MS LifeLines®

ONE-ON-ONE SUPPORT FOR PATIENTS TAKING EMD SERONO PRODUCTS

# Navigating the Formulary Exception Request and Appeals Process

Educational Toolkit for Healthcare Professional Offices

EMD Serono

MS LifeLines is an educational support service for people living with RMS and their families, and is sponsored by EMD Serono, Inc.

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## INDICATION and IMPORTANT SAFETY INFORMATION for MAVENCLAD® (cladribine) tablets

MAVENCLAD® (cladribine) 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.

## SELECT 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.**

Please see Important Safety Information on pages 14-15 and the full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

## INDICATION and IMPORTANT SAFETY INFORMATION for REBIF® (interferon beta-1a) for subcutaneous injection

### INDICATION

REBIF is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

## SELECT IMPORTANT SAFETY INFORMATION

**Contraindication:** REBIF is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation.

Please see Important Safety Information on pages 16-17 and the full **Prescribing Information** and **Medication Guide** for additional information.

# UNDERSTANDING THE EXCEPTION AND APPEALS PROCESS

## Coverage Barriers May Be Resolved Through a Formulary Exception Request or an Appeals Process

When a product is not covered by an insurance plan, it is sometimes referred to as non-formulary, National Drug Code (NDC) blocked, or requiring a medical exception.[1]

A formulary exception describes the process whereby a healthcare provider (HCP) can request that a payer consider covering a product not on formulary for a specific patient due to medical necessity. When an HCP has determined that a drug not on formulary is medically necessary, the HCP can submit a formulary exception request to ask the payer to approve the treatment.[1]

Additionally, if a prior authorization or formulary exception request is denied, the appeals process can be used to request payer approval of the treatment for an individual patient. Similar forms and processes are typically used, whether requesting an appeal to a previous prior authorization denial or a formulary exception.[1]

**Contact MS LifeLines at 1-877-447-3243 for payer-specific details and forms**

**Please submit all formulary exception request or appeals paperwork directly to the insurer, and forward copies of any determinations to MS LifeLines so we can better support your patient.**

Similar to a traditional prior authorization process, the formulary exception request or appeals process varies by payer, so it is important to follow the steps required, submit all requested documentation, and use the correct forms.

Commercial payer formulary exception request or appeals processes may be obtained by contacting the payer's provider relations department and may also be available online.

Additionally, MS LifeLines can provide payer-specific details.

For Medicare Part D plans, instructions for submitting an exception request or appeal, as well as downloadable sample forms, are available from the Centers for Medicare & Medicaid Services **here**.

Part D plans do not require specific forms, so use of the sample form is optional.

MS LifeLines can describe payer processes and forms required.

Reference:
1. Centers for Medicare & Medicaid Services. Medicare prescription drug appeals and grievances. Accessed July 23, 2025. https://www.cms.gov/medicare/appeals-grievances/prescription-drug

# DOCUMENTATION CHECKLIST

*Each Payer May Require Different or Additional Documentation*

*Please review the denial notification, payer-specific guidelines, and any required forms to determine what to include in your patient's formulary exception request or appeals submission.*

## INFORMATION FROM PATIENT'S MEDICAL RECORD AND CHART NOTES

**Patient's Condition**

- ☐ Diagnosis
- ☐ Detailed history of patient's condition
- ☐ Current symptoms

If applicable:

- ☐ Clinical relapse(s), including hospitalization(s), in the prior year
- ☐ MRI scan with additional lesion(s) in the past 6 months

**Prior Treatments: Including ALL Tried and Failed Therapies**

- ☐ Names
- ☐ Duration
- ☐ Reasons for discontinuation (e.g., new evidence of disease activity or increased disability, worsening symptoms, adverse events)

## PRESCRIBER INFORMATION

- ☐ Name
- ☐ National Provider Identifier (NPI) number
- ☐ Specialty
- ☐ Contact information

## MEDICATION REQUESTED

- ☐ **MAVENCLAD (cladribine) tablets**
  - ☐ Dosage strength (based on patient's weight)
- ☐ **REBIF (interferon beta-1a) subcutaneous injection**
  - ☐ Dosage strength (indicate loading and maintenance doses where applicable)
  - ☐ Injection delivery method: REBIF Rebidose® (interferon beta-1a) or prefilled syringe

## FORMULARY EXCEPTION AND APPEALS REQUEST CRITERIA

- ☐ Follow payer processes and use applicable forms
- ☐ Explanation of medical necessity for the specific patient type, (e.g., patient has high disease activity)
- ☐ Reason why other available formulary drugs are not appropriate

