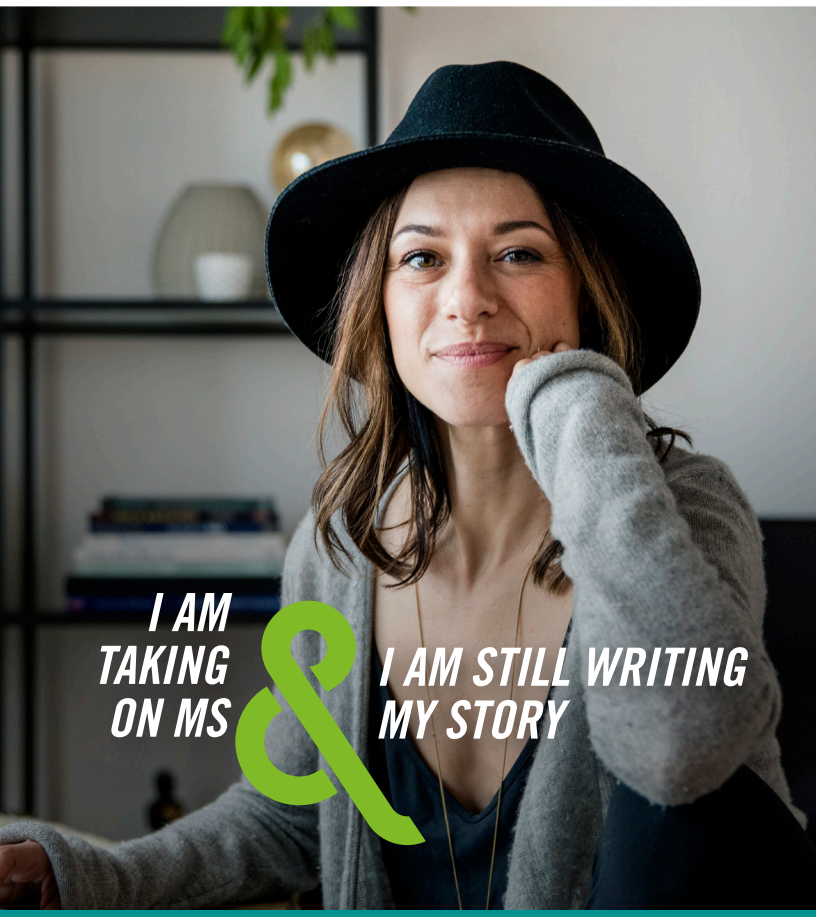
Rebif®
(interferon beta-1a)
subcutaneous injection



