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Press Release

AbbVie GK
Eisai Co., Ltd.

AbbVie and Eisai Clear All-Case Surveillance Condition for Approval of HUMIRA®, a Fully Human Anti-TNF-α Monoclonal Antibody, in the Treatment of Ankylosing Spondylitis

AbbVie GK (Headquarters: Tokyo, President: Esteban Plata, "AbbVie") and Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") 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 HUMIRA® Pre-filled Syringe 40 mg / 0.8 mL (adalimumab; [genetical recombination], "HUMIRA"), a fully human anti-TNF-α monoclonal antibody formulation, has been lifted for use in patients with ankylosing spondylitis.

In October 2010, the MHLW approved the indication of ankylosing spondylitis for HUMIRA® with the following condition 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."

The MHLW lifted this condition for approval based on a review of requirements in the approval condition for HUMIRA®, i.e., early collection of the safety and efficacy data on HUMIRA® and necessary measures for its proper use, which were submitted to the MHLW in an interim report of the all-case surveillance in 127 patients with ankylosing spondylitis. The analysis results supported the previously established safety and efficacy of HUMIRA®.

Clinical studies of HUMIRA® have been carried out extensively to date and a wide literature of clinical data exists on the drug. In Japan, AbbVie is the marketing and manufacturing authorization holder for HUMIRA®, while Eisai is responsible for distribution. The two companies are working together to promote the product under a one-brand, one-channel, two-promotion scheme.

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

Media Inquiries	
Public Affairs AbbVie GK Tel: +81-3-4577-1112	Public Relations Department Eisai Co., Ltd. Tel: +81-3-3817-5120

[Notes to editors]

1. Results of the special drug use-results survey*

The report submitted to the MHLW includes the results of analysis of the data obtained from 127 patients who were evaluated during the period between October 27, 2010 and March 15, 2013.
Adverse drug reactions developed in 27.6% of patients (35 of 127). The most common adverse drug reactions were “rash,” “gastroenteritis,” “nasopharyngitis,” and “abnormal hepatic function.” Serious adverse drug reactions developed in 3.9% of patients (5 of 127) including “dermatofibrosarcoma,” “anaphylactic shock,” “gastric ulcer perforation,” “hemorrhoids,” and “lupus-like syndrome” in 1 patient each. The outcome was “recovered/resolved” or “recovering/resolving” in all patients.
The efficacy of HUMIRA® in the treatment of ankylosing spondylitis was evaluated by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and global improvement. In patients who were evaluated with BASDAI at baseline and Week 24 of treatment, the BASDAI50 response rate (the proportion of patients achieving ≥50% improvement in BASDAI from baseline) was 50.0% (25 of 50) at Week 24. At Week 24, the global improvement as subjectively assessed by the physician was complete response in 38.8% (38 of 98). Responders and complete responders together accounted for 91.8% (90 of 98). This survey demonstrated that HUMIRA® improved symptoms in patients with ankylosing spondylitis who had an inadequate response to conventional therapy.

* Special drug use-results survey is a type of drug use-results survey. Please refer to 5) under Glossary of Terms.

2. Glossary of Terms

1) Ankylosing spondylitis

Ankylosing spondylitis (AS) is a chronic systemic inflammatory disease that manifests first as joint pain and stiffness in the neck, lower back, and hips, and in some cases the hands and feet, followed by fusion and rigidity of affected joints over time. This is nationally designated as an intractable disease. In rare cases, patients may develop severe AS with bony ankylosis or deformation of the spine and other joints. AS typically develops in young individuals, most often men, in their teens and twenties, and progresses slowly over several decades. Although the cause of AS is unknown, it is believed that genetic factors play a role in the etiology of the disease. The prevalence of AS is lower in Japanese (0.0065%) than Caucasians (0.9%), and AS is regarded as a rare disease in Japan.

Ankylosing spondylitis is diagnosed based on clinical symptoms characteristic of this disease and X-ray images of the sacroiliac joints. The diagnosis is difficult to establish at the early stage of the disease, and time to diagnosis of approximately 10 years on average has been pointed out as a problem.

The mainstay of treatment is exercise therapy and non-steroidal anti-inflammatory drugs. It is believed that neutralization of TNFα may alleviate inflammation of affected joints, since concentration of TNFα, an inflammatory cytokine, is found at high levels in affected areas such as the sacroiliac joint.