**Supporting Documentation (may be required by some payers)**

- ☐ Chart documentation
- ☐ Letter of medical necessity

**If you have questions about formulary exceptions or the appeals process, MS LifeLines may be able to help—call 1-877-447-3243.**

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

TEMPLATES

# GUIDANCE FOR TEMPLATES

**Important Tips for Completing Letters**

## Formulary Exception Request Letter

- The MS LifeLines Patient Access Team can assist in obtaining payer-specific forms and can further describe payer processes
- To avoid delays in a coverage decision, it is recommended that you provide as much documentation as possible when submitting your request
- It is important to note that supplying information in your request does not guarantee coverage, and this information is not intended to substitute for or influence the physician's independent medical judgment

VIEW SAMPLE TEMPLATE

## Appeals Letter

If a prior authorization or formulary exception request is denied by the patient's health plan, the payer may require an appeals letter. The denials and appeals process varies by health plan.

- Review the denial provided by the plan so your appeals letter can address the specific reasons for the denial
- Contact the health plan with any questions about the denial, appeals process, or deadlines
- Use the template letters provided to create appeals for your patients, and then send back to the health plan

VIEW SAMPLE TEMPLATE

## Medical Necessity Letter

HCPs can use the letter of medical necessity to provide an explanation for treatment decisions and supporting documentation for exception and appeal requests. Medical necessity letters may be required by some health plans when submitting an appeals letter.

- Ensure all pertinent identifying information is included: patient's full name, date of birth, and plan identification number
  - If a decision was previously made, include the case identification (ID) number
- Provide a copy of the patient's medical records with the following included: medical history, diagnosis with specific International Classification of Diseases, Tenth Revision (ICD-10) codes, current condition and symptoms, and severity
- Provide a list of prior treatment trials/failures
  - Indicate formulary appropriateness, duration of each treatment, and rationale for treatment discontinuation
- Provide rationale for current treatment recommendations

VIEW SAMPLE TEMPLATE

**Templates can also be obtained by calling MS LifeLines at 1-877-447-3243**

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# FORMULARY EXCEPTION REQUEST SAMPLE TEMPLATE LETTER

*This template letter is provided for your guidance only.*

[Physician's letterhead]

[Date]
[Health Plan Contact Name]
[Title]
[Health Plan Organization Name]
[Address]
[City, State, ZIP]

Re: [Patient Name], Date of Birth [Date], Insurance Policy ID Number: [Policy ID Number], Group Number: [Group Number]

Dear [Health Plan Contact Name],

I am writing to request a formulary exception for my patient, [Patient], for the treatment of relapsing forms of multiple sclerosis with [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection]. It is my professional opinion that [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] is medically appropriate and necessary and should be approved for this patient.

[Patient] has been under my care for [insert diagnosis] since [date of onset/diagnosis]. Included for your consideration are [Patient]'s medical history and diagnosis (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] code), and a statement summarizing my reasons for requesting treatment of [Patient] with [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection].

[Insert summary of patient history, including treatment history, response to past therapies, and recent symptoms and conditions, and any other factors that are guiding your recommendation for this patient.]

[Insert key clinical information, including indications and usage, safety and efficacy outcomes, and any other key data that support your recommendation for the patient.]

Based on this information, I feel strongly that [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] is medically necessary for this patient, and it is in my patient's best interest to begin [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] therapy immediately.

After reviewing the information provided with a healthcare provider specializing in multiple sclerosis treatment, if you do not believe that this information establishes clear medical necessity for [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] for this patient, please provide a detailed rationale and further appeal options and contacts.

I would appreciate any efforts to expedite this review process. If you have any questions or require additional information, please contact me as soon as possible at [phone number].

Sincerely,
[Physician's name, degree(s), and signature]

Enclosures: [Attach additional documentation, as appropriate or required]

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# APPEAL SAMPLE TEMPLATE LETTER

*This template letter is provided for your guidance only.*

[Physician's letterhead]

[Date]
[Health Plan Contact Name]
[Title]
[Health Plan Organization Name]
[Address]
[City, State, ZIP]

Re: [Patient Name], Date of Birth [Date], Insurance Policy ID Number: [Policy ID Number], Group Number: [Group Number]

Dear [Health Plan Contact Name],

I am writing to appeal the denial of [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] treatment for my patient, [Patient]. For your convenience, I have attached documentation supporting the appeal request for this denial:

[Insert summarized rationale for prescribing MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection specifically for your patient or attach letter of medical necessity. Address any specific reasons for denial.]

