

MSLifeLines®

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

Navigating the Formulary Exception Request and Appeals Process

Educational Toolkit for Healthcare Professional Offices



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



TABLE OF CONTENTS

UNDERSTANDING THE FORMULARY EXCEPTION AND APPEALS PROCESS	3
DOCUMENTATION CHECKLIST	4
TEMPLATES	5
Formulary Exception Request Sample Template Letter	6
Appeal Sample Template Letter	7
Medical Necessity Sample Template Letter	8
Reference Compendium	9
MS LIFELINES	13
Overview of MS LifeLines Services	13
Submitting the Service Request Form	14
MS LifeLines Pro™ Portal	15
IMPORTANT SAFETY INFORMATION	16

INDICATION 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 16-17 and the full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

INDICATION for REBIF® (interferon beta-1a) for subcutaneous injection

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 18-19 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
- Relevant clinical information and data (e.g., clinical trials and publications)

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 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 and full [Prescribing Information](#) and [Medication Guide](#) for additional information.



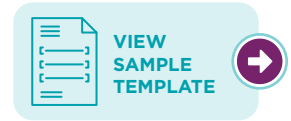
TEMPLATES

GUIDANCE FOR TEMPLATES

Important Tips for Completing Letters

Formulary Exception Request Letter

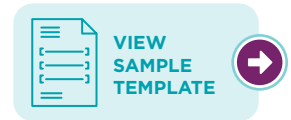
- The MS LifeLines Patient Access Team can assist in obtaining payer-specific forms and can further describe payer processes
- To avoid delays in a coverage decision, it is recommended that you provide as much documentation as possible when submitting your request
- It is important to note that supplying 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



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.

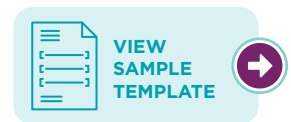
- Review the denial provided by the plan so your appeals letter can address the specific reasons for the denial
- Contact the health plan with any questions about the denial, appeals process, or deadlines
- Use the template letters provided to create appeals for your patients, and then send back to the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



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



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

Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 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].

[Clinical Considerations:]

- [Patient's diagnosis, date of diagnosis, and other relevant medical history]
- [Patient disease activity (including highly active disease, if applicable)]
- [Response to past therapies (branded and generics)]
- [Adverse events related to past therapies or method of administration]
- [Concerns related to dosing]
- [Treatment continuity]
- [Adherence concerns]
- [Any additional concerns, including any related to patient's general health, age-related factors, or co-morbidities]
- [Summary of your professional opinion explaining the patient's need for branded treatment]

[Insert key clinical information, including indications and usage, safety and efficacy outcomes, and any other key data that support your recommendation for the patient. Consider including additional references from clinical trials and peer-reviewed publications to support your request.]

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.

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]

Refer to Appendix A in this form for information about MAVENCLAD® (cladribine) tablets 10 mg 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.

Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 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]. I understand from your denial letter[s] dated [month, date, year] that [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] has been denied because [quote denial reason as communicated in the denial letter.] After reviewing the letter[s], I still maintain that [MAVENCLAD (cladribine) tablets/REBIF (interferon beta-1a) subcutaneous injection] is the appropriate treatment for my patient, due to the below considerations and have attached documentations 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. Summarized rationale may include the below factors. Address any specific reasons for denial.]

- [Patient's diagnosis, date of diagnosis, and other relevant medical history]
- [Patient disease activity (including highly active disease, if applicable)]
- [Response to past therapies (branded and generics)]
- [Adverse events related to past therapies or method of administration]
- [Concerns related to dosing]
- [Treatment continuity]
- [Adherence concerns]
- [Any additional concerns, including any related to patient's general health, age related factors, or co-morbidities]
- [Summary of your professional opinion explaining the patient's need for branded treatment]

[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 information from clinical trials, peer-reviewed publications, and additional data.)]

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 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 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 brand-name [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 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 and full [Prescribing Information](#) and [Medication Guide](#) for additional information.



REFERENCE COMPENDIUM

Information to support further documentation for your appropriate patients regarding payer coverage for MAVENCLAD and REBIF.

