CHUGAI PHARMACEUTICAL CO., LTD.
Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome,
Chuo-ku Tokyo, 103-8324 Japan
TEL:+81-(0)3-3273-0881
FAX:+81-(0)3-3281-6607
E-mail:pr@chugai-pharm.co.jp
URL:http://www.chugai-pharm.co.jp

CHUGAI
Roche Roche Group

Translation

"ACTEMRA®" Humanized Anti-Human IL-6 Receptor Monoclonal Antibody Conditions for Approval (All Patients Surveillance) Lifted in Japan

August 4, 2010 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Head Office: Chuo-ku, Tokyo; President: Osamu Nagayama (hereafter, "Chugai") announced today that it has received a notification from the Japanese Ministry of Health, Labour and Welfare(MHLW) that the conditions for approval (surveillance of all patients[*1]) are lifted with “rheumatoid arthritis(RA)” and "polyarticular-course juvenile idiopathic arthritis (pJIA)" indications for the humanized anti-human IL-6 receptor monoclonal antibody, ACTEMRA®.

For ACTEMRA®, additional approval of indications of "RA (including prevention of structural damage of joints)," "pJIA" and "systemic-onset juvenile idiopathic arthritis (sJIA)” was obtained in April 2008. As one of the conditions for this approval, it had been required that "data on the safety and efficacy of this drug shall be swiftly collected by conducting surveillance of uses in all patients and that the necessary measures shall be taken for the proper use of the drug until data on a certain number of patients is accumulated after marketing."

Data on 3,987 patients with RA and pJIA was submitted to the Japanese MHLW as the interim analysis results of the above surveillance[*2]. Based on the results, it has been determined that there is no problem necessitating additional measures for the safety and efficacy of this drug at this time. Accordingly, the conditions for approval involving the all patient surveillance have been lifted. For the surveillance, over 10,000 patients have been enrolled up to date. The final analysis of safety data will be done on the 8,300 patients enrolled by November 15, 2009, and will be reported as soon as they become available.

Among the indications of this drug, surveillance of all patients with sJIA and Castleman's disease is still conducted and new patients continue to be enrolled.

ACTEMRA®, the first antibody drug (humanized monoclonal antibody) originating from Japan, was created by Chugai in collaboration with Osaka University, utilizing genetic recombinant technology to produce a monoclonal antibody against the anti-IL6 receptor. It works by inhibiting biological activity of IL-6 through competitively blocking the binding of IL-6 to its receptor.

Rheumatoid arthritis is a systemic inflammatory disease that mainly causes progressive and multiple joint destructions, for which the cause is unknown. It appears more commonly in females in their 40s and 50s, and the disease is causing serious psychological and social problems not only for the patients but also for their families, and measures to counter the disease are seriously needed. Patients are often forced to spend a long time fighting the disease, causing various difficulties in social life such as school life and employment.

Chugai focuses on bone and joint diseases area as one of the strategic domains, and hopes to contribute to the treatment by providing innovative therapeutic options for patients and medical professionals. The company will continue to make efforts for promoting the proper use and supplying information while giving the highest priority to the safety of patients.

[References]

***1. Objective of surveillance of all patients**
For those patients who receive treatment with ACTEMRA®, the data will be evaluated in order to obtain information on the safety (adverse effects of the drug) and efficacy of the drug at an early date and to ensure the safe use of the drug.

***2. Result of interim analysis**
For the interim analysis, data on 3,987 patients with RA (3,881 patients) and pJIA (106 patients) who were enrolled between April 16, 2008 and July 15, 2009 was evaluated.

<Rheumatoid arthritis>
- The incidence of adverse drug reaction was 37.9%, in which the incidence of serious adverse drug reactions accounted for 8.0%. The most frequent adverse drug reactions were "abnormal laboratory test values" and "infections and infestations." The most frequent serious adverse drug reactions were "infections and infestations" including pneumonia. The safety profile was almost the same as in the clinical trials.
- The efficacy was evaluated using DAS28 (*). Among 2,072 patients whose DAS28 values were collected before the administration of ACTEMRA® and at the 28th week, the high disease activity score of DAS28 (mean±SD) 5.53±1.30 before administration markedly improved to 3.00±1.49 at the 28th week. The remission rate at the 28th week was 45.0%.

<Polyarticular-course juvenile idiopathic arthritis (pJIA)>
- The incidence of adverse drug reactions was 41.7%, in which the incidence of serious adverse drug reactions accounted for 10.7%. The most frequent adverse drug reactions were "infections and infestations" same as in the case with RA patients.
- For the efficacy, the general improvement levels at the 28th week were evaluated, showing "markedly effective" in 54.2%, "effective" in 42.2%, "ineffective" in 2.4%, and "cannot be evaluated" in 1.2%.

(*) The Disease Activity Score (DAS) 28 is a combined index that measures disease activity in patients with RA. It combines information from 28 tender and swollen joints (range 0-28), erythrocyte sedimentation rate, and a general health assessment on a visual analog scale. The level of disease activity is interpreted as low (DAS28 < 3.2), moderate (3.2 < DAS28 < 5.1) or high (DAS28 >5.1). DAS28 <2.6 corresponds to being in remission according to the criteria of the American Rheumatism Association (ARA).