2) TNFα

The tumor necrosis factors (TNFs) are a group of cytokines mediating intercellular communication that have been found to damage tumor cells.

TNFα 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. TNFα, when produced in excess, plays a central role in the inflammatory responses involved in some immune-mediated diseases.

3) 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.

4) Drug use-results survey

A drug use-results survey is defined as follows by the MHLW ordinance (Good Post-marketing Study Practice [GPSP] Ministerial Ordinance).

"Among post-marketing surveys, a drug use-results survey refers to a survey by the manufacturing/marketing authorization holder to screen or confirm information related to the incidence of each disease due to adverse drug reactions, together with the quality, efficacy and safety of drugs, without specifying the condition of the patients that use the drugs."

5) Special drug use-results survey

A special drug use-results survey is a type of drug use-results surveys. A special drug use-results survey is defined as follows by the MHLW ordinance (GPSP Ministerial Ordinance). The all-case surveillance condition for approval which was cleared as announced in this press release concerns a special drug use-results survey.

"Among drug use result surveys, special drug use-results survey refers to a survey by the manufacturing/marketing authorization holder to screen or confirm information relating to the incidence of each disease due to adverse drug reactions, together with the quality, efficacy and safety of drugs, in specified populations of patients, such as pediatric patients, elderly patients, pregnant women, patients with renal and/or hepatic disorders, and patients using the drug for long periods."

6) BASDAI (Bath Ankylosing Spondylitis Disease Activity Index)

This is a disease activity index for ankylosing spondylitis. This activity index represents patients' subjective assessment of the following 6 parameters during the past week using the Visual Analog Scale (VAS)* on the questionnaire (a 0 – 10 scale for each parameter).

[1] Level of fatigue; [2] neck, back or hip pain; [3] pain/swelling in joints other than neck, back or hips; [4] discomfort from any areas tender to touch or pressure; [5] morning stiffness severity; [6] morning stiffness duration

BASDAI＝0.2［[1]＋[2]＋[3]＋[4]＋0.5([5]＋[6])］

BASDAI50 refers to ≥50% improvement in the total BASDAI score from baseline.

*VAS (Visual Analog Scale): a method that tries to indicate the current level of pain along a 10-cm line marked 0 (no pain) at one end and 100 (worst pain imaginable [worst pain ever experienced]) at the other.

3. About HUMIRA®

HUMIRA® is a fully human anti-TNF-α monoclonal antibody, and has already been approved for the following indications in Japan: “treatment of rheumatoid arthritis (including prevention of structural joint damage) and the following diseases that do not sufficiently respond to the existing treatments: psoriasis vulgaris; arthropathic psoriasis; ankylosing spondylitis; juvenile idiopathic arthritis affecting multiple joints; intestinal Behçet’s disease; moderate to severe active Crohn’s disease as remission induction and maintenance therapy; and moderate to severe ulcerative colitis.”

4. About AbbVie

AbbVie is a global, research-based biopharmaceutical company formed in 2013 following separation from Abbott Laboratories. The company’s mission is to use its expertise, dedicated people and unique approach to innovation to develop and market advanced therapies that address some of the world’s most complex and serious diseases. Together with its wholly-owned subsidiary, Pharmacyclics, AbbVie employs more than 28,000 people worldwide and markets medicines in more than 170 countries. For further information on the company and its people, portfolio and commitments, please visit www.abbvie.com. Follow @abbvie on Twitter or view careers on our Facebook or LinkedIn page.

AbbVie GK was established in Japan in 2013. The company employs approximately 800 people, dedicated to developing and delivering treatments in our therapeutic areas focused on immunology, neonatology, liver disease and neuroscience, where we believe we can make a remarkable impact on the lives of patients. For further information, please visit www.abbvie.co.jp.

5. About Eisai

Eisai Co., Ltd. is a Japan-based global research-based pharmaceutical company, and aims to be a “*human health care* (*hhc*)” company that gives first thought to patients and their families, and to increasing the benefits health care provides. Eisai Co., Ltd. has a global network of research facilities, manufacturing sites, and marketing subsidiaries, and more than 10,000 employees worldwide are engaged in development and provision of innovative new drugs in areas of unmet medical needs. For further information on Eisai Co., Ltd., please visit www.eisai.com.