APPENDIX A

MAVENCLAD® (CLADRIBINE) TABLETS REFERENCE COMPENDIUM

MAVENCLAD® Clinical Profile Information

The following references may be used to support coverage communications related to:

- **The clinical profile of MAVENCLAD®**
- **CLARITY pivotal trial data, which evaluated the use of MAVENCLAD to treat RMS in adults over 96 weeks, & CLARITY-Extension, a 2-year extension study that assessed the safety & efficacy of MAVENCLAD over four years**
- **MAGNIFY-MS, a phase IV, open-label, single-arm multicenter study, that looked at clinical and safety outcomes with MAVENCLAD, including impact on lymphocyte subgroups**

MAVENCLAD. Prescribing Information. EMD Serono, Inc.

[CLICK HERE TO VIEW INFORMATION](#)



Giovannoni G, Comi G, Cook S, et al; for the CLARITY Study Group. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. *N Engl J Med*. 2010;362(5):416-426

[CLICK HERE TO VIEW INFORMATION](#)



Giovannoni G, Soelberg Sorensen P, Cook S, et al. Safety and efficacy of cladribine tablets in patients with relapsing-remitting multiple sclerosis: Results from the randomized extension trial of the CLARITY study. *Mult Scler*. 2018;24(12):1594-1604.

[CLICK HERE TO VIEW INFORMATION](#)



Wiendl H, Barkhof F, Montalban X, et al. Blood biomarker dynamics in people with relapsing multiple sclerosis treated with cladribine tablets: results of the 2-year MAGNIFY-MS study. *Front Immunol*. 2025;16:1512189.

[CLICK HERE TO VIEW INFORMATION](#)



Treatment Factors Based on Patient Disease Activity

The following references may be used to support coverage communications related to:

MAVENCLAD

- **MAVENCLAD efficacy and safety data in patients with highly active disease**

Giovannoni G, Soelberg-Sorensen P, Cook S, et al. Efficacy of cladribine tablets in high disease activity subgroups of patients with relapsing multiple sclerosis: a post hoc analysis of the CLARITY study. *Mult Scler*. 2019;25(6):819-827.

[CLICK HERE TO VIEW INFORMATION](#)



DISEASE EDUCATION

- **Efficacy classification and utility of early use**

Samjoo IA, Worthington E, Drudge C, et al. Efficacy classification of modern therapies in multiple sclerosis. *J Comp Clin Res*. 2022;10(6):495-507.

[CLICK HERE TO VIEW INFORMATION](#)



Freeman L, Longbrake EE, Coyle PK, et al. High-efficacy therapies for treatment-naïve individuals with relapsing-remitting multiple sclerosis. *CNS Drugs*. 2022;36:1285-1299.

[CLICK HERE TO VIEW INFORMATION](#)



Fillippi M, Pia Amato M, Centonze D, et al. Early use of high-efficacy disease modifying therapies makes the difference in people with multiple sclerosis: expert opinion. *J Neurol*. 2022;269:5382-5394.

[CLICK HERE TO VIEW INFORMATION](#)



Sorensen PS, Sellebjerg F. Pulsed immune reconstitution therapy in multiple sclerosis. *Ther Adv Neurol Disord*. 2019;(12):1-16.

[CLICK HERE TO VIEW INFORMATION](#)



Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 and full [Prescribing Information](#) and [Medication Guide](#) for additional information.



REFERENCE COMPENDIUM (Cont.)

Information to support further documentation for your appropriate patients regarding payor coverage for MAVENCLAD and REBIF.

APPENDIX A

MAVENCLAD® (CLADRIBINE) TABLETS REFERENCE COMPENDIUM (CONTINUED)

Dosing and Administration Considerations

The following references may be used to support coverage communications related to:

MAVENCLAD

- **The weight-based dosing schedule of MAVENCLAD®, with 2-year cumulative dosing of 3.5mg/kg & no treatment in years 3 & 4**
 - **Approved dosing for MAVENCLAD is 3.5mg/kg. Higher dosages were associated with increased adverse events**

Giovannoni G, Comi G, Cook S, et al; for the CLARITY Study Group. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. *N Engl J Med.* 2010;362(5):416-426

[CLICK HERE TO VIEW INFORMATION](#)

Giovannoni G, Soelberg Sorensen P, Cook S, et al. Safety and efficacy of cladribine tablets in patients with relapsing-remitting multiple sclerosis: Results from the randomized extension trial of the CLARITY study. *Mult Scler.* 2018;24(12):1594-1604.

