

REBIF[®] SOLUTION FOR INJECTION

Interferon Beta-1a (22mcg, 44mcg per 0.5ml)

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What Rebif is used for

Rebif is used in ambulatory people who have relapsing forms of multiple sclerosis (MS). It is also approved for use in those who have experienced a single clinical event likely to be a first sign of multiple sclerosis.

How Rebif works

Rebif belongs to a class of medicine known as interferons. The active substance of Rebif is interferon beta-1a, a recombinant human interferon beta produced in Chinese hamster ovary cells.

Rebif has been shown to reduce the number of attacks that occur, decrease the severity of attacks and increase the time between attacks.

Treatment with Rebif also delays the progression in disability and lowers the number of times people need to be hospitalised because of attacks.

Before you use Rebif

- When you must not use it

Do not use if you have an allergy to:

- interferon beta
- any of the other ingredients listed at the end of this leaflet.

Some of the symptoms of an allergic reaction may include:

- shortness of breath
- wheezing or difficulty breathing
- swelling of the face, lips, tongue or other parts of the body
- rash, itching or hives on the skin.

Do not use Rebif if:

- you are feeling depressed (feeling of severe sadness and unworthiness) or have thoughts of suicide.
- you are pregnant or intend to become pregnant as there may be an increased risk of spontaneous abortion. Rebif may be considered during pregnancy if clinically needed.
- you want to have children; you should discuss this matter with your doctor.
- after the expiry date (EXP) printed on the pack or if the packaging is torn or shows signs of tampering. If it has expired or is damaged, return it to your pharmacist for disposal.
- you want to use of Rebif in children.
- you are not sure whether you should.

- Before you start to use it

Tell your doctor before you start to use Rebif if you are breastfeeding or intend to breastfeed.

It is not known whether Rebif passes into breast milk. No harmful effects on the breastfed newborn are anticipated. Rebif can be used during breast-feeding.

Before starting Rebif, tell your doctor if you have or have had any of the following:

- fits that is not adequately controlled by treatment
- heart disorders
- kidney disease
- liver disease
- problems with your thyroid
- blood disorder (e.g. low counts of platelets, red and white blood cells)
- allergy to any other medicines, foods, dyes or preservatives
- alcohol abuse

Rebif has a potential for causing severe liver injury. Therefore, liver enzyme monitoring, blood cell counts and platelet counts are recommended

at regular intervals (1, 3 and 6 months).

- Taking other medicines

Tell your doctor if you are taking any other medicines, including:

- all prescription medicines
- all medicines, vitamins, herbal supplements or natural therapies that you buy without a prescription from your pharmacy, supermarket, naturopath or health food shop.

Rebif may interact with some other medicines that are broken down by the liver:

- medicine to treat epilepsy
- medicine to treat depression

Your doctor may have to adjust the dose of your other medicines while you are using Rebif.

If you are not sure if you are taking any of these medicines, ask your doctor or pharmacist.

The following medicines, which are commonly used by people with MS, may be taken while using Rebif:

- Corticosteroid
- Adrenocorticotrophic hormone (ACTH)

How to use Rebif

Rebif is intended for you to inject yourself by subcutaneous (under the skin) injection.

Your doctor or nurse will instruct and assist you in the procedure and technique of self-injection.

Do not attempt self-injection until you are sure of how to do it.

You may be prescribed:

- Rebif pre-filled syringe (Rebif PFS) for single injection. Rebif PFS can be used on its own.
- Rebif PFS in a RebiDose[®] single use autoinjector (RebiDose). Rebif PFS is preassembled in the RebiDose injection device and is also for single injection.

• Rebif Cartridge for multidose use and it is to be used with the RebiSmart electronic injection device
Follow the Directions for Use supplied in the pack.

Before the injection, you should allow the cold Rebif solution to reach room temperature. This will minimise discomfort during administration. Do not inject Rebif if it contains particles or is not clear.

- Where to inject

The best areas for injection are loose and soft (flabby) skin away from joints and nerves.

Use a different injection site each time you inject to lessen the risk of damage to the fat and tissues under the skin.

Suitable injection sites are:

- arms (upper back portion)
- stomach (except around navel and waistline)
- upper buttocks
- thighs (front and sides except at groin and knee).

Do not inject into any areas that have lumps, firm knots, depressions, pain or discolouration.

Talk to your doctor if you experience anything

- How much to use

Your doctor will tell you how much Rebif to inject.

When first starting treatment with Rebif, it is recommended to start at a lower dose and then increase the dose gradually over the first few weeks until you reach your maintenance dose.

- When to use it

The usual dose for those with multiple sclerosis or those who have experienced a single clinical event is 44 micrograms injected subcutaneously three times a week.

- How long to use it

Your doctor or nurse will advise you on which days you should use it.

- If you forget to use it

If you forget an injection by one day, take it the day after the missed dose and push back the days of injection for

the remainder of the week by one day. Resume your regular schedule the following week.

If you miss an injection by two days, skip the missed injection (do not double dose on any day) and resume regular schedule.

Ask your doctor if you are not sure what to do or have trouble remembering to inject your medicine.

- If you use too much (overdose)

Immediately contact your doctor if you are concerned that you have given yourself too much or someone else has injected themselves with Rebif

If you have any further questions on the use of this product, ask your doctor or pharmacist.

While you are using Rebif

- Things you must do

Tell your doctor immediately if you become pregnant while using Rebif. Change the injection site each time you inject.