[Insert description of MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection and include supporting clinical trial information. (Refer to Appendix A in this form for information about MAVENCLAD (cladribine) tablets and Appendix B for information about REBIF (interferon beta-1a) subcutaneous injection, including the approved indications, Important Safety Information, and data from the clinical trials.)]

Based on this information, I feel strongly that [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] is medically necessary for this patient, and it is in my patient's best interest to [begin/continue MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] therapy immediately.

After reviewing the information provided with a healthcare provider specializing in multiple sclerosis treatment, if you do not believe that this information establishes clear medical necessity for [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] for this patient, please provide a detailed rationale and further appeal options and contacts. A determination letter can be sent via [fax number or email address].

I would appreciate any efforts to expedite this appeal process. If you have any questions or require additional information, please contact me as soon as possible at [phone number].

Sincerely,
[Physician's name, degree(s), and signature]

Enclosures: [Attach additional documentation, as appropriate or required]

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# APPEAL SAMPLE TEMPLATE LETTER (CONTINUED)

*This template letter is provided for your guidance only.*

## APPENDIX A

**About MAVENCLAD (cladribine) tablets**

MAVENCLAD was approved in March 2019 by the US Food and Drug Administration (FDA) and 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. MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS). The use of MAVENCLAD may cause serious side effects such as malignancy and teratogenicity. MAVENCLAD is associated with an increased risk of infections and lymphopenia.[1]

MAVENCLAD is an oral treatment that is a maximum of 10 days of treatment per year for 2 years and demonstrates efficacy at 96 weeks.[1]

In the clinical trial program of cladribine in MS, 1,976 patients received therapy for a total of 9,509 patient-years, of which the mean time on study including follow-up was approximately 4.8 years and 24% of the follow-up was for 8 years.[1] The efficacy of MAVENCLAD was demonstrated in a 96-week, randomized, double-blind, placebo-controlled pivotal clinical trial in patients (n=1,326) with relapsing forms of MS[2]:

- Patients experienced a 58% relative reduction in the annualized relapse rate with MAVENCLAD compared to placebo (0.14 vs 0.33; *P*<0.001) at 96 weeks.[2]
- 81% of patients were free of relapses after 96 weeks of oral treatment with MAVENCLAD, compared to 63% of patients who received placebo (nominal *P*<0.05).[1]
- Patients treated with MAVENCLAD had a 33% reduction in risk of 3-month confirmed disability progression as measured by Expanded Disability Status Scale (EDSS) at 96 weeks compared to placebo (nominal *P*<0.05).[1]
- Patients taking MAVENCLAD experienced a lower median number of T1-weighted gadolinium-enhanced brain lesions and new or enlarging T2 brain lesions at 96 weeks compared to patients with placebo (0 vs 0.33 and 0 vs 0.67; *P*<0.001).[1]

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.[1]

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.[1]

The most common (>20%) adverse reactions reported in the pivotal phase 3 study, CLARITY, were upper respiratory tract infection, headache, and lymphopenia.[1] Serious adverse reactions reported in the clinical program included malignancies (0.27 events per 100 patient-years) in MAVENCLAD treatment arms, compared to placebo patients (0.13 events per 100 patient-years), and herpes zoster infections (2.0% vs 0.2%) and oral herpes (2.6% vs 1.2%).[1]

Please go to https://www.emdserono.com/us-en/pi/mavenclad-pi.pdf for the full Prescribing Information, including **BOXED WARNING**.

References:

1. MAVENCLAD® (cladribine) [Prescribing Information]. Rockland, MA: EMD Serono, Inc.
2. Giovannoni G, Comi G, Cook S, et al; CLARITY Study Group. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. *N Engl J Med*. 2010;362(5):416-426.

# APPEAL SAMPLE TEMPLATE LETTER (CONTINUED)

*This template letter is provided for your guidance only.*

## APPENDIX B

**About REBIF (interferon beta-1a) subcutaneous injection**

REBIF is approved by the US Food and Drug Administration (FDA) for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.[1] The FDA approved REBIF for the treatment of relapsing forms of MS in 2002, based upon the results of 2 large multi-center studies (PRISMS and EVIDENCE)* in patients with relapsing MS.[1] Some details of the PRISMS and EVIDENCE trials are discussed below.

