

Medication Guide

Rebif[®] (Re-bif)

interferon beta-1a
(in-ter-feer-on beta-one-â)

Please read this leaflet carefully before you start to use Rebif[®] and each time your prescription is refilled since there may be new information. The information in this medication guide does not take the place of regularly talking with your doctor or health care provider.

What is the most important information I should know about Rebif[®]?

Rebif[®] will not cure multiple sclerosis (MS) but it has been shown to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. Rebif[®] can cause serious side effects, so before you start taking Rebif[®], you should talk with your doctor about the possible benefits of Rebif[®] and its possible side effects to decide if Rebif[®] is right for you. Potential serious side effects include:

- **Depression.** Some patients treated with interferons, including Rebif[®], have become seriously depressed (feeling sad). Some patients have thought about killing themselves and a few have committed suicide. Depression (a sinking of spirits or sadness) is not uncommon in people with multiple sclerosis. However, if you are feeling noticeably sadder or helpless, or feel like hurting yourself or others, you should tell a family member or friend right away and call your doctor as soon as possible. Your doctor may ask that you stop using Rebif[®]. You should also tell your doctor if you have ever had any mental illness, including depression, and if you take any medications for depression.
- **Liver problems.** Your liver may be affected by taking Rebif[®] and a few patients have developed severe liver injury. Your health care provider may ask you to have regular blood tests to make sure that your liver is working properly. If your skin or the whites of your eyes become yellow or if you are bruising easily you should call your doctor right away.
- **Risk to pregnancy.** If you become pregnant while taking Rebif[®] you should call your doctor right away. Rebif[®] may cause you to lose your baby (miscarry) or may cause harm to your unborn child. You and your doctor will need to decide whether the potential benefit of taking Rebif[®] is greater than the risks are to your unborn child.

- **Allergic reactions.** Some patients taking Rebif[®] have had severe allergic reactions leading to difficulty breathing, and loss of consciousness. Allergic reactions can happen after your first dose or may not happen until after you have taken Rebif[®] many times. Less severe allergic reactions such as itching, flushing or skin bumps can also happen at any time. If you think you are having an allergic reaction, stop using Rebif[®] immediately and call your doctor.

- **Injection site problems.** Rebif[®] may cause redness, pain or swelling at the place where an injection was given. Some patients have developed skin infections or areas of severe skin damage (necrosis) requiring treatment by a doctor. If one of your injection sites becomes swollen and painful or the area looks infected and it doesn't heal within a few days, you should call your doctor.

What is Rebif[®]?

Rebif[®] is a type of protein called beta interferon that occurs naturally in the body. It is used to treat relapsing forms of multiple sclerosis. It will not cure your MS but may decrease the number of flare-ups of the disease and slow the occurrence of some of the physical disability that is common in people with MS. MS is a life-long disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers. The way Rebif[®] works in MS is not known.

Who should not take Rebif[®]?

Do not take Rebif[®] if you:

- have had an allergic reaction such as difficulty breathing, flushing or hives to another interferon beta or to human albumin.

If you have any of the following conditions or serious medical problems, you should tell your doctor before taking Rebif[®]:

- Depression (a sinking feeling or sadness), anxiety (feeling uneasy or fearful for no reason), or trouble sleeping
- Liver diseases
- Problems with your thyroid gland
- Blood problems such as bleeding or bruising easily and anemia (low red blood cells) or low white blood cells
- Epilepsy
- Are planning to become pregnant

Tell your doctor about all medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. Rebif[®] and other medicines may affect each other causing serious side effects. Talk to your doctor before you take any new medicines.

How should I take Rebif[®]?

Rebif[®] is given by injection under the skin (subcutaneous injection) on the same

three days a week (for example, Monday, Wednesday and Friday). Your injections should be at least 48 hours apart so it is best to take them the same time each day. Your doctor will tell you what dose of Rebif[®] to use, and may change the dose based on how your body responds. You should not change the dose without talking with your doctor.