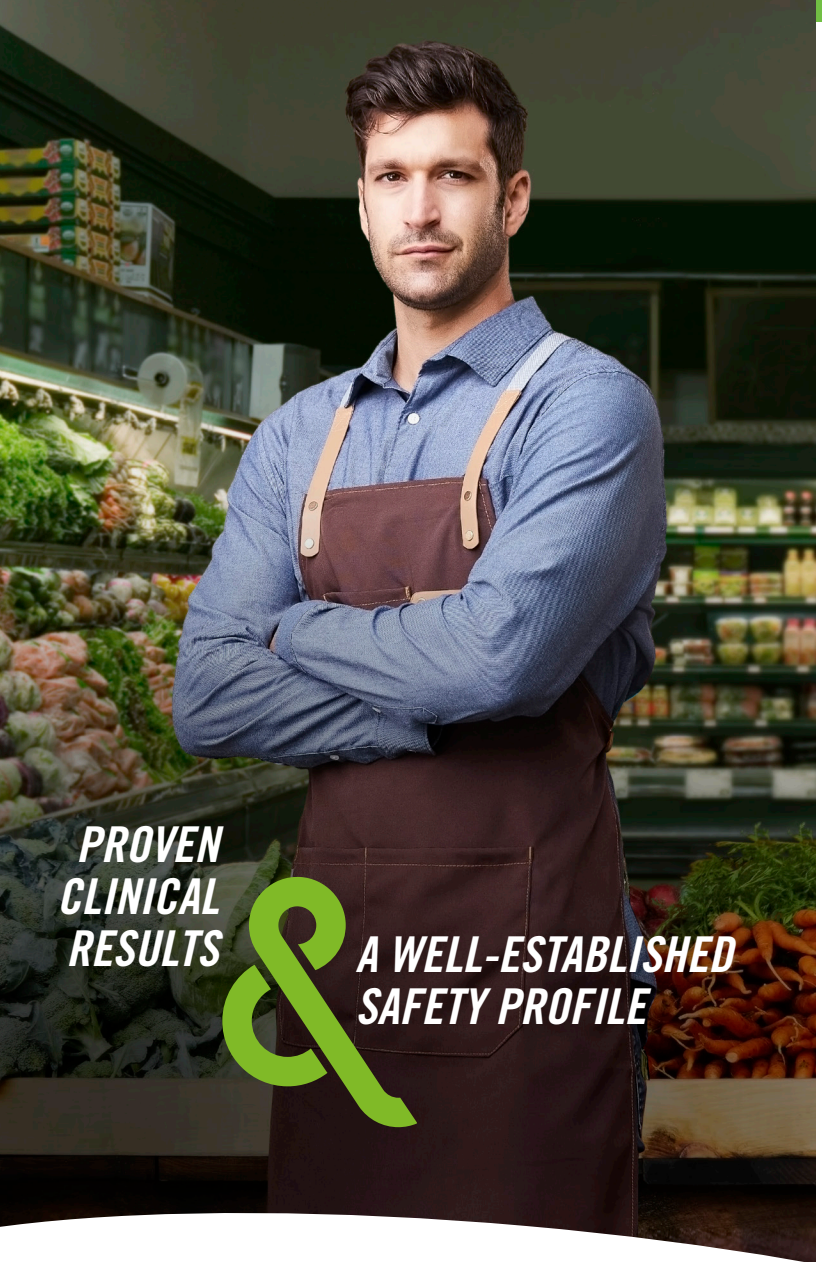
Discover Rebif®

Taking on your MS means knowing your options. Ask your healthcare provider if Rebif might be right for you.

INDICATION

Rebif® (interferon beta-1a) is a prescription medicine used to treat relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is not known if Rebif is safe and effective in children.

Please see Rebif Prescribing Information and Medication Guide and Important Safety Information on pages 11-12.



More than **150,000** people in the US have been prescribed Rebif for relapsing multiple sclerosis (RMS) since it was approved. There are many good reasons why healthcare providers continue to trust Rebif for their patients.

Rebif by the numbers

3 treatment goals met

2 ways Rebif was proven superior to another RMS treatment

20+ years of combined clinical trial data and real-world patient experience support our safety profile

3 injection options to choose from

1 on 1 support from MS LifeLines®

As little as

$0 co-pay or co-insurance for Rebif may be available if you're eligible*

*Some limitations are required by law. Patients covered by federal or state healthcare programs, including Medicare and Medicaid, are not eligible for assistance. See details on page 8.

INDICATION

Rebif® (interferon beta-1a) is a prescription medicine used to treat relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is not known if Rebif is safe and effective in children.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

IMPORTANT SAFETY INFORMATION

Do not take Rebif if you are allergic to interferon beta, human albumin, or any of the ingredients in Rebif.

Rebif® was shown to help with 3 important treatment goals

When compared to a placebo (an inactive substance), Rebif 44 mcg was proven effective at **(1) reducing relapses, (2) reducing new or enlarging MRI brain lesions, and (3) slowing the time to disability progression.**

32% fewer relapses in 2 years

1.73 relapses, on average, with Rebif (n=184) | 2.56 relapses, on average, with placebo (n=187)

84% fewer T1 lesions at 9 months

1.3 lesions with Rebif (n=68) | 8.0 lesions with placebo (n=66)

T1-weighted gadolinium-enhanced* (T1-Gd+) brain lesions†‡§

78% fewer new or enlarging T2 lesions at 2 years

0.5 lesions with Rebif (n=171) | 2.25 lesions with placebo (n=172)

Nearly 2x longer to disability progression‖

21.3 months for Rebif (n=184) | 11.9 months for placebo (n=187)

The 2-year study looked at 560 people to see how they responded. 189 people took Rebif 22 mcg; 184 took Rebif 44 mcg; and 187 took a placebo, all given under the skin 3 times a week.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

It's important to inform your healthcare provider of any side effects that you experience. There may be things you can do to help manage them.

Rebif can cause serious side effects:

- Behavioral health problems including depression and suicidal thoughts
- Liver problems or worsening of liver problems including liver failure
- Serious allergic and skin reactions
- Injection site problems
- Blood problems
- Seizures

The most common side effects of Rebif include:

- Flu-like symptoms
- Stomach pain
- Change in liver blood tests

*Refers to new lesions and total lesion burden or area as defined in the American Academy of Neurology (AAN) and MS Council guidelines.

†From a subgroup of 134 patients in the PRISMS study who received 11 consecutive monthly T2 and T1-Gd+ MRI scans beginning 1 month before treatment initiation.