PRISMS was a double-blind, placebo-controlled study conducted over 2 years. Patients were randomly assigned REBIF 44 mcg (n=184), REBIF 22 mcg (n=189), or placebo (n=187), given 3 times weekly (tiw) by subcutaneous (SC) injection. The primary efficacy endpoint was the number of clinical exacerbations. Numerous secondary efficacy endpoints were also evaluated and included exacerbation-related parameters, effects of treatment on progression of disability, and magnetic resonance imaging (MRI)–related parameters.[1,2]

In the 2-year PRISMS clinical trial, the mean number of relapses per patient during the first 2 years of PRISMS was significantly lower in the REBIF 44 mcg group (1.73, n=184) compared with the placebo group (2.56, n=187) with a relative reduction of 32% for REBIF vs placebo ($P$<0.0001). Moreover, REBIF 44 mcg SC tiw led to a 30% reduction in the proportion of relapsing MS patients with sustained disability progression (secondary endpoint, 26% with REBIF vs 37% with placebo; $P$=0.01).[1,2]

In this trial, REBIF 44 mcg tiw significantly increased the median time to first relapse relative to placebo over 2 years. In fact, REBIF more than doubled the time to first relapse (9.6 months vs 4.5 months with placebo; $P$<0.0001).[1]

The MRI scans of relapsing MS patients taking REBIF showed significantly less lesion activity (the median number of T2-active lesions per patient per scan was 0.5 for REBIF [n=171] vs 2.25 for placebo [n=172]; $P$<0.0001) and T2 lesion area (the median percent change of T2 lesion area at 2 years was -3.8% for REBIF [n=171] vs 11% for placebo [n=172]).[1] The exact correlation between MRI findings and the current or future clinical status of patients, including disability progression, is unknown.

EVIDENCE was an assessor-blinded, parallel-group study conducted over an average of 64 weeks. Patients were randomized to receive REBIF 44 mcg SC tiw (n=339) or Avonex®† 30 mcg intramuscularly (IM) once weekly (qw) (n=338). The primary endpoint of EVIDENCE was the proportion of relapse-free patients at 24 weeks. The secondary endpoints included additional relapse measures, disability progression, safety, and MRI outcomes, such as number of combined unique active lesions at 24 weeks, T1 gadolinium-enhanced lesions at 24 weeks, T2 lesions over 64 weeks, and post-transition T2 lesions.[1,3]

In the EVIDENCE clinical trial, REBIF 44 mcg SC tiw demonstrated superior efficacy over Avonex in reducing the frequency of relapses at 24 weeks in patients with relapsing MS: 75% of the patients who received REBIF 44 mcg SC tiw (n=339) did not have a relapse, compared to 63% of patients in the study who received Avonex 30 mcg IM (n=338) ($P$<0.001). In the EVIDENCE trial, side effects in REBIF and Avonex groups were generally similar with some exceptions: the group of patients taking REBIF had a higher incidence of low white blood cell counts, liver enzyme elevation, and injection site reactions, and the group of patients on Avonex had a higher incidence of flu-like symptoms.[1,3]

REBIF has 2 dosing options: 44 mcg tiw and 22 mcg tiw. The dose can be reduced if low white blood cell counts or liver enzyme elevation issues arise. REBIF comes from a pre-filled syringe or the REBIF Rebidose pre-filled auto-injector.[1] Other disease-modifying drugs may require additional steps for preparation.

The most common reported side effects with REBIF include flu-like symptoms, stomach pains, and changes in liver blood tests. Potential serious side effects of REBIF include depression and suicidal ideation, liver problems or worsening liver problems, including liver failure, serious allergic and skin reactions, and injection site problems. There are no adequate and well-controlled studies in pregnant women. REBIF should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.[1]

Please go to https://www.emdserono.com/us-en/pi/rebif-pi.pdf for full Prescribing Information.

*PRISMS (Prevention of Relapses and Disability by Interferon Beta-1a Subcutaneously in Multiple Sclerosis) trial and EVIDENCE (Evidence of Interferon Dose-response: European North American Comparative Efficacy) trial.

†Avonex is a registered trademark of Biogen.

References:
1. REBIF® (interferon beta-1a) [Prescribing Information]. Rockland, MA: EMD Serono, Inc.
2. PRISMS Study Group. Randomised double-blind placebo-controlled study of interferon β-1a in relapsing/remitting multiple sclerosis. *Lancet*. 1998;352(9139):1498-1504.
3. Panitch H, Goodin DS, Francis G, et al; EVIDENCE Study Group. Randomized, comparative study of interferon β-1a treatment regimens in MS: the EVIDENCE Trial. *Neurology*. 2002;59(10):1496-1506.

