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FDA Grants Supplemental Approval for ACTEMRA

ACTEMRA now includes labeling for the inhibition and slowing of structural joint damage, improvement of physical function, and achievement of major clinical response in rheumatoid arthritis

Roche today announced that the United States (U.S.) Food and Drug Administration (FDA) has extended the ACTEMRA (tocilizumab, RoACTEMRA in the European Union) label to include inhibition and slowing of structural joint damage, improvement of physical function, and achievement of major clinical response in adult patients with moderately to severely active rheumatoid arthritis (RA), when given in combination with methotrexate (MTX). The supplemental approval comes one year after initial U.S. approval and supports the efficacy of ACTEMRA in treating RA.

RA is a chronic, progressive inflammatory disease of the joints and surrounding tissues that is associated with intense pain, irreversible joint destruction and systemic complications. Joint damage often begins early in the disease and can lead to permanent disability; therefore, inhibiting structural damage to patients' joints is a critical measure of the effectiveness of an RA treatment.

The new U.S. license extension was based on positive data from the Phase III LITHE trial which demonstrated that patients receiving either dose of ACTEMRA (4 mg/kg or 8mg/kg) in combination with MTX had significantly less damage to their joints at one year, compared to patients in the control group. The outcome was determined by X-rays which measured the progression of bone erosions and narrowing of joint spaces over time.

"This FDA approval further supports the efficacy of ACTEMRA and follows a similar approval in the EU," said Hal Barron, M.D, Head of Global Development and Chief Medical Officer. "For those who are faced with the daily challenges of RA, inhibition and slowing of joint damage is imperative if patients are to truly achieve their treatment goals."

The LITHE study also showed that patients who received either dose of ACTEMRA (4 mg/kg or 8 mg/kg) plus MTX showed significant improvement in physical function, compared with patients who received MTX plus placebo at week 52. More patients treated with ACTEMRA also achieved major clinical response, defined as achieving an ACR 70 response for a continuous 24-week period, compared to MTX plus placebo. No new or unexpected safety signals were identified with ACTEMRA, and safety was consistent with previous studies.

ACTEMRA was approved by the FDA on January 8, 2010 as the first interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody to treat moderately to severe active RA in adult patients after an inadequate response to one or more tumour necrosis factor (TNF) antagonist therapies. It can be used as monotherapy or in combination with MTX or other disease modifying anti-rheumatic drugs (DMARDS).

The treatment is also approved for use in the European Union and a growing number of other countries including Japan, Mexico, India, Brazil, Switzerland and Australia.

About the LITHE (TociLIzumab Safety and THE Prevention of Structural Joint Damage) Study

The LITHE study, a randomised, double-blind, placebo-controlled trial was designed to evaluate the efficacy of tocilizumab plus MTX in preventing structural joint damage and improving physical function over two years. LITHE was an international study, including 15 countries and 1,196 patients with moderate to severe RA who had an inadequate response to MTX. In this randomised study, patients received either ACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with MTX or MTX plus placebo. Results from the 12-month analysis showed that ACTEMRA 4 mg/kg slowed (less than 75 percent inhibition compared to the control group) and ACTEMRA 8 mg/kg inhibited (at least 75 percent inhibition compared to the control group) the progression of structural damage compared to MTX plus placebo. At 52 weeks, total Genant-modified Sharp Score change from baseline for the ACTEMRA 8mg/kg and 4mg/kg plus MTX, and MTX plus placebo groups was: 0.25, 0.33 and 1.17 respectively. By week 104, the mean change from baseline was 0.34 and 0.47 for the 8mg/kg plus MTX and 4mg/kg plus MTX groups respectively.

The Genant-modified Sharp score focuses on 14 specific sites for evidence of bone erosion and 13 sites for narrowing of the joint space, both key measures of ongoing structural damage to the joints. A high score or an increase in the score over time represents a greater extent of damage. Improvement in physical function was measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI). The HAQ-DI is a questionnaire that asks about physical functioning in the categories of dressing and grooming, arising, eating, walking, hygiene, reach, grip and daily activities. Sixty-three percent and 60 percent of patients in the ACTEMRA 8mg/kg plus MTX and ACTEMRA 4mg/kg plus MTX groups respectively, achieved a clinically relevant improvement in HAQ-DI (change from baseline of ≥0.3 units) at week 52 compared to 53 percent in the MTX plus placebo group. Major clinical response, defined as achieving an ACR 70 response for a continuous 24 week period, was achieved in seven percent and four percent in the ACTEMRA 8mg/kg plus MTX, ACTEMRA 4mg/kg plus MTX groups, respectively, compared with one percent in the MTX plus placebo group.

About ACTEMRA

ACTEMRA is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. ACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development programme of five Phase III trials was designed to evaluate clinical findings of ACTEMRA, all of which met their primary endpoints.

ACTEMRA was first approved in Japan, and launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan. ACTEMRA was approved in the European Union in January 2009 for the treatment of RA in patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) inhibitors. It is also approved for use in over 90 other countries, including India, Brazil, Switzerland, and Australia. ACTEMRA was approved in the United States in January 2010 for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors.

The overall safety profile of ACTEMRA is consistent across all global clinical studies. The serious adverse events reported in ACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse events reported in clinical studies were upper respiratory tract infection, nasopharyngitis, headache, hypertension and increased ALT. Increases in liver enzymes (ALT and AST) were seen in some patients; these increases were generally mild and reversible, with no evidence of hepatic injuries or any observed impact on liver function. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients without association with clinical outcomes. Treatments that suppress the immune system, such as ACTEMRA, may cause an increase in the risk of malignancies.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2009, Roche had over 80,000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.