October 28, 2010

Press Release

Abbott Japan Co., Ltd.
Eisai Co., Ltd

Abbott Japan and Eisai have Cleared the Condition for Approval of Humira®, a Fully Human Anti-TNF-alpha Monoclonal Antibody, for Rheumatoid Arthritis in Terms of the All-Case Surveillance

Abbott Japan Co., Ltd. (Pharmaceutical Products Group Headquarters: Tokyo, President: Gary M. Winer, "Abbott Japan") and Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that the Ministry of Health, Labor and Welfare (MHLW) of Japan has notified them of clearance of the condition for approval of Humira® pre-filled syringe 40 mg/0.8 mL for subcutaneous injection (generic name: adalimumab [genetic recombination]), a fully human anti-TNF-alpha monoclonal antibody, in terms of the use results survey (all-case surveillance) on rheumatoid arthritis, the first approved indication for this drug.

In April 2008, Humira® was approved for the treatment of rheumatoid arthritis with the following condition for approval: "Until data for a pre-determined number of cases have been accumulated following the approval of Humira®, a use-results survey in all patients receiving the drug should be continued to promptly obtain safety and efficacy data for Humira® and take appropriate measures to ensure proper use of the drug."

The MHLW cleared the condition for approval on the basis of the review of the safety and efficacy of Humira® in 3,084 patients with rheumatoid arthritis who participated in the all-case surveillance. In the survey, we confirmed the use of Humira® by more than 10,000 patients up to the present in Japan. We will provide a final report of the results for a predetermined number of patients (about 8,000) to the MHLW.

Humira® is a fully human anti-TNF-alpha monoclonal antibody that exerts its effects by neutralizing TNF-alpha, a cytokine that plays a central role in inflammatory responses. While Abbott Japan is the marketing authorization holder of Humira® in Japan and Eisai is responsible for its distribution, the two companies are working together to promote the drug.

On the basis of the evidence obtained in the survey, Abbott Japan and Eisai will promote the proper use of Humira® and accumulate additional information to contribute to improving the quality of life of patients.

[Please refer to the following notes for the results of the use results survey of Humira® on rheumatoid arthritis, a glossary of terms, product and company information, and an outline on Eisai and Abbott's Commitment to Immunology]

Media Inquiries:	
Public Relations Department Eisai Co., Ltd. Tel: +81-3-3817-5120	Public Affairs Department Abbott Japan Co., Ltd. Tel: +81-3-4588-4602

< Notes to editors >

1. Results of the use results survey of Humira® on rheumatoid arthritis

The report submitted to the MHLW includes the results of analysis of the data obtained from 3,084 patients who were evaluated during the period between June 18, 2008 and December 31, 2009.

The efficacy of Humira® in the treatment of rheumatoid arthritis was evaluated with Disease Activity Score 28 (DAS28). In the group of 1,971 patients for whom DAS28 was evaluated at baseline and week 24 of treatment, the mean DAS28 (mean ± SD) was improved substantially from 5.3 ± 1.3, which indicates highly active disease, to 3.9 ± 1.5 at week 24 of treatment, with a response rate of 21.1%. Stratified analysis revealed that Humira® was especially effective in patients in the early phase of disease (Class I or II), those naïve to biological therapy, and those receiving methotrexate concomitantly with Humira®.

Adverse drug reactions developed in 27.1% of the patients. The most common ADRs were “skin disorders,” “general disorders and administration site conditions,” and “infections and infestations.” Serious ADRs were observed in 4.2% of the patients, and included “infections and infestations.” The profile of these ADRs was consistent with that observed in clinical studies during the development of Humira®.

2. Glossary of Terms

1) Rheumatoid arthritis (RA)

Rheumatoid arthritis is an autoimmune disease in which joints are inflamed, which may lead to damage to the interior of joints and the surrounding bone. The joints most commonly affected early in the disease are the smaller joints of the fingers, feet, and wrists. The elbows, knees, ankles, and hips can also be affected. Although there is no cure for RA, people continue to seek treatments that not only alleviate the pain and inflammation associated with it but also slow disease progression, and thereby inhibit the joint damage that can hinder performance of daily activities. It is estimated that over 5 million patients in Japan, the United States, and Europe, mostly between the ages of 22 and 55, are receiving antirheumatic drugs for the treatment of rheumatoid arthritis.

More information on RA and current treatment options can be found at www.RA.com (English).

Humira® Information Net was established in June 2008 to provide information on Humira® and RA for healthcare professionals and patients with RA and their families.

The pages for patients include clear descriptions of the disease, examinations for it, and its treatment, including anti-TNF-alpha drugs, while the pages for healthcare professionals include detailed proper use information and information on benefits of treatment including the safety and efficacy of Humira®.

Humira® Information Net is located at http://www.e-humira.jp/.

2) DAS28

DAS is an abbreviation for Disease Activity Score. DAS 28 is an index developed by the European League Against Rheumatism (EULAR) to score the disease activity of rheumatoid arthritis (RA).