[CLICK HERE TO VIEW INFORMATION](#)

Lizak N, Hodgkinson S, Butler E, et al. Real-world effectiveness of cladribine for Australian patients with multiple sclerosis: An MS Base registry substudy. *Mult Scler J.* 2020;27(3):465-474.

[CLICK HERE TO VIEW INFORMATION](#)

DISEASE EDUCATION

- **Patient preference factors, including method of administration**

Hincaple AL, Penm J, Burns CF. Factors associated with patient preferences for disease-modifying therapies in multiple sclerosis. *J Managed Care Spec Pharm.* 2017;23(8):822-830.

[CLICK HERE TO VIEW INFORMATION](#)

- **Considerations about adherence and persistence**

Hersh CM, Brook RA, Beren IA, et al. The implications of suboptimal year-1 outcomes with disease-modifying therapy in employees with multiple sclerosis. *J Med Econ.* 2021;24(1):479-486.

[CLICK HERE TO VIEW INFORMATION](#)

Nicholas JA, Edwards NC, Edwards RA, et al. Real-world adherence to, and persistence with, once- and twice-daily oral disease modifying drugs in patients with multiple sclerosis: a systematic review and meta-analysis. *BMC Neurol.* 2020;20:1-15.

[CLICK HERE TO VIEW INFORMATION](#)

Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 and full [Prescribing Information](#) and [Medication Guide](#) for additional information.



REFERENCE COMPENDIUM (Cont.)

Information to support further documentation for your appropriate patients regarding payor coverage for MAVENCLAD and REBIF.

APPENDIX A

MAVENCLAD® (CLADRIBINE) TABLETS REFERENCE COMPENDIUM (CONTINUED)

Additional Treatment Considerations Related to Patient Comorbidities, Age-Related Factors, and Other Considerations

The following references may be used to support coverage communications related to:

MAVENCLAD

Giovannoni G, Coyle PK, Vermersch P, et al. Integrated lymphopenia analysis in younger and older patients with multiple sclerosis treated with cladribine tablets. *Front Immunol.* 2021;12:763433.

[CLICK HERE TO VIEW INFORMATION](#)



de Seze J, Dive D, Ayrignac X, et al. Narrative Review on the Use of Cladribine Tablets as Exit Therapy for Stable Elderly Patients with Multiple Sclerosis. *Neurol Ther.* 2024;13(3):519-533.

[CLICK HERE TO VIEW INFORMATION](#)



DISEASE EDUCATION

- **Age-related treatment considerations**

Macaron G, Larochelle C, Arbour N, et al. Impact of aging on treatment considerations for multiple sclerosis patients. *Front Neurol.* 2023;14:1197212.

[CLICK HERE TO VIEW INFORMATION](#)



Moccia et al. Emergency medical care for multiple sclerosis: A five-year population study in the Campania Region (South Italy). *Mult Scler.* 2022.

[CLICK HERE TO VIEW INFORMATION](#)



Knapp R, Hardtstock F, Krieger J, et al. Serious infections in patients with relapsing and progressive forms of multiple sclerosis: A German claims data study. *Mult Scler Relat Disord.* 2022;68:104245.

[CLICK HERE TO VIEW INFORMATION](#)



- **Generics & Bioequivalence**

- **The US Food and Drug Administration (FDA) considers a generic bioequivalent if, in a well-designed same-dose study, there's no meaningful difference in how fast or how much the active drug reaches the body. Practically, the 90% confidence interval for key pharmacokinetic ratios (for e.g., AUC, Cmax) must lie entirely between 0.80 and 1.25 (in other words within 80% and 125% of the value for perfect bioequivalence)^{2, 3}**

Straka, R; Keohane, D; Liu, L. Potential Clinical and Economic Impact of Switching Branded Medications to Generics. *American Journal of Therapeutics.* 24(3):p e278-e289, 2017.