If you miss a dose, you should take your next dose as soon as you remember or are able to take it, then skip the following day. **Do not take Rebif[®] on two consecutive days.** You should return to your regular schedule the following week. If you accidentally take more than your prescribed dose, or take it on two consecutive days, call your doctor right away.

You should always follow your doctor's instructions and advice about how to take this medication. If your doctor feels that you, or a family member or friend may give you the injections then you and/or the other person should be trained by your doctor or health care provider in how to give an injection. Do not try to give yourself (or have another person give you) injections at home until you (or both of you) understand and are comfortable with how to prepare your dose and give the injections.

Always use a new, unopened, pre-filled syringe of Rebif[®] or Rebidose[®] autoinjector for each injection. Do not reuse pre-filled syringes or Rebidose[®] autoinjectors.

It is important that you change your injection site each time Rebif[®] is injected. This will lessen the chance of your having a serious skin reaction at the spot where you inject Rebif[®]. You should always avoid injecting Rebif[®] into an area of skin that is sore, reddened, infected or otherwise damaged.

At the end of this leaflet, there are detailed instructions on how to prepare and give an injection of Rebif[®] using a pre-filled syringe. For the Rebidose[®] autoinjector, refer to the Instructions for Use that comes with the Rebidose[®] autoinjector. You should become familiar with all instructions and follow your doctor's orders before injecting Rebif[®].

What should I avoid while taking Rebif[®]?

- **Pregnancy.** You should avoid becoming pregnant while taking Rebif[®] until you have talked with your doctor. Rebif[®] can cause you to lose your baby (miscarry).
- **Breast feeding.** You should talk to your doctor if you are breast feeding an infant. It is not known if the interferon in Rebif[®] can be passed to an infant in mother's milk, and it is not known whether the drug could harm the infant if it is passed to an infant.

• Rebif® and other medicines may affect each other causing serious side effects. Talk to your doctor before you take any new medicines.

What are the possible side effects of Rebif®?

• **Flu-like symptoms.** Most patients have flu-like symptoms (fever, chills, sweating, muscle aches and tiredness). For many patients, these symptoms will lessen or go away over time. You should talk to your doctor about whether you should take an over the counter medication for pain or fever reduction before or after taking your dose of Rebif®.

• **Skin reactions.** Soreness, redness, pain, bruising or swelling may occur at the place of injection. See “What is the most important information I should know about Rebif®?”

• **Depression and anxiety.** Some patients taking interferons have become very depressed and or anxious. There have been patients taking interferons who have had thoughts about killing themselves. If you feel sad or hopeless you should tell a friend or family member right away and call your doctor immediately. See “What is the most important information I should know about Rebif®?”

• **Liver problems.** Your liver function may be affected. If you develop symptoms of changes in your liver, including yellowing of the skin and whites of the eyes and easy bruising, call your doctor immediately. See “What is the most important information I should know about Rebif®?”

• **Blood problems.** You may have a drop in the levels of infection-fighting blood cells, red blood cells or cells that help to form blood clots. If the drop in levels are severe, they can lessen your ability to fight infections, make you feel tired or sluggish or cause you to bruise or bleed easily.

• **Thyroid problems:** Your thyroid function may change. Symptoms of changes in the function of your thyroid include feeling cold or hot all the time, change in your weight (gain or loss) without a change in your diet or amount of exercise you are getting.

• **Allergic reactions:** Some patients have had hives, rash, skin bumps or itching while they were taking Rebif®. Other patients have had more serious allergic reactions such as difficulty breathing, or feeling light-headed. You should tell your doctor if you think you are having an allergic reaction. See “What is the most important information I should know about Rebif®?”

Whether you experience any of these side effects or not, you and your doctor should periodically talk about your general health. Your doctor may want to monitor you more closely and ask you to have blood tests done more frequently.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Storage Conditions

Rebif® is packaged in pre-filled syringes with needles already attached to the syringe and in pre-assembled, single-use autoinjectors, called Rebidose®, with needles already attached within the autoinjector.

