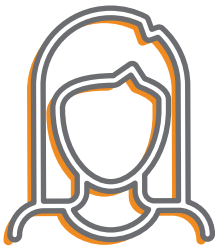
REAL-WORLD PATIENT CASE STUDY

A working parent who is looking to switch her DMT due to previous intolerance to infusion and oral DMTs[1]*



- 40-year-old female
- Working mother of two
- Previous intolerance to infusion and oral DMTs

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

DMT: disease-modifying therapy.

To protect patient privacy, patient details have been modified.

REAL-WORLD PATIENT CASE STUDY:

A working mother of two who switched due to previous intolerance to infusion and oral DMTs[1]

Disease and treatment history

- 2011: Diagnosed with RRMS while pregnant, presented with leg tingling and numbness, and postponed starting DMT until after pregnancy
- 2012: After giving birth, experienced a relapse with optic neuritis and initiated first infusion DMT, which she continued for 3 years
- 2015: Discontinued infusion DMT due to second pregnancy
- 2011–2016: Patient had multiple brain lesions, cervical and thoracic spine lesions consistent with long-standing disease with mild brain atrophy
- 2016: After giving birth to second child, started on an oral DMT but discontinued after 6 months due to intolerable side effects. MRI scans showed 4 new enhancing brain lesions
- 2017: Transitioned to another oral DMT but discontinued after 8 months and remained treatment free for 5 months
- 2018: Relapsed with 2 new T spine lesions

Recent disease activity

- 2018: Experienced chest tightness and leg weakness, and started on another infusion DMT
- February 2020: Received treatment with infusion DMT
- Patient experiencing cognitive disability and fatigue, urinary frequency and urgency

Treatment plan

- Fall 2020: EDSS = 3.0. Completed pre-screening assessments and informed of the risk of teratogenicity and counseled regarding birth control requirements. Started treatment with MAVENCLAD

Treatment follow-up and outcomes

- Patient has reported satisfaction with dosing regimen after year 1
- Follow-up blood monitoring scheduled for 3, 7, and 11 months

Factors the healthcare provider considered

- Working parent who appreciates the convenient dosing but understands that monitoring and doctor visits are part of her treatment plan
- Patient's intolerance of previous infusion and oral DMTs

DMT: disease-modifying therapy; EDSS: Expanded Disability Status Scale; RRMS: relapsing-remitting multiple sclerosis.

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. In clinical studies, patients who received additional MAVENCLAD treatment within 2 years after the first 2 treatment courses had an increased incidence of malignancy. 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.

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

MAVENCLAD®
(cladribine) tablets 10 mg

Assessments prior to starting each MAVENCLAD treatment course[3]

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/μL 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/μL. 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 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
- 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 breastfeeding is not advised on MAVENCLAD treatment days 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.

Administer all immunizations according to immunization guidelines prior to starting MAVENCLAD

Administer live-attenuated vaccines 4 to 6 weeks prior to starting MAVENCLAD because of the risk of active vaccine infection. Vaccination of patients who are antibody-negative for varicella zoster virus is recommended prior to initiation of MAVENCLAD. 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.

During each treatment course[1]

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

There are other important considerations when starting and continuing treatment with MAVENCLAD. Please refer to the full Prescribing Information, including boxed WARNING, for more information.

IMPORTANT SAFETY INFORMATION (con't)

WARNINGS AND PRECAUTIONS (con't)

- **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. Renown Institute for Neuroscience web site location page. Available at: https://www.renown.org/locations/institutes/neurosciences/. Accessed December 18, 2020.
3. MAVENCLAD [prescribing information]. Rockland, MA: EMD Serono, Inc; 2019..

What would you consider in an MS treatment for a patient who is a working parent with previous intolerance to infusion and oral DMTs?

In this real-world patient case study, Dr. Melissa Bloch evaluated the following issues when choosing a treatment for this patient[1]:

- Is it effective in my patient's type of MS?
- What are the safety/tolerability considerations for use in this patient?
- Do the administration requirements meet the personal needs of my patient?

Scan here to see more real-world patient case studies

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