[CLICK HERE TO VIEW INFORMATION](#)



Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 and full [Prescribing Information](#) and [Medication Guide](#) for additional information.

References:

2. U.S. Food and Drug Administration. Statistical Approaches to Establishing Bioequivalence. 2001. <https://www.fda.gov/media/70958/download>.
3. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Bioequivalence for Immediate Release Solid Oral Dosage Forms. 2024. https://database.ich.org/sites/default/files/ICH_M13A_Step4_Final_Guideline_2024_0723.pdf



REFERENCE COMPENDIUM (Cont.)

Information to support further documentation for your appropriate patients regarding payer coverage for MAVENCLAD and REBIF.

APPENDIX B

REBIF® (INTERFERON BETA-1A) FOR SUBCUTANEOUS INJECTION REFERENCE COMPENDIUM

REBIF Clinical Profile Information

The following references may be used to support coverage communications related to:

- **The clinical profile of REBIF**
- **PRISMS, a double-blind, placebo-controlled study conducted over 2 years, with a primary endpoint of number of clinical exacerbations/relapses**
- **EVIDENCE, an assessor-blinded, parallel-group study conducted over an average of 64 weeks against Avonex, evaluating efficacy and safety outcomes**

Rebif. Prescribing Information. EMD Serono, Inc.

[CLICK HERE TO VIEW INFORMATION](#)



PRISMS Study Group. Randomised double-blind placebo-controlled study of interferon β -1a in relapsing/remitting multiple sclerosis. *Lancet*. 1998;352(9139):1498-1504.

[CLICK HERE TO VIEW INFORMATION](#)



Panitch H, Goodin DS, Francis G, et al; EVIDENCE Study Group and the University of British Columbia MS/MRI Research Group. Randomized, comparative study of Interferon β -1a treatment regimens in MS: the EVIDENCE trial. *Neurology*. 2002;59(10):1496-1506.

[CLICK HERE TO VIEW INFORMATION](#)



Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 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



Patient and Provider

Field Reimbursement Manager

- Works directly with HCP offices to navigate patient access barriers
- Provides education on local payer policies and coverage landscape
- Field-based partner to Patient Support Specialist

Nurse Support Specialist

- Provides supplementary product education to patients
- Contacts patients throughout their treatment journey to offer support
- 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

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

Please see Important Safety Information for MAVENCLAD on pages 16-17 and full [Prescribing Information](#), including **BOXED WARNING**, and [Medication Guide](#) for additional information.

Please see Important Safety Information for REBIF on pages 18-19 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](https://www.hipaahipaa.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™. If prior authorizations are required, CoverMyMeds can help streamline the process.

Service Request Forms can be provided by your Area Business Manager or downloaded for [MAVENCLAD](#) or [REBIF](#).

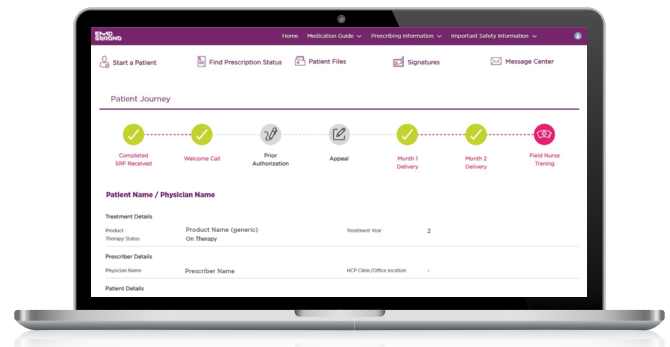


WELCOME TO MS LifeLines Pro™

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**.



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 embryoletality 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.

Please see full [Prescribing Information](#) and [Medication Guide](#) for additional information.



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

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.