Rebif® should be stored refrigerated between 36°F to 46°F (2°C to 8°C). **Do Not Freeze.** If a refrigerator is not available, Rebif® may be stored between 36°F to 77°F (2°C to 25°C) for up to 30 days and away from heat and light.

General Information About Prescription Medicines

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This medication has been prescribed for your particular medical condition. Do not use it for another condition or give this drug to anyone else. If you have any questions you should speak with your doctor or health care provider. You may also ask your doctor or pharmacist for a copy of the information provided to them with the product.

Keep this and all drugs out of the reach of children.

Instructions for Preparing and Giving Yourself an Injection of Rebif® using a Rebidose® autoinjector

Refer to the Instructions for Use that comes with the Rebidose® autoinjector.

Instructions for Preparing and Giving Yourself an Injection of Rebif® using a pre-filled syringe

Before you begin, gather all of the supplies listed below:

- Rebif® pre-filled syringe or Rebidose® autoinjector.
- Alcohol swabs (wipes) or cotton balls and rubbing alcohol
- Small adhesive bandage strip (if desired)
- Puncture resistant safety container for disposal of used syringes
- Antibacterial soap
- An over-the-counter pain or fever reducing medication, if your doctor has recommended that you take this prior to, at the same time, or after you give yourself Rebif® to help minimize the fever, chills, sweating and muscle aches (flu-like symptoms) that may occur.

When first starting treatment with Rebif®, your doctor may prescribe either the 22 mcg or 44 mcg dose of Rebif®. You should gradually increase the dose over 4 weeks, starting at 20% of the prescribed dose for the first 2 weeks, half-dose for the second 2 weeks (weeks 3 and 4), and then the full dose prescribed by your doctor.

If your prescribed dose is 22 mcg dose of Rebif®, a Rebif® Titration Pack containing 6 pre-filled syringes with 8.8 mcg and 6 pre-filled syringes with 22 mcg should be prescribed to you for use during the 4 week titration period. Table 1 explains the amount to inject using the Rebif® Titration Pack syringes to gradually increase to 22 mcg.

Table 1: Titration Schedule for a 22 mcg Prescribed Dose*

| Week of Use | Syringe to Use | Amount of syringe |
|------------------|--------------------------------|----------------------------------|
| Week 1 Titration | 8.8 mcg syringe | Use half of syringe |
| Week 2 Titration | 8.8 mcg syringe | Use half of syringe |
| Week 3 Titration | 22 mcg syringe | Use half of syringe |
| Week 4 Titration | 22 mcg syringe | Use half of syringe |
| Week 5 and on | 22 mcg syringe or autoinjector | Use full syringe or autoinjector |

* Only pre-filled syringes can be used to titrate to 22 mcg Prescribed Dose

If your prescribed dose is 44 mcg, you may be prescribed either a Rebif® Titration Pack (described above) or Rebif® Rebidose® Titration Pack containing 6 autoinjectors with 8.8 mcg and 6 autoinjectors with 22 mcg for use during the 4 week titration period. Table 2 explains the amount to inject using the Rebif® Titration Pack or Rebif® Rebidose® Titration Pack to gradually increase to 44 mcg.

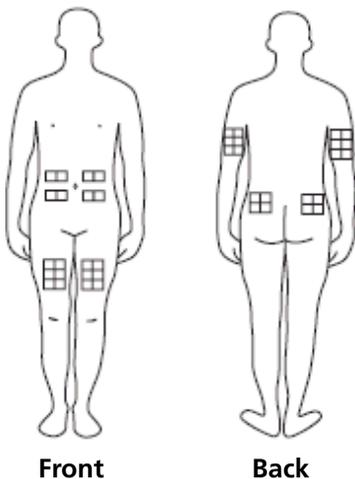
Table 2: Titration Schedule for a 44 mcg Prescribed Dose**

| Week of Use | Syringe or Autoinjector to Use | Amount of syringe or autoinjector |
|------------------|---------------------------------|-----------------------------------|
| Week 1 Titration | 8.8 mcg syringe or autoinjector | Use full syringe or autoinjector |
| Week 2 Titration | 8.8 mcg syringe or autoinjector | Use full syringe or autoinjector |
| Week 3 Titration | 22 mcg syringe or autoinjector | Use full syringe or autoinjector |
| Week 4 Titration | 22 mcg syringe or autoinjector | Use full syringe or autoinjector |
| Week 5 and on | 44 mcg syringe or autoinjector | Use full syringe or autoinjector |

