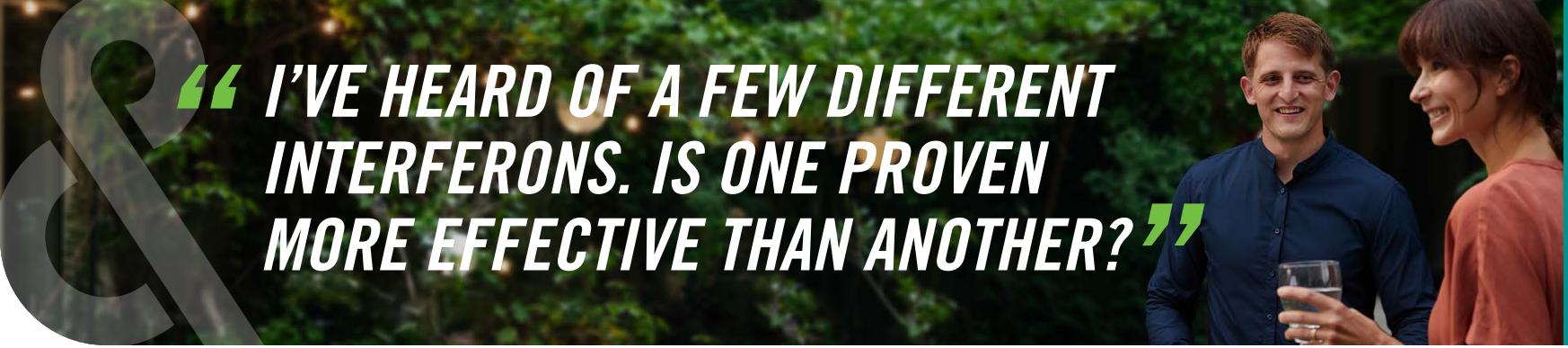


CLICK HERE FOR MORE INFO ABOUT PRESCRIBING REBIF®

## HIGH-DOSE, HIGH-FREQUENCY REBIF® WAS PROVEN SUPERIOR TO LOW-DOSE, LOW-FREQUENCY AVONEX® IN RELAPSE AND MRI CLINICAL MEASURES[1-5]

### MORE PATIENTS RELAPSE-FREE

AT 24 WEEKS*

**75%**

vs 63% with Avonex

Rebif® 44 mcg sc tiw: 75% (n=339) vs Avonex 30 mcg im qw: 63% (n=338), *P*<0.001

### MORE PATIENTS T2- ACTIVE LESION-FREE

AT 64 WEEKS

**58%**

vs 38% with Avonex

Rebif® 44 mcg sc tiw: 58% (n=325) vs Avonex 30 mcg im qw: 38% (n=325), *P*<0.001

### EVIDENCE STUDY DESIGN

**EV**idence of **I**nterferon **D**ose-response: **E**uropean **N**orth American **C**omparative **E**fficacy (**EVIDENCE**) was an assessor-blinded, parallel-group study conducted over an average of 64 weeks. Patients were randomized to receive Rebif® 44 mcg subcutaneously 3 times weekly (n=339) or Avonex 30 mcg intramuscularly once weekly (n=338). Outcomes measured included percentage relapse-free, MRI, safety, and antigenicity and were determined at 24, 48, and an average of 64 weeks.[2,3]

The primary endpoint of the EVIDENCE trial was the proportion of relapse-free patients at 24 weeks. Compared with Avonex, adverse events were similar over an average of 64 weeks, despite higher, more frequent dosing with Rebif. Exceptions included injection site disorders (85% vs 33%), hepatic function disorders (18% vs 10%), and white blood cell disorders (14% vs 5%), which were more frequent with Rebif. Flu-like symptoms were more frequent with Avonex (53% vs 45%).[2]

*Logistic regression model adjusted for treatment and center, intent-to-treat analysis.

## NOT ALL INTERFERONS ARE THE SAME

Your patients should know that there are different kinds of interferon treatments, and they may differ in many ways, including formulation, method of delivery, frequency, and dose.[1,6-8]

### INDICATION

Rebif® (interferon beta-1a) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

### IMPORTANT SAFETY INFORMATION

Rebif® is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation.

Please see additional Important Safety Information on page 2 and the Full Prescribing Information and Medication Guide.