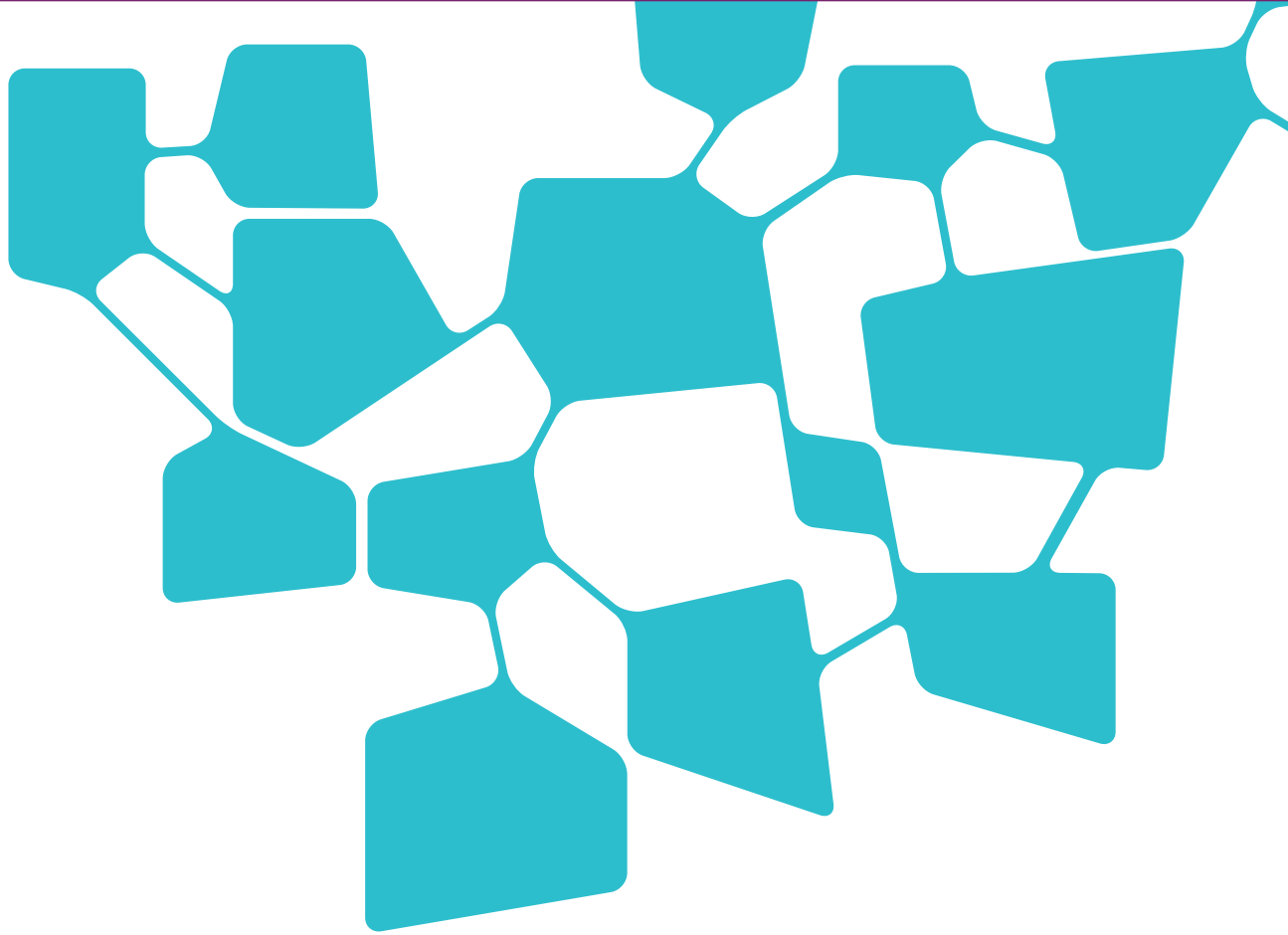
Adverse Reactions: The most common adverse reactions with REBIF are injection-site disorders, influenza-like symptoms, abdominal pain, depression, elevated liver enzymes, and hematologic abnormalities.

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.



© 2026 Merck KGaA, Darmstadt, Germany or its affiliates. All rights reserved. EMD Serono is the Healthcare business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada.

MAVENCLAD, REBIF, REBIF Rebidose, and MS LifeLines are registered trademarks of Merck KGaA, Darmstadt, Germany or its affiliates. MS LifeLines Pro is a trademark of Merck KGaA, Darmstadt, Germany.