



Your Contact

Phyllis Carter
Phone +49 6151 72-7144

News Release

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Merck Receives European Approval to Expand Use of Rebif in Patients with Early Multiple Sclerosis

Darmstadt, January 25, 2012 – Merck KGaA announced today that the European Commission (EC) has approved extension of the indication of Rebif® (interferon beta-1a), Merck's leading treatment for relapsing forms of multiple sclerosis (MS). This EC approval is for the use of Rebif 44 micrograms three times weekly in patients who have experienced a single demyelinating event, an early sign of the disease, and who are at high risk of converting to MS. This approval was based on the results of the REFLEX study¹⁻², which showed the safety and efficacy of Rebif in this patient population.

"We are delighted by the European Commission decision," said Dr Annalisa Jenkins, Head of Global Drug Development and Medical at the Merck Serono division. "Multiple sclerosis has an initial stage when clinical manifestations are not pronounced but irreversible neurological damage is taking place. Throughout the European Union, neurologists will now be able to prescribe Rebif for patients with early signs of this devastating disease."

The new labelling for Rebif is valid immediately in all 27 member states of the European Union³.

Merck has a long-standing commitment to the therapeutic area of MS. The company continues to invest in discovering and developing treatment options in this area, including active life-cycle management initiatives for Merck's foundation therapy, Rebif. In addition, the company continues to strengthen existing and establish new

Page 1 of 3

Merck KGaA

Frankfurter Strasse 250
64293 Darmstadt
Hotline +49 6151 72-5000
www.merckgroup.com

Head External Communications -2386
Spokesmen: -9591 / -7144 / -6328
Fax +49 6151 72-7707
media.relations@merckgroup.com



News Release

collaborations to advance research and bring innovative solutions to patients living with MS.

¹ REFLEX: REbif FLEXible dosing in early multiple sclerosis: A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial of the HSA-free formulation of Rebif (44 micrograms three times a week and 44 micrograms once a week) in Subjects at High Risk of Converting to Multiple Sclerosis

² Comi G, De Stefano N, Freedman MS, Barkhof F, Polman CH, Uitdehaag BMJ, *et al.* Comparison of two dosing frequencies of subcutaneous interferon beta-1a in patients with a first demyelinating event suggestive of multiple sclerosis (REFLEX): a phase 3 randomised controlled trial. *Lancet Neurol* 2012; 11:33-41

³ The indication of Rebif in the United States is not extended by this approval.

About the REFLEX study design

The REFLEX study was a two-year (24-month), randomized, double-blind, placebo-controlled, international Phase III trial. It randomized 517 patients considered at risk of developing MS due to a recently experienced isolated demyelinating event (e.g. optic neuritis, myelopathy or brainstem syndrome) and having magnetic resonance imaging (MRI) brain scans consistent with early signs of MS. Study participants were randomized in a 1:1:1 ratio to receive either Rebif[®] 44 micrograms three times weekly, Rebif[®] 44 micrograms once weekly, or placebo as a subcutaneous injection. Patients were treated for a period of two years, or up to the time when they experienced a second attack leading to a diagnosis of clinically definite MS. At this point, patients were offered open-label treatment with Rebif[®] 44 micrograms three times a week. The primary endpoint of the study was "time to conversion to McDonald MS" (2005). Further endpoints include "time to conversion to clinically definite MS" (the main secondary endpoint), assessments of MRI brain scans and clinical relapses.

The REFLEX study was conducted with the human serum albumin (HSA)-free formulation of Rebif, which is not available in the United States.

A three-year double blind extension of the REFLEX study, called REFLEXION (REFLEX extensION study), is currently ongoing in order to provide long-term follow-up data.

About Rebif[®]

Rebif[®] (interferon beta-1a) is a disease-modifying drug used to treat relapsing forms of multiple sclerosis (MS) and is similar to the interferon beta protein produced by the human body. The efficacy of Rebif[®] in chronic progressive MS has not been established. Interferons are thought to help reduce inflammation. The exact mechanism is unknown.

Rebif[®], which was approved in Europe in 1998 and in the US in 2002, is registered in more than 90 countries worldwide. Rebif[®] has been proven to delay the progression of disability, reduce the frequency of relapses and reduce MRI lesion activity and area*. Rebif[®] is available in a 22 micrograms and 44 micrograms ready-to-use pre-filled syringe and a titration pack (8.8 micrograms). Rebif[®] is also now available in two multidose cartridges [132 micrograms (three doses of 44 micrograms) and 66 micrograms (three doses of 22 micrograms)] for the use with the RebiSmart[™] electronic auto-injection device, in several EU member countries, Switzerland and Canada, as well as in Australia. RebiDose[™], a single-use disposable pen, which is pre-filled with Rebif[®], is approved in the European Union, Australia and Canada, and was launched in several EU member countries in 2011. RebiSmart[™] and RebiDose[™] are not available in the United States.

Rebif[®] should be used with caution in patients with a history of depression, liver disease and seizures. Most commonly reported side effects are flu-like symptoms, injection site disorders, elevation of liver enzymes and blood cell abnormalities. Patients, especially those with depression, seizure disorders, or liver problems, should discuss treatment with Rebif[®] with their doctors.

* The exact correlation between MRI findings and the current or future clinical status of patients, including disability progression, is unknown.



News Release

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 two 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.

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Merck is a global pharmaceutical and chemical company with total revenues of € 9.3 billion in 2010, a history that began in 1668, and a future shaped by more than 40,000 employees in 67 countries. Its success is characterized by innovations from entrepreneurial employees. Merck's operating activities come under the umbrella of Merck KGaA, in which the Merck family holds an approximately 70% interest and shareholders own the remaining approximately 30%. In 1917 the U.S. subsidiary Merck & Co. was expropriated and has been an independent company ever since.