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# MEDICAL NECESSITY SAMPLE TEMPLATE LETTER

*This template letter is provided for your guidance only.*

[Physician's letterhead]

[Date]
[Health Plan Contact Name]
[Title]
[Health Plan Organization Name]
[Address]
[City, State, ZIP]

Re: [Patient Name], Date of Birth [Date], Insurance Policy ID Number: [Policy ID Number], Group Number: [Group Number], Claim Number: [Claim Number]

Dear [Health Plan Contact Name],

I am writing to provide additional information supporting my prescription for the treatment of [Patient]'s relapsing form of multiple sclerosis with [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection]. It is my belief that treatment with [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] is medically necessary and appropriate for this patient. This letter will provide supporting documentation that details the patient's medical history, prior treatments, and current symptoms and disease severity.

**Patient's Diagnosis:**
Patient has been diagnosed with a relapsing form of multiple sclerosis.

[Attach medical records and other supporting documentation, including all relevant clinical evaluation and scoring forms.]

**Treatment History:**
History of medications tried and/or failed for multiple sclerosis. Include rationale for why formulary agents were not tried, where applicable (eg, contraindications, comorbidities).

| Treatment: | Dose: | Start Date: | Stop Date: | Reason for Discontinuation: |
|---|---|---|---|---|
| | | | | |

**Additional Considerations:**
[Insert reason(s) the patient would benefit from your recommendation as a part of their multiple sclerosis care plan. Provide support for your rationale based on clinical peer-reviewed literature and/or package inserts.]

After reviewing the information provided with a healthcare provider specializing in multiple sclerosis treatment, if you do not believe that this information establishes clear medical necessity for [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] for this patient, please provide a detailed rationale and further appeal options and contacts.

I would appreciate any efforts to expedite this review process. If you have any questions or require additional information, please contact me as soon as possible at [phone number].

Sincerely,
[Physician's name, degree(s), and signature]

Enclosures: [Attach additional documentation, as appropriate or required]

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# MS LifeLines®

**SUPPORT** YOU CAN COUNT ON

## YOUR EMD SERONO PATIENT SUPPORT TEAM

An integrated team for you and your patients

### Patient Support Specialist

- Primary patient and healthcare provider (HCP) contact through the pre-treatment access journey
- Provides access and reimbursement support

### Field Reimbursement Manager

- Works directly with HCP offices to navigate patient access barriers
- Field-based partner to Patient Support Specialist


### Field Nurse Educator

- Provides supplementary product education during patient visits
- Updates HCPs on patient visits and adherence status as requested

### Nurse Support Specialist

- Contacts patients throughout their treatment journey to offer support and education
- Available to answer patient questions

**For more information, or to obtain a Service Request Form:**

Visit: Mavenclad.com/hcp or REBIF.com/hcp

Call: 1-877-447-3243
Fax: 1-866-227-3243

Hours: Monday through Friday: 8 AM to 8 PM ET;
Saturday: 9 AM to 5 PM ET

**Individualized support to help patients start and stay on therapy, including access to MS-certified nurse educators and financial assistance for eligible patients.**

Please see Important Safety Information for MAVENCLAD on pages 14-15 and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

Please see Important Safety Information for REBIF on pages 16-17 and full **Prescribing Information** and **Medication Guide** for additional information.

# SUBMITTING THE MS LIFELINES SERVICE REQUEST FORM

## Service Request Form

You can prescribe EMD Serono RMS products using a Service Request Form. Just print it, fill it out, and fax it to MS LifeLines to get started. Completing this form with your patient also gives them access to the one-on-one support services provided by MS LifeLines.

## Completing the Service Request Form

- ☑ Have your patient read the Patient Consent Information and **sign the Patient Authorization section** of the Service Request Form, either in writing or electronically via **HIPAAconsent.com**
  - Obtaining the patient's signature will help expedite their enrollment in the MS LifeLines Patient Support Program, which includes determining eligibility for financial assistance programs
  - If the patient signs electronically, the form can be submitted without their physical signature (Prescriber signature still required)
- ☑ Complete all requested form fields and **sign the Prescriber Authorization section**
  - An incomplete form may delay treatment or patient enrollment in MS LifeLines
- ☑ Fax to MS LifeLines at **1-866-227-3243**

## Prescribing Electronically

Prescriptions and Service Request Forms can be submitted electronically through MS LifeLines Pro™. CoverMyMeds also offers free electronic prior authorization services.

Service Request Forms can be provided by your Area Business Manager or downloaded for **MAVENCLAD** or **REBIF**.

## SELECT IMPORTANT SAFETY INFORMATION for MAVENCLAD® (cladribine) tablets

**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.

Please see Important Safety Information on pages 14-15, and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

## SELECT IMPORTANT SAFETY INFORMATION for REBIF® (interferon beta-1a) for subcutaneous injection

**Depression and Suicide:** Use REBIF with caution in patients with depression, a common condition in people with multiple sclerosis. Depression, suicidal ideation, and suicide attempts have been reported to occur with increased frequency in patients receiving interferon compounds, including REBIF.

