

## News Release

Your Contact  
[alice.mcgrail@emdserono.com](mailto:alice.mcgrail@emdserono.com)  
+1 781 738 8791

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### **CHMP Issues Positive Opinion for Rebif® (interferon beta-1a) EU Label Amendment Regarding Use of Rebif During Pregnancy and While Breastfeeding**

Darmstadt, Germany, September 23, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion to update the product label of Rebif®, an interferon beta-1a, to include that women with relapsing multiple sclerosis (RMS) may continue treatment with Rebif, if clinically needed, during pregnancy and while breastfeeding. The EU label update applies to the interferon beta (IFNβ) class of drugs. The EU CHMP opinion will remove the current contraindication against treatment initiation during pregnancy as well as the requirement to use contraception while on Rebif.

In the U.S., Rebif is classified as “Pregnancy Category C” and the prescribing information states that: “There are no adequate and well-controlled studies in pregnant women. Rebif should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.”

The EU label update also includes that “Rebif can be used during breastfeeding.” The U.S. label states that: “It is not known whether Rebif is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Rebif is administered to a nursing woman.”

#### **About Rebif® (interferon beta-1a)**

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. It is used to decrease the frequency of relapses and delay the occurrence of some of the physical disability that is common in people with MS. The efficacy and safety of Rebif in controlled clinical trials beyond 2-years has not been established.

#### **IMPORTANT SAFETY INFORMATION:**



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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.

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.

There are no adequate and well-controlled studies in pregnant women. Rebif should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Please see the full Prescribing Information for additional information:

[http://www.emdserono.com/ms.country.us/en/images/Rebif\\_PI\\_tcm115\\_140051.pdf?Version=](http://www.emdserono.com/ms.country.us/en/images/Rebif_PI_tcm115_140051.pdf?Version=)

### **About Multiple Sclerosis**

Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that approximately 2.3 million people have MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

### **Merck KGaA, Darmstadt, Germany in Neurology and Immunology**

Merck KGaA, Darmstadt, Germany, has a long-standing legacy in neurology and immunology, with significant R&D and commercial experience in multiple sclerosis (MS). The company's current MS portfolio includes two products for the treatment of relapsing MS, with a robust pipeline focusing on discovering new therapies that have the potential to modulate key pathogenic mechanisms in MS. Merck KGaA, Darmstadt, Germany, aims to improve the lives of those living with MS, by addressing areas of unmet medical needs.

The company's robust immunology pipeline focuses on discovering new therapies that have the potential to modulate key pathogenic mechanisms in chronic diseases such as MS, systemic lupus erythematosus (SLE) and forms of arthritis, including rheumatoid arthritis (RA) and osteoarthritis (OA).

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### **About Merck KGaA, Darmstadt, Germany**

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 52,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2018, Merck KGaA, Darmstadt, Germany, generated sales of € 14.8 billion in 66 countries.

Scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. This is how Merck KGaA, Darmstadt, Germany, has thrived since its founding in 1668. The founding family remains the majority owner of the publicly listed company. Merck KGaA, Darmstadt, Germany, holds the global rights to the Merck name and brand. The only exceptions are the United States and Canada, where the business sectors of Merck operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials.