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Eisai Co., Ltd.
Toyama Chemical Co., Ltd.

EISAI AND TOYAMA CHEMICAL CLEAR ALL-CASE SURVEILLANCE CONDITION FOR APPROVAL OF ANTIRHEUMATIC AGENT IGURATIMOD (BRAND NAMES: CARERAM® TABLETS 25 MG/KOLBET® TABLETS 25 MG)

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Fujifilm Group company Toyama Chemical Co., Ltd. (Headquarters: Tokyo, President: Masuji Sugata, "Toyama Chemical") announced today that they have received notification from Japan's Ministry of Health, Labour and Welfare (MHLW) to the effect that the "all-case surveillance" special drug use-results survey condition required for approval of the antirheumatic agent iguratimod (Eisai brand name: Careram®, Toyama Chemical brand name: KOLBET®) has been lifted.

In June 2012, the MHLW approved iguratimod indicated for rheumatoid arthritis with the following condition for approval: "After the launch of iguratimod, the use-results survey should be conducted for all patients treated with this product until adequate data from a certain number of cases have been collected, in order to understand the background of those patients, and efficacy and safety data on this product be collected just after marketing of the product so that actions necessary for the proper use of the drug can be taken." Eisai and Toyama Chemical jointly conducted an all-case drug use-results survey on all patients who had been treated with iguratimod between launch on September 12, 2012 to April 14, 2013, and submitted the results of an interim analysis on the first 24 weeks of treatment for 2,246 patients to the MHLW. Based on the safety and efficacy data submitted, the MHLW lifted this condition for approval after determining that there are no issues that require new measures to ensure proper use of the product.

Discovered by Toyama Chemical, iguratimod is a disease-modifying antirheumatic drug (DMARD) and was the first oral antirheumatic agent in Japan to demonstrate efficacy in domestic clinical trials as an add-on therapy to methotrexate (MTX), the standard of care, in rheumatoid arthritis patients who did not achieve satisfactory benefit with MTX alone. As an antirheumatic drug, it is believed that iguratimod provides a new option for drug therapy of rheumatoid arthritis and enables rheumatoid arthritis patients to choose a drug therapy regime that matches their condition. Eisai and Toyama Chemical conducted joint development of the agent in Japan based on a co-development and license agreement previously concluded between the two companies. After receiving approval, Eisai and Taisho Toyama Pharmaceutical Co., Ltd. launched iguratimod under the brand names Careram® Tablets 25 mg and KOLBET® Tablets 25 mg, respectively, with each company working to market their product and provide information on its proper use.

Eisai and Toyama Chemical will continue to promote and provide information on the proper use of iguratimod while making further contributions to improve the quality of life of patients.

Media Inquiries	
Public Relations Department Eisai Co., Ltd. +81-(0)3-3817-5120	General Affairs Group, General Affairs and Personnel Department Toyama Chemical Co., Ltd. +81-(0)3-5381-3818

[Notes to editors]

1. Results of the All-Case Surveillance

2,736 patients who commenced treatment with iguratimod between launch on September 12, 2012 and April 14, 2013 were enrolled for all-case surveillance, and out of these patients, 2,246 were included for an interim safety analysis. The adverse reaction incidence for up to 24 weeks after the start of treatment was 31.34% (704 cases), with 3.07% (69 cases) being serious adverse reactions. The most common adverse drug reactions were gastrointestinal disorder (8.41%), abnormal clinical laboratory test results (7.08%), and infections and infestations (5.03%). In addition, the most common serious reactions were infections and infestations (1.16%), respiratory, thoracic and mediastinal disorder (0.76%) and gastrointestinal disorder (0.49%).

Regarding efficacy, the response rates based on EULAR response criteria using DAS28-ESR and DAS28-CRP at 24-week (LOCF) were 55.4% (586/1,057 cases) and 54.8% (757/1,382 cases), respectively.

2. About Rheumatoid Arthritis

Rheumatoid arthritis is a disease that leads to the inflammation of multiple joints throughout the body, causing joint swelling and pain. With joint destruction progressing right from the early stages of the disease, rheumatoid arthritis causes joint deformities and functional impairment over the long term. Rheumatoid arthritis is an autoimmune disease in which synovial cells, which line the inner surface of the joint cavity, proliferate due to an unknown cause. The number of blood vessels in joints also increases, resulting in the migration of lymphocytes, macrophages and other white blood cells from inside blood vessels to the synovial tissue of joints. An immune reaction in localized joints causes an inflammatory reaction and the progression of cartilage and bone destruction due to the effects of cytokines produced by lymphocytes and macrophages. In Japan, rheumatoid arthritis is said to affect an estimated 700,000 to 800,000 patients.

3. About Disease-Modifying Antirheumatic Drugs (DMARDs)

DMARDs (disease-modifying antirheumatic drugs) are a category of drugs that work to control the underlying processes of rheumatoid arthritis. They are expected to control the immune abnormalities that are thought to cause inflammation in the disease.

4. About DAS28-ESR and DAS28-CRP

Short for Disease Activity Score, DAS is widely used in general as a clinical index of disease activity in patients with rheumatoid arthritis. It is calculated using the number of swollen joints, the number of tender joints, blood testing and the patient's own global assessment of health. DAS28-ESR is calculated by combining these results with the patient's erythrocyte sedimentation rate (ESR) and DAS28-CRP using their C reactive protein (CRP) level.