** Pre-filled syringes or autoinjectors can be used to titrate to 44 mcg Prescribed Dose

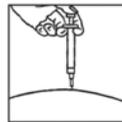
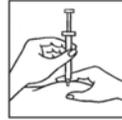
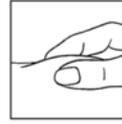
Preparing for an injection:

- Check the expiration date; **do not use if the medication is expired.** The expiration date is printed on the syringe, plastic syringe packaging and carton.
- You may wish to remove your medication from the refrigerator at least 30 minutes prior to use so it can warm to room temperature. Do not heat or microwave the medication.
- Be sure that the dose, either, 8.8 mcg, 22 mcg or 44 mcg, described on the carton is the same as the dose prescribed by your doctor.
- Remove the Rebif® syringe or autoinjector from the plastic packaging. Keep the needle capped.
- Examine the contents of the syringe carefully. The liquid should be clear to slightly yellow. **Do not use if the liquid is cloudy, discolored or contains particles.**
- Choose only one site for injection. The best sites for giving yourself an injection are those areas with a layer of fat between the skin and muscle, like your thigh, the outer surface of your upper arm, your stomach or buttocks. Do not use the area near your waistline or within 2 inches of your navel. If you are very thin, use only the thigh or outer surface of the arm for injection. Use a different site each time you inject (thigh, hip, stomach or upper arm, see Figure below). Do not inject Rebif® into an area of your body where the skin is irritated, reddened, bruised, infected or abnormal in any way.
- Keep a record of the date and location of each injection.
- Wash your hands thoroughly with antibacterial soap before preparing to inject the medication.
- Clean the injection site with an alcohol swab (wipe) or cotton ball with rubbing alcohol using a circular motion. To avoid stinging, you should let your skin dry before you inject Rebif®.



Giving yourself an injection of Rebif® using a pre-filled syringe

- Remove the needle cap from the syringe needle.
- If your doctor has told you to use less than the full 0.5 mL dose, slowly push the plunger in until the amount of medication left in the syringe is the amount your doctor told you to use.
- Use your thumb and forefinger to pinch a pad of skin surrounding the cleaned injection site (see adjacent figure). Hold the syringe like a pencil with your other hand.
- While still pinching the skin, swiftly insert the needle like a dart at about a 90 degree angle (just under the skin) into the pad of tissue as shown.
- After the needle is in, remove the hand that you used to pinch your skin and inject the drug using a slow, steady push on the plunger until all the medication is injected and the syringe is empty.
- Withdraw the needle and apply gentle pressure to the injection site with a dry cotton ball or sterile gauze. Applying a cold compress or ice pack to the injection site after injection may help reduce local skin reactions.
- Put a small adhesive bandage strip over the injection site, if desired.
- After 2 hours, check the injection site for redness, swelling, or tenderness. If you have a skin reaction and it doesn't clear up in a few days, contact your doctor or nurse.



Disposing of Needles, Syringes and Rebidose® autoinjectors

There are special state or local laws for properly disposing used needles, syringes and Rebidose® autoinjectors. Your doctor or health care provider will instruct you on the discarding procedure and may provide you with a FDA-cleared disposal container called a Sharps container.

Put your used needles, syringes, or Rebidose® autoinjectors in a Sharps container right away after use. Do not throw away (dispose of) any sharps in your household trash.

If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,

- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Always keep your disposal container out of the reach of children.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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