Rebif®

(REE bif)

Generic name: interferon beta-1a (in ter FEER on, BAY ta, won ay)

What is Rebif®?
Interferons are proteins made in the body to regulate the immune system. They provide chemical signals that increase or decrease the activity of various cell types within the immune system. Rebif® was made by splicing the human gene for interferon beta-1a into mammalian cells that are grown in tissue culture. The interferon made by these cells is isolated and purified to make the medication.

Rebif® decreases the activity of certain white blood cells that are believed to be involved in the immune system attack on the nervous system in multiple sclerosis. It also makes it more difficult for white blood cells to cross from the bloodstream into the brain. This medicine does not suppress the immune system, and patients taking it do not have an increased risk of infection.

Rebif® slows the course of multiple sclerosis when used regularly over long periods of time. It does not improve existing symptoms and is not used to treat acute MS attacks.

Starting on Rebif®
To obtain Rebif®

1. A start form must be completed and faxed to the MS Lifelines program. This program, operated by EMD Serono (the manufacturer of Rebif®), will start the process of obtaining the medication. Pharmacotherapy clinic staff can assist with completion of these forms and getting insurance approval. It takes 1-2 weeks to get insurance approval. Sometimes, insurance denials and appeals may take longer.

2. Insurance often pays only part of the cost of Rebif®. The contract between the patient and the insurance company specifies the amount of deductibles and copayments.
   a. The deductible is the amount patients must pay each year before their insurance starts covering costs.
   b. The copayment is the amount patients must pay for each medical bill. For medications, the copayment is often a percent of the medication’s cost. Pharmacotherapy clinic staff can assist in getting the manufacturer or foundations to decrease the cost of deductibles and copayments.

3. The medication is not stocked in your pharmacy. It must be shipped overnight from a distributor to either your home or your pharmacy (depending on insurance requirements). Pharmacotherapy clinic staff can assist in the shipping process.

After the medication arrives, those living near the Center should contact our nurse for training on how to administer the Rebif®. Those living outside our region will have training done by visiting nurses.
When first starting Rebif®, it should be started at a low dose and tapered upwards. Rebif® provides a titration kit that has numbered syringes for titration. The typical titration is as follows:

- Weeks 1-2: 8.8 mcg three times a week
- Weeks 3-4: 22 mcg three times a week
- Weeks 5+: 44 mcg three times a week

Rebif® often causes aching and fevers (flu-like side effects) when first starting on the medication. These occur about an hour after the injection, and last about 8 hours. These side effects can be minimized by:

- Taper upwards from a low dose when starting the medication (see above)
- Take medications for this in the beginning. These should be taken at the time of the injection and if needed the following day. They should be taken with each dose until the full dose of Rebif® is achieved. At that time, if side effects are tolerable then the medications to prevent these side effects can be tapered. For patients with kidney or liver impairment, check with your healthcare provider on the maximum daily dose of these medications. Medications that help minimize the flu-like side effects include:
  - Ibuprofen (Advil, Motrin): can take up to 800mg three times a day
  - Naproxen (Aleve): can take up to 250-550mg twice a day
  - Aspirin: can take up to 650mg every six hours
  - Acetaminophen (Tylenol and others): can take up to 650-1000mg every 6 hours
- Inject the medication at bedtime so that most of the side effects occur during sleep

Safety Monitoring

- Blood counts and liver function. There is no standard frequency for these tests, but our Center does blood tests about every three months during the first year with lesser frequencies after that.
- Thyroid testing is indicated if symptoms of thyroid dysfunction develop.

How should Rebif® be taken?

Rebif® is given by injection under the skin (subcutaneous).
Volume injected: 0.5 mL (0.5 cc).
Needle size: 29 gauge, ½ inch length
Autoinjector: available for those who want to use it.
Frequency: 3 times a week (no less than 48 hours apart).
Injection site locations: Injections should be rotated among various sites. Sites include front of the thighs, back of arms, buttocks and abdomen.
**Injection sites:** The medication guide provided by the manufacturer contains a diagram of where injections can be given. However, injections can be given in a wider territory than described in the medication guide. Below are the areas that we recommend using.

**Abdomen:**
- Avoid hitting ribs
- Avoid belly button
- Inject into fat on flank but not into muscle
- Avoid crease between abdomen and thigh

**Buttock:**
- Stay below the bones where your beltline is
- Avoid midline where there is not much fat below the skin
- Avoid skin that you would sit on
- 3-4 inches below top of leg
- 3-4 inches above kneecap
- From inside pant seam to outside pant seam
- Keep to areas that you can pinch some fat for injections
**What if a dose is missed?**
Take the next dose as soon as you can after remembering. Doses should be given about 48 hours apart.

**How should Rebif® be stored?** Rebif® should be refrigerated. However, it may be kept at room temperature for up to 30 days.

**How supplied:** Rebif® comes in prepackaged kits containing all needed supplies. It comes in single dose prefilled syringes. There are 12 syringes per carton.

**What are the common side effects?**
- Injection site reactions: Injection site pain, or a lump under the skin at the injection site are common. In 3% of people, the injection site may break down into a sore (necrosis) that may be slow to heal. Injection site reactions can be minimized by:
  - Keep the needle and other equipment clean.
  - Rotating the injection sites.
  - Some find that applying warm packs before or after the injection may help. Others find that cool packs help. Experiment to see which works best for you.
  - Be sure the needle is deep enough to keep the medication from reacting just beneath the skin.
  - Don’t remove the air bubble, and don’t squirt the drug out the end of the needle that you use to inject with. The medication left on the tip of the needle may track to the surface of the skin.
  - Lidocaine creams such as Emla® or Elamax® may decrease injection site pain on the surface of the skin.
  - Hydrocortisone cream may decrease the inflammation.
- Injection site bruising: This is caused by blood leaking along the needles tract. This can be minimized by applying firm pressure to the injection site for a full minute, immediately after removing the needle.
- Flu-like side effects: Aching and fevers are common after these injections. Gastrointestinal symptoms (nausea, vomiting, diarrhea) are not usually seen with this medication. This side effect responds to tapering of the dose, use of analgesics, and taking the medication at bedtime (see above).
- White blood counts commonly decrease. Anemia and low platelet levels are rarely seen.
What are the rare side effects?

- Liver injury. Rarely, liver injury may occur. This is monitored with periodic blood tests. Action is usually not needed unless laboratory tests are elevated more than three times above normal.
- Depression. This medication may cause or worsen depression. Depression should be monitored in those taking the medication. In patients with depression, Rebif® may be used but patients should notify their provider if their depression worsens.
- Thyroid dysfunction may occur. If symptoms develop then blood testing for thyroid function is recommended.
- Allergic reactions may occur.
- Heart failure has rarely been reported with Rebif®.
- Thrombotic microangiopathy has rarely been reported with Rebif®. This is a condition with damage to small blood vessels that can result in damage to several organs.
- Seizures have rarely been reported. Multiple sclerosis and fevers may also increase the risk of seizures. It is uncertain whether the Rebif® or fever from the flu-like side effect caused the seizure.

Sharps container: Needles must be disposed of properly. We recommend using a needle clipper such as the Becton Dickinson Safe-Clip™ (www.bd.com/us/diabetes). This clips off the needles, allowing the rest of the syringe to be disposed of in the trash. Other disposal options may be available through your local solid waste disposal company.

Company Support:
MS LifeLines® 1-877-447-3243 Provides financial assistance, insurance assistance, information about Rebif® and multiple sclerosis.
www.Rebif.com
Insurance billing code: J3490