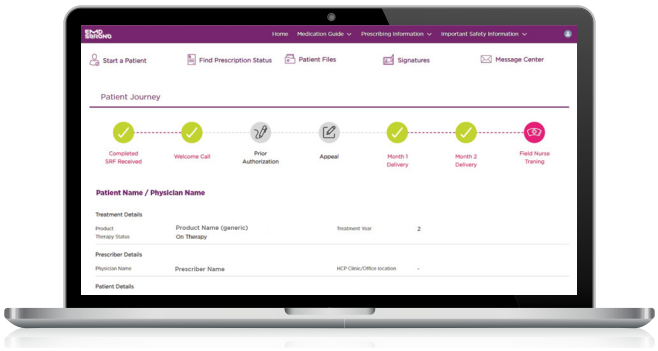
Please see Important Safety Information on pages 16-17, and full **Prescribing Information** and **Medication Guide** for additional information.

# WELCOME TO MSLifeLines Pro™

## Are you taking full advantage of MS LifeLines Pro?

The portal allows you to manage all of your patients who are enrolled in MS LifeLines in one place. Through the portal you can:

- Electronically submit and sign prescriptions for EMD Serono RMS products
- View real-time patient journey status
- Take action on outstanding tasks or next steps
- Invite other office staff and prescribers to help manage patients on your behalf
- Send messages to the MS LifeLines team




Green indicates task completed

Pink indicates task started, but not completed

Grey indicates task not started

***Note:*** *Colors indicate different steps in the prescription journey.*

**MS**LifeLines®

**Don't miss out. Register today!**

To register, visit **mslifelinespro.com** or contact MS LifeLines at **1-877-447-3243**.

MS LifeLines is an educational support service for people living with RMS and their families, and is sponsored by EMD Serono, Inc.

## INDICATION and IMPORTANT SAFETY INFORMATION for MAVENCLAD® (cladribine) tablets

MAVENCLAD® (cladribine) 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 infected 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 on a MAVENCLAD treatment day 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. Concomitant use of MAVENCLAD with hematotoxic drugs may increase the risk of adverse reactions because of the additive hematological effects. Monitor lymphocyte counts before, during, and after treatment.
- **Infections:** Serious, including life-threatening or fatal, infections have occurred. MAVENCLAD reduces the body's immune defense, and an increased risk of infections has been observed in patients receiving MAVENCLAD. Infections occurred in 49% of MAVENCLAD-treated patients compared to 44% of patients treated with placebo in clinical studies; serious or severe infections occurred in 2.4% of MAVENCLAD-treated patients and 2.0% of placebo-treated patients. The most frequent serious infections included herpes zoster and pyelonephritis. Fungal infections were observed, including cases of coccidioidomycosis. Single fatal cases of tuberculosis and fulminant hepatitis B were reported in the clinical program.

Please see additional Important Safety Information on next page, and full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

## IMPORTANT SAFETY INFORMATION for MAVENCLAD® (cladribine) tablets (CONTINUED)

**WARNINGS AND PRECAUTIONS** (continued)

- Screen patients for active and latent infections (tuberculosis, hepatitis B or C). Delay treatment until infection is fully resolved or controlled.
- Vaccinate patients who are seronegative for varicella zoster virus (VZV) prior to treatment. Vaccinate patients who are seropositive to VZV with recombinant, adjuvanted zoster vaccine either prior to or during treatment, including when their lymphocyte counts are less than or equal to 500 cells per microliter.
- Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections.
- Progressive multifocal leukoencephalopathy (PML) has been reported in patients treated with parenteral cladribine for oncologic indications. No case of PML has been reported in clinical studies of cladribine in patients with MS. Obtain a baseline magnetic resonance imaging (MRI) within 3 months before initiating the first treatment course of MAVENCLAD. At the first sign of PML, withhold MAVENCLAD and perform an evaluation.
- 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 due to risk of infection.

- **Hematologic Toxicity:** In addition to lymphopenia, decreases in other blood cells and hematological parameters have been reported with MAVENCLAD in clinical studies. Obtain complete blood count (CBC) with differential including lymphocyte count before and during treatment, periodically thereafter, and when clinically indicated.
- **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. In patients who require blood transfusion, irradiation of cellular blood components is recommended.
- **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 MAVENCLAD if clinically significant liver injury is suspected. .
- **Hypersensitivity:** 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. Instruct patients to seek medical advice if they experience symptoms of cardiac failure (e.g., shortness of breath, rapid or irregular heartbeat, swelling).

