OF TERATOGENICITY

- **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**
- **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**

CONTRAINDICATIONS

- Patients with current malignancy.
- Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during and for 6 months after the last dose in each treatment course. May cause fetal harm.
- Patients with human immunodeficiency virus (HIV).
- Patients with active chronic infections (e.g., hepatitis or tuberculosis).
- Patients with a history of hypersensitivity to cladribine.
- Women intending to breastfeed while taking MAVENCLAD tablets and for 10 days after the last dose.

WARNINGS AND PRECAUTIONS

- **Malignancies:** Treatment with MAVENCLAD may increase the risk of malignancy. After the completion of 2 treatment courses, do not administer additional MAVENCLAD treatment during the next 2 years. The risk of malignancy with reinitiating MAVENCLAD more than 2 years after the completion of 2 treatment courses has not been studied. Follow standard cancer screening guidelines in patients treated with MAVENCLAD.
- **Risk of Teratogenicity:** MAVENCLAD may cause fetal harm when administered to pregnant women. In females of reproductive potential, exclude pregnancy before initiation of each treatment course of MAVENCLAD and prevent by the use of effective contraception during MAVENCLAD dosing and for at least 6 months after the last dose of each treatment course. Women who become pregnant during treatment with MAVENCLAD should discontinue treatment.
- **Lymphopenia:** MAVENCLAD causes a dose-dependent reduction in lymphocyte count. In clinical studies, 87% of MAVENCLAD-treated patients experienced lymphopenia. The lowest absolute lymphocyte counts occurred approximately 2 to 3 months after the start of each treatment course and were lower with each additional treatment course. Concomitant use of MAVENCLAD with hematotoxic drugs may increase the risk of adverse reactions because of the additive hematological effects. Monitor lymphocyte counts before and during treatment, periodically thereafter, and when clinically indicated.

Assessments prior to starting each MAVENCLAD treatment course²

Complete blood count (CBC)

Obtain a CBC with differential including lymphocyte count. Lymphocytes must be:

- ✓ within normal limits before initiating the first treatment course
- ✓ at least 800 cells/ μ L 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/ μ L. If this recovery takes more than 6 months, the patient should not receive further treatment with MAVENCLAD.

Infections

- ✓ Exclude HIV infection
- ✓ Perform tuberculosis screening, exclude active chronic infection
- ✓ Screen for hepatitis B and C, exclude active chronic infection
- ✓ Evaluate for acute infection. Consider a delay in MAVENCLAD treatment until any acute infection is fully controlled
- ✓ Vaccination of patients who are antibody-negative for varicella zoster virus is recommended prior to initiation of MAVENCLAD
- ✓ Administer all immunizations 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) MRI prior to the first treatment course because of the risk of progressive multifocal leukoencephalopathy (PML)

Cancer screening

Exclude current malignancy. In patients with a prior malignancy, evaluate the benefits and risks from an individual patient basis. Follow standard cancer screening guidelines.

Pregnancy

Exclude pregnancy prior to treatment with MAVENCLAD in females of reproductive potential.

- ✓ Females of reproductive potential should prevent pregnancy by use of effective contraception during MAVENCLAD dosing and for at least 6 months after the last dose in each treatment course
- ✓ Women using systemically acting hormonal contraceptives should add a barrier method during MAVENCLAD dosing and for at least 4 weeks after the last dose in each treatment course
- ✓ Male patients of reproductive potential should take precautions to prevent pregnancy of their partner during MAVENCLAD dosing and for at least 6 months after the last dose in each treatment course

Breastfeeding

Inform women that they cannot breastfeed on a MAVENCLAD treatment day and for 10 days after the last dose.

Liver injury

Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels.

Drug interactions

Initiation of MAVENCLAD in patients currently receiving immunosuppressive or myelosuppressive therapy is not recommended.