DAS 28 scores are calculated based on different indexes of RA disease activity using absolute values. The most commonly used DAS 28 score is calculated based on tender joint count (TJC) and swollen joint count (SJC), which are obtained through evaluation of 28 joints in the body for tenderness and swelling; the results of general health assessment made by patients themselves using a visual analog scale (VAS); and erythrocyte sedimentation rate (ESR) using the following formula:

$$DAS28ESR = 0.555 \times \sqrt{(TJC)} + 0.284 \times \sqrt{(SJC)} + 0.7 \times LN(ESR) + 0.0142 \times (VAS)$$

where LN indicates natural logarithm, ESR is expressed in millimeters in 1 hour, and VAS ranges

from 0–100 mm.

RA activity is considered low, intermediate, and high when DAS28 is < 3.2, 3.2–5.1, and > 5.1, respectively. Patients with a DAS 28 of < 2.6 are considered in a state of remission.

3) TNF-alpha

The tumor necrosis factors (TNFs) are a group of cytokines (i.e., substances mediating cell-cell interactions) mediating intercellular communication that have been found to damage tumor cells. TNF-alpha is produced by many types of cells, including macrophages, lymphocytes, and vascular endothelial cells, and is known to cause and enhance inflammatory responses and to activate inflammatory cells. TNF-alpha, when produced in excess, plays a central role in the inflammatory responses involved in some immune-mediated diseases.

4) Monoclonal antibody

A monoclonal antibody is a protein produced from clones of a single antibody-producing cell (known as a monoclone). It is a homologous population of antibody molecules identical in affinity and specificity to the target antigen.

5) Use results survey

A use results survey is conducted after the approval of a drug to evaluate the safety and efficacy of the drug according to the Pharmaceutical Affairs Law by investigating those who receive the drug, what types of adverse drug reactions develop, and how effective the drug is. The use results survey of Humira® in the treatment of RA was requested as a condition for approval of Humira®, and was to be performed in all patients receiving Humira® after approval.

3. About Humira®

Humira® resembles antibodies normally found in the human body. It works by blocking tumor necrosis factor alpha (TNF-alpha), a protein that plays a central role in inflammatory responses.

As of June 2010, Humira® has been approved for the treatment of rheumatoid arthritis in 86 countries, psoriatic arthritis in 79 countries, ankylosing spondylitis in 76 countries, Crohn's disease in 75 countries, plaque psoriasis in 75 countries, and juvenile idiopathic arthritis in 50 countries, and more than 460,000 people worldwide have been treated with it.

Humira® has been extensively investigated in a wide range of clinical studies, and a large-scale safety information database has been established containing data on approximately 24,000 patients who received adalimumab for a variety of indications between April 1, 1997 and November 6, 2009. A number of clinical trials are also underway to evaluate the potential of Humira® in treating immune-mediated diseases other than those for which it is currently indicated.

4. Eisai's Commitment to Immunology

Eisai, whose strength lies in low-molecular-weight drugs, is aggressively addressing the development of biologics. Having acquired Morphotek, Inc., a U.S. bio-venture specialized in the research and development of antibody drugs, in April 2007, Eisai is now involved in the creation of antibody drugs for the treatment of cancer, rheumatoid arthritis, and infectious diseases using Morphotek's proprietary technologies, such as Human Morphodoma® and Libradoma™. In addition, Eisai is working with Sweden-based BioArctic Neuroscience Inc. to investigate potential immunotherapies for Alzheimer's disease, and is developing and marketing Humira®, a fully human anti-TNF-alpha monoclonal antibody, in Japan in cooperation with Abbott Japan, thus demonstrating its commitment to improving the quality of life (QOL) of patients and their families by producing antibody drugs.

5. About Abbott

Headquartered in Chicago, Illinois, Abbott is a global, broad-based health care company devoted to the discovery, development, manufacture and marketing of pharmaceuticals and medical products, including nutritionals, devices and diagnostics. The company employs more than 90,000 people and markets its products in more than 130 countries.

In Japan, approximately 2,500 Abbott employees are devoted to the manufacture, development, distribution, and marketing of pharmaceuticals and medical products, including nutritionals, devices, diagnostics, and products for vision care. Abbott's main offices in Japan are located in Tokyo, Fukui, and Chiba. News releases issued by Abbott Japan and Abbott Headquarters are available at www.abbott.co.jp and www.abbott.com, respectively.

6. Abbott's Commitment to Immunology

Abbott is focused on the discovery and development of innovative treatments for immunologic diseases. The Abbott Bioresearch Center, founded in 1989 in Worcester, Mass., United States, is a world-class discovery and basic research facility committed to finding new treatments for autoimmune diseases.

More information about Humira®, including full prescribing information, is available on the Web sites http://www.e-humira.jp (Japanese only) and www.HUMIRA.com (English).