**Adverse Reactions:** The most common adverse reactions (incidence of >20%) are upper respiratory tract infection, headache, and lymphopenia.

**Drug Interactions:** Concomitant use 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. Monitor for additive effects on the hematological profile with use of hemotoxic drugs. Avoid concomitant use of 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 >65 years, pregnant or breastfeeding women. Use in patients with moderate to severe renal or hepatic impairment is not recommended.

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

Please see full **Prescribing Information**, including **BOXED WARNING**, and **Medication Guide** for additional information.

## INDICATION AND IMPORTANT SAFETY INFORMATION for REBIF® (interferon beta-1a) for subcutaneous injection

### INDICATION

REBIF is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

## IMPORTANT SAFETY INFORMATION

**Contraindication:** REBIF is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation.

**Depression and Suicide:** Use REBIF with caution in patients with depression, a common condition in people with multiple sclerosis. Depression, suicidal ideation, and suicide attempts have been reported to occur with increased frequency in patients receiving interferon compounds, including REBIF.

**Hepatic Injury:** There have been rare reports of severe liver injury, including some cases of hepatic failure requiring liver transplantation, in patients taking REBIF. Consider the potential for hepatic injury when REBIF is used in combination with other products associated with hepatotoxicity. Monitor liver function tests and patients for signs and symptoms of hepatic injury. Consider discontinuing REBIF if hepatic injury occurs.

**Anaphylaxis and Other Allergic Reactions:** Anaphylaxis and other allergic reactions (some severe) have been reported. Discontinue REBIF if anaphylaxis occurs.

**Injection Site Reactions Including Necrosis:** In controlled clinical trials, injection site reactions occurred more frequently in REBIF-treated patients than in placebo-treated and Avonex-treated patients. Injection site reactions including injection site pain, erythema, edema, cellulitis, abscess, and necrosis have been reported in the postmarketing setting with the use of REBIF. Do not administer REBIF into affected area until fully healed; if multiple lesions occur, change injection site or discontinue REBIF until skin lesions are healed. Some cases of injection site necrosis required treatment with intravenous antibiotics and surgical intervention (debridement and skin grafting). Some cases of injection site abscesses and cellulitis required treatment with hospitalization for surgical drainage and intravenous antibiotics. Rotate site of injection with each dose to minimize likelihood of severe injection site reactions, including necrosis or localized infection.

**Decreased Peripheral Blood Counts:** Decreased peripheral blood counts in all cell lines, including pancytopenia, have been reported in REBIF-treated patients. In controlled clinical trials, leukopenia occurred at a higher frequency in REBIF-treated patients than in placebo and Avonex-treated patients. Thrombocytopenia and anemia occurred more frequently in 44 mcg REBIF-treated patients than in placebo-treated patients. Monitor patients for symptoms or signs of decreased blood counts. Monitoring of complete blood and differential white blood cell counts is also recommended.

**Thrombotic Microangiopathy:** Cases of thrombotic microangiopathy (TMA), some fatal, have been reported with interferon beta products, including REBIF, up to several weeks or years after starting therapy. Discontinue REBIF if clinical symptoms and laboratory findings consistent with TMA occur and manage as clinically indicated.

**Pulmonary Arterial Hypertension:** Cases of pulmonary arterial hypertension (PAH) have been reported in patients treated with interferon beta products, including REBIF. Patients who develop unexplained symptoms (e.g., dyspnea, new or increasing fatigue) should be assessed for PAH. If alternative etiologies have been ruled out and a diagnosis of PAH is confirmed, discontinue treatment and manage as clinically indicated.

**Seizures**: Seizures have been temporally associated with the use of beta interferons, including REBIF, in clinical trials and in postmarketing reports. Monitor for seizures when administering REBIF to patients, particularly those with pre-existing seizure disorders.

**Laboratory Tests:** New or worsening thyroid abnormalities have developed in some patients treated with REBIF. Thyroid function tests are recommended every 6 months in patients with history of thyroid dysfunction or as clinically indicated.

**Adverse Reactions:** The most common adverse reactions with REBIF are injection-site disorders, influenza-like symptoms, abdominal pain, depression, elevated liver enzymes, and hematologic abnormalities.

Please see full **Prescribing Information** and **Medication Guide** for additional information.