During each treatment course²

Obtain lymphocyte count at 2 and 6 months after start of treatment in each treatment course

- ✓ If the lymphocyte count at month 2 is below 200 cells/ μ L, monitor monthly until month 6. Hold MAVENCLAD therapy if the lymphocyte count is below 200 cells/ μ L
 - Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells/ μ L
- ✓ Monitor periodically thereafter and when clinically indicated

IMPORTANT SAFETY INFORMATION (con't)

WARNINGS AND PRECAUTIONS

- **Infections:** MAVENCLAD can reduce the body's immune defense and may increase the likelihood of infections. Infections occurred in 49% of MAVENCLAD-treated patients compared to 44% of patients treated with placebo in clinical studies. The most frequent serious infections included herpes zoster and pyelonephritis. Single fatal cases of tuberculosis and fulminant hepatitis B were reported in the clinical program. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting MAVENCLAD. Screen patients for latent infections; consider delaying treatment until infection is fully controlled. Vaccinate patients antibody-negative to varicella zoster virus prior to treatment. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections. In patients treated with parenteral cladribine for oncologic indications, cases of progressive multifocal leukoencephalopathy (PML) have been reported. No case of PML has been reported in clinical studies of cladribine in patients with MS.
- **Hematologic Toxicity:** In addition to lymphopenia, decreases in other blood cells and hematological parameters have been reported with MAVENCLAD in clinical studies. In general, mild to moderate decreases in neutrophil counts, hemoglobin levels, and platelet counts were observed. Severe decreases in neutrophil counts were observed in 3.6% of MAVENCLAD-treated patients, compared to 2.8% of placebo patients. Obtain complete blood count (CBC) with differential including lymphocyte count before and during treatment, periodically thereafter, and when clinically indicated.
- **Risk of Graft-versus-Host Disease With Blood Transfusions:** Transfusion-associated graft-versus-host disease has been observed rarely after transfusion of nonirradiated blood in patients treated with cladribine for non-MS treatment indications.
- **Liver Injury:** In clinical studies, 0.3% of MAVENCLAD-treated patients had liver injury (serious or causing treatment discontinuation) compared to 0 placebo patients. Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment. Discontinue if clinically significant injury is suspected.
- **Hypersensitivity:** In clinical studies, 11% of MAVENCLAD-treated patients had hypersensitivity reactions, compared to 7% of placebo patients. Hypersensitivity reactions that were serious and/or led to discontinuation of MAVENCLAD, occurred in 0.5% of MAVENCLAD-treated patients, compared to 0.1% of placebo patients. If a hypersensitivity reaction is suspected, discontinue MAVENCLAD therapy. Do not use MAVENCLAD in patients with a history of hypersensitivity to cladribine.
- **Cardiac Failure:** In clinical studies, one MAVENCLAD-treated patient experienced life-threatening acute cardiac failure with myocarditis, which improved after approximately one week. Cases of cardiac failure have also been reported with parenteral cladribine used for treatment indications other than multiple sclerosis.

Adverse Reactions: The most common adverse reactions with an incidence of >20% for MAVENCLAD are upper respiratory tract infection, headache, and lymphopenia.

Drug Interactions/Concomitant Medication: Concomitant use of MAVENCLAD with immunosuppressive or myelosuppressive drugs and some immunomodulatory drugs (e.g., interferon beta) is not recommended and may increase the risk of adverse reactions. Acute short-term therapy with corticosteroids can be administered.

Avoid concomitant use of certain antiviral and antiretroviral drugs. Avoid concomitant use of BCRP or ENT/CNT inhibitors as they may alter bioavailability of MAVENCLAD.

Use in Specific Populations: Studies have not been performed in pediatric or elderly patients, pregnant or breastfeeding women. Use in patients with moderate to severe renal or hepatic impairment is not recommended.

Please see the accompanying full Prescribing Information, including **boxed WARNING** for additional information.

REFERENCES

1. Data on File. EMD Serono, Inc.
2. MAVENCLAD [prescribing information]. Rockland, MA: EMD Serono, Inc; 2019.

What would you consider in an MS treatment for a patient who has difficulty tolerating alternate treatments?

In this real-world patient case study, an MS Specialist evaluated the following issues when choosing a treatment for this patient¹:



Is it effective in my patient's type of MS?



What are the safety/tolerability considerations for use in this patient?



Is the dosing schedule appropriate for my patient?



What are the patient's risk factors?

Please see accompanying full Prescribing Information, including **boxed WARNING**.