‡Median number of lesions, per patient per scan, based on comparisons from rank-based ANOVA. Lesions detected with both T1-Gd+ and T2-weighted MRI. Median = a value in an ordered set that has an equal number of values higher and lower.

§The number of lesions represents new or enlarging lesions, per patient per scan.

‖Disability progression was defined as an increase of at least 1 point in the EDSS that was sustained for at least 3 months.

IMPORTANT SAFETY INFORMATION (cont'd)

Rebif can cause serious side effects. Tell your healthcare provider right away if you have any of the symptoms listed below while taking Rebif.

- **Behavioral health problems including depression and suicidal thoughts.** You may have mood problems including depression (feeling hopeless or feeling bad about yourself), and thoughts of hurting yourself or suicide.

A head-to-head study proved Rebif® was superior to another interferon beta-1a

High-dose, high-frequency Rebif (interferon beta-1a) was proven superior to low-dose, low frequency Avonex® (interferon beta-1a)* in 2 important ways.

Relapses

More people on Rebif remained free from relapses

75% On Rebif (n=339) vs **63%** On Avonex® (n=338)

Average of 24 weeks on treatment

MRI Lesions

More people on Rebif were free of T1-weighted gadolinium-enhanced (T1-Gd+) lesions

55% On Rebif (n=325) vs **38%** On Avonex® (n=325)

Average of 24 weeks on treatment

More people on Rebif showed no new or enlarging T2 brain lesions

60% On Rebif (n=325) vs **43%** On Avonex® (n=325)

Average of 24 weeks on treatment

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

The EVIDENCE† study compared Rebif to Avonex® to see which treatment was more effective.

In the EVIDENCE study, the side effects of Rebif and Avonex® were generally similar, with the following exceptions:

Side effects	% of people Rebif 44 mcg	% of people Avonex® 30 mcg
Flu-like symptoms	45%	53%
Injection-site reactions	85%	33%
Liver disorders	18%	10%
White blood cell disorders	14%	5%

Represents adverse events reported over an average of 64 weeks.

*The approved Avonex® dose is 30 mcg per week.

† **EV**idence of **I**nterferon **D**ose-response: **E**uropean **N**orth American **C**omparative **E**fficacy. 339 people received Rebif 44 mcg 3 times a week under the skin. 338 people received Avonex® 30 mcg 1 time a week into the muscle.

See the study details at rebif.com/evidence

IMPORTANT SAFETY INFORMATION (cont'd)

- **Liver problems or worsening of liver problems including liver failure.** Symptoms may include nausea, loss of appetite, tiredness, dark colored urine and pale stools, yellowing of your skin or the white part of your eye, bleeding more easily than normal, confusion, and sleepiness. During your treatment with Rebif you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.
- **Serious allergic and skin reactions.** Symptoms may include itching, swelling of your face, eyes, lips, tongue or throat, trouble breathing, anxiousness, feeling faint, skin rash, hives, sores in your mouth, or skin blisters and peels.

Rebif® has a well-established safety profile

The safety profile of Rebif is supported by more than 20 years of combined clinical trial data* and real-world patient experience. Here are some topics to discuss with your healthcare provider:

20+ years

of combined clinical trial data and real-world patient experience

150 thousand +

US patients prescribed since approval

NO PML

Rebif has not been associated with progressive multifocal leukoencephalopathy, a rare brain disease.

*Common adverse events have been consistent across trials.

Rebif (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

Rebif (interferon beta-1a) is an immunomodulator, a medication used to help regulate the immune system. It doesn't continuously suppress your immune system.

Infection information

When it comes to the risk of infection, clinical studies showed:

Patients treated with Rebif showed a similar incidence of infections compared to placebo

Rebif did not result in increases in the incidence of viral, bacterial, or fungal infections

Some people develop lower white blood cell counts which could increase the risk of infection. Your doctor should monitor your white blood cell count during the course of your therapy with Rebif

Vaccination while using Rebif

Getting vaccinated is a key part of medical care, and that is no different for people with MS. Some inactivated vaccines may provide protection and may be administered while treating your MS with an interferon, like Rebif.

Ask your healthcare provider about your ability to be vaccinated while taking Rebif. They will use their clinical judgment and refer to the latest medical information to decide what is right for you.

IMPORTANT SAFETY INFORMATION (cont'd)

Injection site problems. Rebif may cause redness, pain, itching or swelling at the place where your injection was given. Call your healthcare provider right away if an injection site becomes swollen and painful or the area looks infected. You may have a skin infection or an area of severe skin damage (necrosis) requiring treatment by a healthcare provider.