Rebif® (interferon beta-1a) subcutaneous injection

# INDICATION AND IMPORTANT SAFETY INFORMATION

## INDICATION

Rebif® is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

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Rebif® should be used with caution in patients with depression, a condition that is common in people with multiple sclerosis. Depression, suicidal ideation, and suicide attempts have been reported to occur with increased frequency in patients receiving interferon compounds, including Rebif®.

Severe liver injury, including some cases of hepatic failure requiring liver transplantation, has been reported rarely in patients taking Rebif®. The potential for liver injury should be considered when used in combination with other products associated with liver injury. Monitor liver function tests and patients for signs and symptoms of hepatic injury. Consider discontinuing Rebif® if hepatic injury occurs.

Anaphylaxis and other allergic reactions (some severe) have been reported as a rare complication of Rebif®. Discontinue Rebif® if anaphylaxis occurs.

In controlled clinical trials, injection site reactions occurred more frequently in Rebif®-treated patients than in placebo-treated and Avonex-treated patients. Injection site reactions including injection site pain, erythema, edema, cellulitis, abscess, and necrosis have been reported in the postmarketing setting. Do not administer Rebif® into affected area until fully healed; if multiple lesions occur, discontinue Rebif® until skin lesions are healed.

Decreased peripheral blood counts in all cell lines, including pancytopenia, have been reported in Rebif®-treated patients. In controlled clinical trials, leukopenia occurred at a higher frequency in Rebif®-treated patients than in placebo and Avonex-treated patients. Thrombocytopenia and anemia occurred more frequently in 44 mcg Rebif®-treated patients than in placebo-treated patients. Patients should be monitored for symptoms or signs of decreased blood counts. Monitoring of complete blood and differential white blood cell counts is also recommended.

Cases of thrombotic microangiopathy (TMA), some fatal, have been reported with interferon beta products, including Rebif®, up to several weeks or years after starting therapy. Discontinue Rebif® if clinical symptoms and laboratory findings consistent with TMA occur, and manage as clinically indicated.

Caution should be exercised when administering Rebif® to patients with pre-existing seizure disorders. Seizures have been temporally associated with the use of beta interferons, including Rebif®, in clinical trials and in postmarketing reports.

The most common side effects with Rebif® are injection-site disorders, headaches, influenza-like symptoms, abdominal pain, depression, elevated liver enzymes, and hematologic abnormalities.

Epidemiological data do not suggest a clear relationship between interferon beta use and major congenital malformations, but interferon beta may cause fetal harm based on animal studies. Data from a large human population-based cohort study, as well as other published studies over several decades, have not identified a drug-associated risk of major birth defects with interferon beta products during early pregnancy. Findings regarding a potential risk for low birth weight or miscarriage with the use of interferon beta products in pregnancy have been inconsistent.

# REFERENCES

**1.** Rebif® [Prescribing Information]. Rockland, MA: EMD Serono, Inc. **2.** Panitch H, Goodin D, Francis G, et al; for EVIDENCE (EVidence of Interferon Dose-response-European North American Comparative Efficacy) Study Group and the University of British Columbia MS/MRI Research Group. Benefits of high-dose, high-frequency interferon beta-1a in relapsing-remitting multiple sclerosis are sustained to 16 months: final comparative results of the EVIDENCE trial. *J Neurol Sci*. 2005;239(1):67-74. **3.** Data on file. EMD Serono, Inc. EVIDENCE study report 2001. **4.** Panitch H, Goodin DS, Francis G, et al; EVIDENCE Study Group and the University of British Columbia MS/MRI Research Group. Randomized, comparative study of interferon beta-1a treatment regimens in MS: the EVIDENCE trial. *Neurology*. 2002;59(10):1496-1506. **5.** Schwid SR, Panitch HS. Full results of the Evidence of Interferon Dose-Response–European North American Comparative Efficacy (EVIDENCE) study: a multicenter, randomized, assessor-blinded comparison of low-dose weekly versus high-dose, high-frequency interferon beta-1a for relapsing multiple sclerosis. *Clin Ther*. 2007;29(9):2031-2048. **6.** Avonex® [Prescribing Information]. Cambridge, MA: Biogen Inc. **7.** Betaseron® [Prescribing Information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc. **8.** Plegridy® [Prescribing Information]. Cambridge, MA: Biogen Inc.



Please see Full Prescribing Information and Medication Guide.