Today's injection should not be given in the same area as the last one. Keep a record of where and when you last gave yourself an injection. You may use a site again, if the skin area is not red or irritated. If all areas become tender, talk to your doctor about choosing other injection sites.

Before starting any new medicine, tell your doctor and pharmacist that you are using Rebif.

Tell any doctors, dentists, and pharmacists who treat you that you are using Rebif.

- Thing you must not do

Do not use Rebif to treat any other complaints unless your doctor tells you to.

Do not give this medicine to anyone else, even if they have the same condition as you.

Do not stop using Rebif without first checking with your doctor.

Do not change the dose unless your doctor tells you to.

This medicinal product contains 2.5 mg benzyl alcohol per 0.5 ml so it must not be given to premature babies or neonates. May cause toxic reactions and anaphylactoid reactions (life-

threatening events that result from an overreactive immune response in infants and children up to 3 years old.

- Things to be careful of

Tell your doctor if you feel depressed or have suicidal ideation while using Rebif.

If Rebif makes you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

Side effects

Tell your doctor as soon as possible if you do not feel well while you are using Rebif.

All medicines can have side effects. Sometimes they are serious, most of the time they are not.

You may need medical treatment if you get some of the side effects.

Tell your doctor if you notice any of the following and they worry you:

- injection site reactions including redness, swelling, bruising, pain
- flu-like symptoms including fever, chills, and muscular pain. Flu-like symptoms can be reduced by taking a fever reducing painkiller, such as paracetamol, before you inject and for 24 hours after you inject Rebif.
- headache or fatigue
- itching or rash
- abdominal pain
- diarrhea or nausea
- muscle pain or aches, back pain or painful joints
- muscle stiffness or spasms,
- numbness, difficulty walking
- increased sweating.

Tell your doctor immediately if you experience:

- shortness of breath
- persistent coughing
- fatigue
- chest pain
- swelling of the ankles, limbs and abdomen

These may indicate pulmonary arterial hypertension (high blood pressure in the arteries that supply the lungs).

Tell your doctor immediately if you experience any of the following:

- infected area at site of injection (swollen and painful area, with or without discharge)
- depression, problems with sleeping or suicidal thoughts
- anxiety/nervousness
- fits
- problems with your eyes or vision
- new onset high blood pressure, fever, central nervous system symptoms (e.g. confusion, muscle weakness)
- loss of appetite accompanied by other symptoms such as nausea, vomiting, jaundice (yellow appearance to your skin colour). Such symptoms can be associated with a liver disorder and, rarely, liver failure.
- swelling, protein in urine and impaired kidney function
- blood disorder (e.g. low counts of platelets, red and white blood cells)
- persistent rapid heartbeat or palpitations, insomnia, weight loss or weight gain, hair loss, tremor, neck lumps, irritability, abnormal menstrual cycles

This symptoms alone or in combination may mean that your thyroid gland is not working properly and needs to be checked by your doctor.

If you experiences any break in the skin, which may be associated with swelling or drainage of fluid from the injection site, you should consult with your physician before continuing injections with Rebif. If you have multiple lesions, Rebif should be discontinued until healing has occurred. Individuals with single lesions may continue provided that the tissue death is not too extensive.

Tell your doctor if you notice anything else that is making you feel unwell. Other side effects not listed above may also occur in some people. Do not be alarmed by this list of possible side effects. You may not experience any of them.

You may report any side effects or adverse drug reactions directly to the

National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website npra.moh.gov.my (Public → Reporting Medicinal Problems / Side Effects / AEFI / Vaccine Safety).

Storage and disposal of Rebif

- Storage

Store in a refrigerator (2°C – 8°C) away from the cooling element. Do not freeze. Store in the original package in order to protect from light. The device (RebiSmart) containing a pre-filled cartridge of Rebif must be stored in the device storage box in a refrigerator (2°C – 8°C). For the purpose of ambulatory use, you may remove Rebif from the refrigerator and store it not above 25°C for one single period of up to 14 days. Rebif must then be returned to the refrigerator and used before the expiry date. After first injection, use within 28 days. Use each prefilled syringe and prefilled pen only once. Use a new syringe for each dose. Do not leave it in the car. Keep it where children cannot reach it.

- Disposal

If you are self-injecting, discard all sharps into a disposal unit. If you have any Rebif that has expired or is left over from your treatment, refer this to your clinic.

Product description

- What it looks like

Rebif pre-filled syringe:

One ml type 1 glass syringe, with a stainless steel needle, containing 0.5 ml solution.

Rebif pre-filled pen:

One mL type 1 glass syringe, with a stainless steel needle, containing 0.5 mL solution.

The syringe is sealed in a disposable pen injector called RebiDose.

Rebif cartridge:

Cartridges 3 mL (type 1 glass) with a plunger stopper (rubber) and crimp cap (aluminium and halobutyl rubber) containing 1.5 ml solution for injection.

Rebif is available as a package of 1, 3 or 12 pre-filled syringes or pre-filled pens and box of 4 cartridges.

Not all pack sizes may be marketed.

- Ingredients

- Active ingredient: interferon beta-1a
- Inactive ingredient: mannitol, poloxamer, methionine, benzyl alcohol, sodium acetate, acetic acid, sodium hydroxide, water for injections

- MAL Numbers:

Rebif 22mcg/0.5ml - MAL20034728ASZ
Rebif 44mcg/0.5ml - MAL20034743ASZ

Manufacturer

Merck Serono S.p.A.
Via delle Magnolie 15 (loc. frazione Zona Industriale)
70026 - Modugno (BA), Italy.

Product Registration Holder

Merck Sdn Bhd (178145-V)
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