Family planning with Rebif®

If you have MS and are thinking about having a child, it's important to choose a treatment that can help you manage your MS while planning for a family.

Although your doctor may determine that you can continue on Rebif until you become pregnant, you should call your healthcare provider immediately and stop taking Rebif if you become pregnant.

It is not known if Rebif can harm your unborn baby.

Rebif may pass into your breastmilk. Talk with your healthcare provider about the best way to feed your baby if you take Rebif.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

MS pregnancy data

The possible effects of interferon beta during pregnancy were evaluated in a pregnancy registry. This registry tracked the outcomes of 2,831 pregnancies of women with multiple sclerosis in Finland from 1996-2014 and Sweden from 2005-2014.

Early in their pregnancies, some women were exposed to interferon beta, including Rebif (n=797 pregnancies), while others were not exposed to any disease-modifying drugs (n=1,647 pregnancies).

THE STUDY DID NOT IDENTIFY:

an increased drug-associated risk of major birth defects among the women exposed to interferon beta in early pregnancy

OR

an increased risk of miscarriage or ectopic pregnancy. However, limitations in obtaining complete data capture for these outcomes made the interpretation of these findings more difficult

IMPORTANT SAFETY INFORMATION (cont'd)

- **Blood problems.** Rebif can affect your bone marrow and cause low red and white blood cell and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising. Your healthcare provider may ask you to have regular blood tests to check for blood problems.
- **Seizures.** Some people have had seizures while taking Rebif.

Rebif® offers 3 injection options

To find the option that's right for you, speak with your healthcare provider. If you have any questions, you can also talk to an MS LifeLines® Nurse at **1-877-447-3243**.

Once you choose an injection option, an MS LifeLines® Nurse can come to your home to help you learn how to use it properly. Learn more about MS LifeLines® on pages 14 and 15.

Rebif should be refrigerated between 36°F to 46°F (2°C to 8°C). Do not freeze. If refrigeration is not available, Rebif can be stored at room temperature above 36°F and below 77°F (2°C to 25°C) for up to 30 days away from heat and light.

For complete injection instructions, please see the Instructions for Use that comes with your Rebif injection option. You should use Rebif only after you have received proper training from a medical professional.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

PREASSEMBLED, PREFILLED SYRINGES*

- Ready to use
- No mixing or assembly required

REBIJECT II® AUTOINJECTOR*

- Works with the Rebif prefilled syringe
- Ability to adjust the injection depth into skin
- Available at no additional cost

REBIF REBIDOSE® (INTERFERON BETA-1A)*

- Portable, prefilled, single-use autoinjector
- Needle remains hidden before and after injecting

*Images shown are not actual size.

IMPORTANT SAFETY INFORMATION (cont'd)

Injection site problems. Rebif may cause redness, pain, itching or swelling at the place where your injection was given. Call your healthcare provider right away if an injection site becomes swollen and painful or the area looks infected. You may have a skin infection or an area of severe skin damage (necrosis) requiring treatment by a healthcare provider.

Get one-on-one support with MS LifeLines®

For patients who have been prescribed Rebif, MS LifeLines® delivers individualized support services that can help you understand your treatment and your financial options.

Our dedicated Financial Support Specialists can help you navigate your insurance coverage for Rebif and find assistance, if you are eligible, for MS LifeLines® programs.

MS LifeLines® Nurses can help answer many questions about relapsing forms of multiple sclerosis and treatment with Rebif (interferon beta-1a), including proper injection techniques.

MSLifeLines®

We're here to help.
Call us at **1-877-447-3243** or visit us at **mslifelines.com**.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

Co-pay support

When you enroll in MS LifeLines®, you may be able to receive Rebif at no cost to you.

As little as $0 co-pay or co-insurance for Rebif may be available if you're eligible* and have insurance

OR

For eligible patients, MS LifeLines® offers other assistance programs, including free medication, to help ensure appropriate patients have access to Rebif

* Some limitations are required by law. Patients covered by federal or state healthcare programs, including Medicare and Medicaid, are not eligible for assistance. This program is open to residents of the US and Puerto Rico with relapsing forms of multiple sclerosis who are starting Rebif or presently taking Rebif.