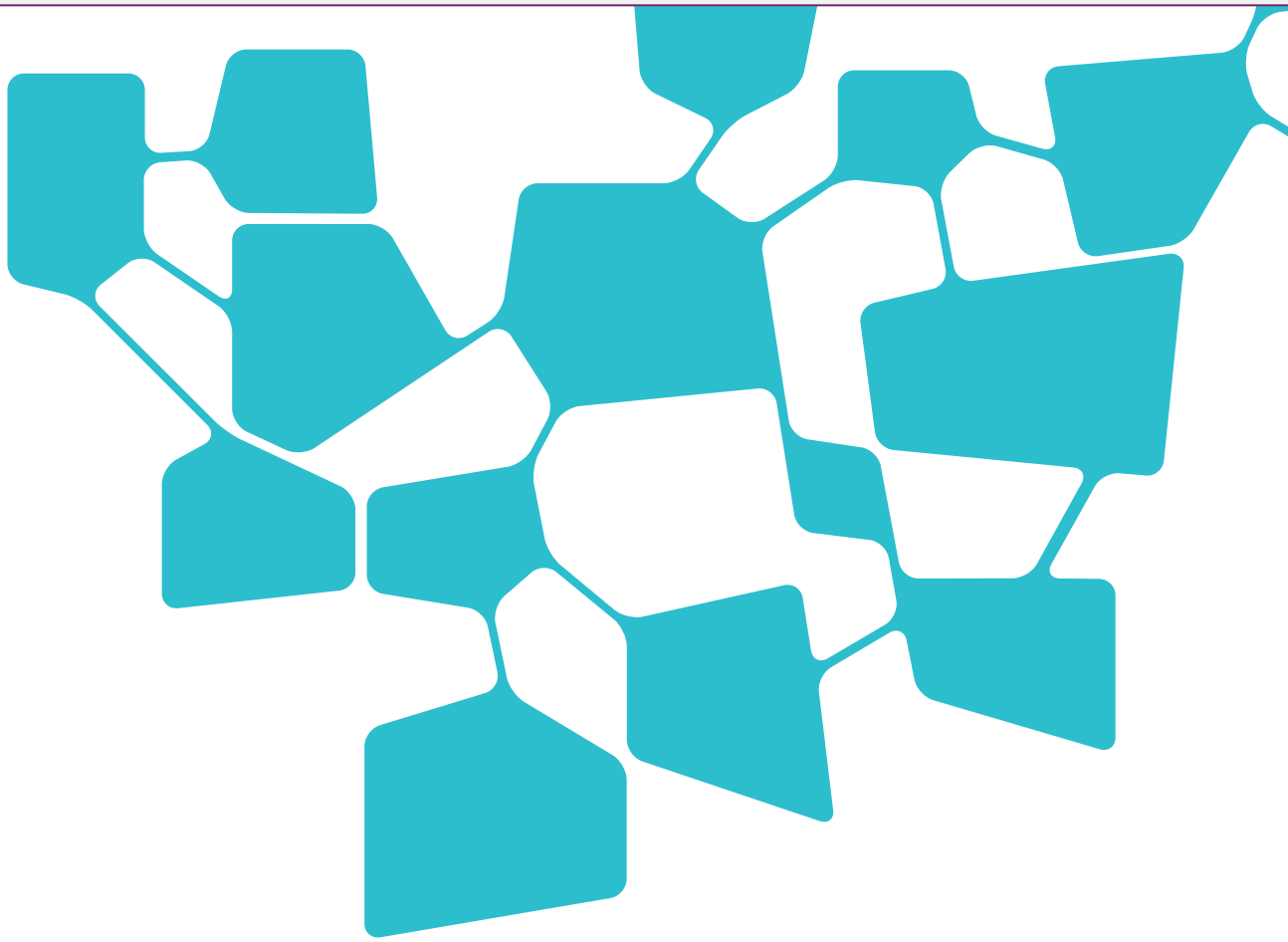
## IMPORTANT SAFETY INFORMATION

**Pregnancy:** Epidemiological data do not suggest a clear relationship between interferon beta use and major congenital malformations, but interferon beta may cause fetal harm based on animal studies. Data from a large human population-based cohort study, as well as other published studies over several decades, have not identified an increased risk of major birth defects with exposure to interferon beta products during early pregnancy. Findings regarding a potential risk for low birth weight or miscarriage with the use of interferon beta products in pregnancy have been inconsistent.

**Lactation:** Limited published literature has described the presence of interferon beta-1a products in human milk at low levels. There are no data on the effects of interferon beta-1a on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for REBIF and any potential adverse effects on the breastfed child from REBIF or from the underlying maternal condition.

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

Please see full **Prescribing Information** and **Medication Guide** for additional information.



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