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Biogen Japan Ltd.
Eisai Co., Ltd.

ALL-CASE SURVEILLANCE CONDITION FOR APPROVAL OF MULTIPLE SCLEROSIS TREATMENT AVONEX® CLEARED IN JAPAN

Biogen Japan Ltd. (Headquarters: Tokyo, President and Representative Director: Shinichi Torii, "Biogen Japan") and Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that they have received notification of the results of reexamination from Japan's Ministry of Health, Labour and Welfare (MHLW) to the effect that the "all-case surveillance" drug use-results survey condition required for approval of Biogen Japan's multiple sclerosis treatment AVONEX® (interferon beta 1a, genetical recombination), has been lifted.

In July 2006, the MHLW approved the indication of relapse prevention of multiple sclerosis for AVONEX® with the following conditions for approval: "Because of the very limited number of subjects treated in the Japanese clinical trials, the applicant is required to conduct all-case drug use-results survey until data from a certain number of patients are accumulated after-market launch, in order to identify the background information of patients treated with the product and collect safety and efficacy data on the product in the early post-marketing period, and thereby take necessary measures to ensure proper use of the product" and "Conduct a clinical study to evaluate the long-term efficacy and safety of the product using indicators such as relapse rate of multiple sclerosis, and report on the results."

Safety data for 1,486 patients, and efficacy data for 1,458 patients, were submitted to the MHLW as the results of analysis of all-case surveillance. Based on these results, MHLW's conclusion from the notification of results of reexamination was that the all-case surveillance had been conducted properly and the necessary measures to ensure proper use of the product are being taken.

In Japan, Biogen Japan is the marketing and manufacturing authorization holder for AVONEX®. On January 9, 2018, Eisai commenced co-promotion of AVONEX®.

Biogen Japan and Eisai will continue to promote and provide information on the proper use of AVONEX® while making further contributions to improve the quality of life of patients.

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<Notes to editors>

1. About the Drug-Use Results Survey

Based on the first condition of approval,[*1] a drug-use results survey on AVONEX® Intramuscular Injection Syringe 30μg and AVONEX® Intramuscular Injection 30μg Pen was carried out using the all-case centralized registration method from November 2006 to July 2016 aiming to assess efficacy and safety under usage conditions, as well as investigate whether or not a special drug use-results survey or post marketing clinical study was required. Data on 1,510 patients was collected from 397 facilities across Japan.

Based on the second condition of approval,[*2] an open-label, multicenter post marketing surveillance study was also conducted to evaluate long-term (two years) safety and efficacy of AVONEX® Intramuscular Injection Syringe 30μg. The target number of patients was 100, and data on 100 patients was collected from 35 facilities across Japan.

[*1]Approval condition 1: Because of the very limited number of subjects treated in the Japanese clinical trials, the applicant is required to conduct all-case drug use-results survey until data from a certain number of patients are accumulated after-market launch, in order to identify the background information of patients treated with the product and collect safety and efficacy data on the product in the early post-marketing period, and thereby take necessary measures to ensure proper use of the product

[*2]Approval condition 2: Conduct a clinical study to evaluate the long-term efficacy and safety of the product using indicators such as relapse rate of multiple sclerosis and report on the results

2. About the Results of the Drug-Use Results Survey

According to the drug-use results survey and various reports on adverse effects and infection, serious adverse effects not predicted from the precautions for use included relapse of multiple sclerosis (26 cases), epididymitis (2 cases), cytomegalovirus infection, shingles, pneumonia, mycotic aneurysm, thynoma, subacute thyroiditis, intent for self-harm, ataxia, cataplexy, generalized tonic-clonic seizure, myasthenia gravis, paralysis, paraplegia, retinopathy, duodenal ulcer, stomatitis, hepatic necrosis, drug-induced liver injury, psoriasis, balanoposthitis, death, and reduced granulocyte count (1 case each).

In the analysis of the available safety information including ongoing investigation activities, there were no new risks or ongoing safety signals confirmed in the report on this drug-use results survey. From this information, it was assessed that the benefit risk profile for this agent was aligned with the key safety information. It was thus determined that there were no changes to the safety profile of the agent, the benefit/risk balance supported treatment with the agent for multiple sclerosis patients, and that no new warnings regarding safety through revision or other change to the attached product information, no new special drug-use results surveys nor post-marketing clinical studies are required.

3. About Multiple Sclerosis

Multiple sclerosis is a serious, chronic, progressive disease of the central nervous system that affects cognitive function, mental and social functions as well as physical functions. It is an autoimmune disease characterized by inflammation throughout the central nervous system, myelin damage, cell death of oligodendrocytes, axon damage, and subsequent death of nerve cells. The incidence of multiple sclerosis differs between races and regions, and the estimated incidence rate reported for Japan is around 10% of the incidence rate in European and American countries.[1] The incidence of multiple sclerosis in Japan is reported as 10.8 to 14.4 per 100,000.[2]

[1] Horiuchi I, Kira J, Tamura A, Matsuya M, Shimizu K. Basic treatment guidelines for disease of neurologic disease based on EBM. *Medical View*, 2002:267-79

[2] Kinoshita M, Obata K, Tanaka M. Latitude has more significant impact on prevalence of multiple sclerosis than ultraviolet level or sunshine duration in Japanese population. *Neurol Sci*. 2015;36(7):1147-51.

4. About Multiple Sclerosis Treatment AVONEX®

AVONEX® is a formulation of interferon beta 1a produced by recombinant DNA technology using genetically engineered Chinese Hamster ovary cells. The agent was approved in May 1996 in the United States and approved in March 1997 in the EU. Development for Japan was undertaken in 1998 by Genzyme Japan K.K., and the agent was designated as an orphan drug in 1999. As a result of clinical studies in Japan, the utility of the agent was confirmed in Japanese people, and based on the results of domestic and international clinical studies, AVONEX® Intramuscular Injection Syringe 30μg was approved as for the relapse prevention of multiple sclerosis in July 2006. Subsequently, Biogen Idec Japan Ltd. (currently Biogen Japan Ltd.) succeeded the marketing and manufacturing approval for the agent from Genzyme Japan K.K. in September 2006. In order to provide an alternative injection method to AVONEX® Intramuscular Injection Syringe 30μg for patients, a pen formulation AVONEX® Intramuscular Injection 30μg Pen was approved in December 2013.

5. About Biogen

At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases. Founded in 1978 as one of the world's first global biotechnology companies by Charles Weissman and Nobel Prize winners Walter Gilbert and Phillip Sharp, today Biogen has the leading portfolio of medicines to treat multiple sclerosis; has introduced the first and only approved treatment for spinal muscular atrophy; and is focused on advancing neuroscience research programs in Alzheimer's disease and dementia, neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry, and acute neurology. Biogen also manufactures and commercializes biosimilars of advanced biologics. We routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Japan is a subsidiary of Biogen in the U.S. Biogen Japan, as the Japan affiliate of one of the oldest independent biotechnology companies, started its operation in Japan in 2000. To learn more about Biogen Japan, please visit www.biogen.co.jp.

6. About Eisai

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in partnership-based initiatives to improve access to medicines in developing and emerging countries.

For more information about Eisai Co., Ltd., please visit www.eisai.com.