IMPORTANT SAFETY INFORMATION (cont'd)

Before you take Rebif, tell your healthcare provider if you have or have had any of the following conditions:

- mental illness, including depression and suicidal behavior
- liver problems
- bleeding problems or blood clots
- low blood cell counts
- seizures (epilepsy)
- thyroid problems
- you drink alcohol
- you are pregnant or plan to become pregnant. It is not known if Rebif will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with Rebif
- you are breastfeeding or plan to breastfeed. It is not known if Rebif passes into your breast milk. You and your healthcare provider should decide if you will use Rebif or breastfeed. You should not do both

Doctor Discussion Starters

These questions can help guide your discussion with your healthcare provider about finding an RMS treatment that works for you.

- ☐ What treatment goals should I consider when looking at my treatment options?
- ☐ Is Rebif® proven effective at helping reduce relapses and lesions, and slowing disability progression?
- ☐ What might make 1 treatment a better choice for me than another?
- ☐ How might my immune system be affected by treatment with Rebif?
- ☐ What are the possible side effects of my treatment options?
- ☐ Can I keep treating my MS while I am trying to get pregnant?
- ☐ Can I change which Rebif injection option I use later on?
- ☐ What kinds of support options are available to me?

Use this space to write down any additional questions or notes.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

Use this space to write down any additional questions or notes.

Rebif® (interferon beta-1a) subcutaneous injection

Please see Rebif® Prescribing Information and Medication Guide, and Important Safety Information on pages 11-12.

INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

Rebif® (interferon beta-1a) is a prescription medicine used to treat relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is not known if Rebif is safe and effective in children.

Important Safety Information

Do not take Rebif if you are allergic to interferon beta, human albumin, or any of the ingredients in Rebif.

Rebif can cause serious side effects. Tell your healthcare provider right away if you have any of the symptoms listed below while taking Rebif.

- **Behavioral health problems including depression and suicidal thoughts.** You may have mood problems including depression (feeling hopeless or feeling bad about yourself), and thoughts of hurting yourself or suicide.
- **Liver problems or worsening of liver problems including liver failure.** Symptoms may include nausea, loss of appetite, tiredness, dark colored urine and pale stools, yellowing of your skin or the white part of your eye, bleeding more easily than normal, confusion, and sleepiness.

  During your treatment with Rebif you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.
- **Serious allergic and skin reactions.** Symptoms may include itching, swelling of your face, eyes, lips, tongue or throat, trouble breathing, anxiousness, feeling faint, skin rash, hives, sores in your mouth, or skin blisters and peels.
- **Injection site problems.** Rebif may cause redness, pain, itching or swelling at the place where your injection was given. Call your healthcare provider right away if an injection site becomes swollen and painful or the area looks infected. You may have a skin infection or an area of severe skin damage (necrosis) requiring treatment by a healthcare provider.
- **Blood problems.** Rebif can affect your bone marrow and cause low red and white blood cell and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising. Your healthcare provider may ask you to have regular blood tests to check for blood problems.
- **Seizures.** Some people have had seizures while taking Rebif.

Rebif® (interferon beta-1a) subcutaneous injection

INDICATION AND IMPORTANT SAFETY INFORMATION (cont'd)

Before you take Rebif, tell your healthcare provider if you have or have had any of the following conditions:

- mental illness, including depression and suicidal behavior
- liver problems
- bleeding problems or blood clots
- low blood cell counts
- seizures (epilepsy)
- thyroid problems
- you drink alcohol
- you are pregnant or plan to become pregnant. It is not known if Rebif will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with Rebif
- you are breastfeeding or plan to breastfeed. It is not known if Rebif passes into your breast milk. You and your healthcare provider should decide if you will use Rebif or breastfeed. You should not do both

Tell your healthcare provider about all medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

The most common side effects of Rebif include:

- flu-like symptoms. You may have flu-like symptoms when you first start taking Rebif. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include muscle aches, fever, tiredness, and chills
- stomach pain
- change in liver blood tests

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of Rebif. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see Rebif® Prescribing Information and Medication Guide.

Rebif® (interferon beta-1a) subcutaneous injection

Rebif®
(interferon beta-1a)
subcutaneous injection

Not all interferons are the same

When choosing a treatment for your RMS, keep in mind that there are several interferon treatment options to choose from. These treatments may differ in many ways, including formulation, method of delivery, frequency, and dose.

Ask your healthcare provider about Rebif®, an interferon that might be right for you.

IMPORTANT SAFETY INFORMATION (cont'd)

The most common side effects of Rebif include:

- flu-like symptoms. You may have flu-like symptoms when you first start taking Rebif. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include muscle aches, fever, tiredness, and chills
- stomach pain
- change in liver blood tests

Want more info about Rebif?

Call MS LifeLines® at 1-877-447-3243

Visit Rebif.com

EMD SERONO