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## EPAR summary for the public

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# Rebif

interferon beta-1a

This document is a summary of the European public assessment report (EPAR) for Rebif. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Rebif.

## What is Rebif?

Rebif is a solution for injection in prefilled syringes, prefilled pens and cartridges. The syringes and pens contain 8.8, 22 or 44 micrograms of the active substance, interferon beta-1a. The cartridges contain a total of 66 or 132 micrograms of interferon beta-1a and are designed for multiple dosing using an electronic injection device that delivers 8.8, 22 or 44 micrograms per dose.

## What is Rebif used for?

Rebif is used to treat patients with relapsing multiple sclerosis (MS). This is the type of MS where the patient has attacks (relapses) in between periods with no symptoms. Rebif's effectiveness has not been shown in patients with secondary progressive MS (the type of MS that comes after relapsing MS) that is not relapsing.

Rebif can also be used in patients who have had a single attack of demyelination (where the protective sheath around nerves is damaged) accompanied by inflammation. It is used when the patient is considered to be at high risk of developing MS. Before using Rebif, doctors need to exclude other causes for the symptoms.

The medicine can only be obtained with a prescription.

## How is Rebif used?

Rebif treatment should be started by a doctor who has experience in the management of MS.

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The recommended dose of Rebif is 44 micrograms given three times a week by injection under the skin. The 22-microgram dose is recommended for patients who cannot tolerate the higher dose.

When first starting treatment with Rebif, the dose should be slowly increased to avoid side effects, starting with 8.8 micrograms three times a week for the first two weeks, followed by 22 micrograms three times a week for the next two weeks after which 44 micrograms three times a week can be given. Special packs with the correct quantities of syringes or cartridges are available when starting treatment. The electronic injection device used with the cartridges is programmed to deliver the correct doses of Rebif at the start of treatment and during the standard-dose phase.

The patients can inject Rebif themselves if they have been trained appropriately. The doctor may advise the patient to take a fever-reducing painkiller before each injection and for 24 hours after injection to reduce the influenza (flu)-like symptoms that may occur as a side effect of treatment. All patients should be assessed at least once every two years.

### **How does Rebif work?**

MS is a disease of the nerves, in which inflammation destroys the protective sheath around the nerves (demyelination). The active substance in Rebif, interferon beta-1a, belongs to the group 'interferons'. Interferons are natural substances produced by the body to help it fight against attacks such as infections caused by viruses. The exact way that Rebif works in MS is not yet fully understood but interferon beta seems to calm the immune system down and prevent relapses of MS.

Interferon beta-1a is produced by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced, which makes them able to produce interferon beta-1a. The replacement interferon beta-1a acts in the same way as naturally produced interferon beta.

### **How has Rebif been studied?**

Rebif has been studied in 560 patients with relapsing MS. The patients had experienced at least two relapses in the previous two years. Patients received either Rebif (22 or 44 micrograms) or placebo (a dummy treatment) for two years. The study was then extended to four years. The main measure of effectiveness was the number of relapses that the patients had. Rebif has also been studied in patients with secondary progressive MS. The study looked at the ability of the medicine to prevent the progression of disability over three years.

Rebif has also been compared with placebo in 515 patients who had experienced a single attack of demyelination. Patients received either placebo or Rebif (44 micrograms given once or three times a week) for two years. The main measure of effectiveness was the time it took for patients to develop MS, using standard criteria for diagnosing MS.

### **What benefit has Rebif shown during the studies?**

Rebif was more effective than placebo in reducing the number of relapses in relapsing MS. Relapses were reduced by about 30% over two years for both Rebif 22 and 44 micrograms compared with placebo, and by 22% (Rebif 22 micrograms) and 29% (Rebif 44 micrograms) over four years.

In the study of patients with progressive MS, Rebif had no significant effect on the progression of disability, but the relapse rate was reduced by about 30%. Some effect on progression of disability could be seen, but only in the patients who had relapses in the two years before the start of the study.

In the study in patients who had experienced a single attack of demyelination, the probability of developing MS over 24 months was lower for patients treated with Rebif than patients treated with placebo. The probability of developing MS over 24 months was 62.5% for patients given Rebif three times a week (or 75.5% for patients given Rebif once a week) compared with 85.8% for patients given placebo.

### **What is the risk associated with Rebif?**

The most common side effects with Rebif (seen in more than 1 patient in 10) are flu-like symptoms, neutropenia, lymphopenia and leucopenia (low white blood cell counts), thrombocytopenia (low blood platelet counts), anaemia (low red blood cell counts), headache, inflammation and other reactions at the injection site, and increases in transaminases (liver enzymes). For the full list of all side effects reported with Rebif, see the package leaflet.

Rebif must not be used in people who are hypersensitive (allergic) to natural or recombinant interferon beta, or any of the other ingredients. Rebif treatment must not be started during pregnancy. If a woman becomes pregnant while taking the medicine, she should consult her doctor. Rebif must also not be used in patients who are suffering from severe depression or having thoughts about committing suicide.

### **Why has Rebif been approved?**

The CHMP decided that Rebif's benefits are greater than its risks and recommended that it be given marketing authorisation.

### **What measures are being taken to ensure the safe and effective use of Rebif?**

A risk management plan has been developed to ensure that Rebif is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Rebif, including the appropriate precautions to be followed by healthcare professionals and patients.

### **Other information about Rebif:**

The European Commission granted a marketing authorisation valid throughout the European Union for Rebif on 4 May 1998.

The full EPAR for Rebif can be found on the Agency's website: [ema.europa.eu/Find\\_medicine/Human\\_medicines/European\\_Public\\_Assessment\\_Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports). For more information about treatment with Rebif, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 01-2014.