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

Roche Release, Basel, 22nd October 2013

Roche Gains FDA Approval for New Subcutaneous Formulation of ACTEMRA for Use in Adult Patients Living with Moderately to Severely Active Rheumatoid Arthritis

- This is the sixth FDA approval for ACTEMRA in four years, following previous approvals for the treatment of adults with moderately to severely active rheumatoid arthritis and children two years of age and older with active polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis.
- ACTEMRA is now approved as a subcutaneous formulation to treat adult patients with moderately to severely active rheumatoid arthritis who have used one or more disease-modifying antirheumatic drugs, such as methotrexate, that did not provide enough relief.
- ACTEMRA is the first and only humanized interleukin-6 receptor-antagonist monoclonal antibody approved by the FDA for both subcutaneous and intravenous administration in rheumatoid arthritis.

Roche today announced that the U.S. Food and Drug Administration (FDA) has approved a subcutaneous formulation of ACTEMRA (tocilizumab) for the treatment of adults with moderately to severely active rheumatoid arthritis (RA), who have used one or more disease-modifying antirheumatics drugs (DMARDs), such as methotrexate, that did not provide enough relief. Like the intravenous (IV) formulation, the subcutaneous (SC) formulation can be used both as a single-agent therapy and in combination with methotrexate or other non-biologic DMARDs. The ACTEMRA pre-filled syringe injection formulation will be available in early November.

"People with moderately to severely active rheumatoid arthritis can suffer irreversible joint damage that may be prevented by earlier treatment with a medicine such as Actemra," said Hal Barron, M.D., chief medical officer and head, Global Product Development. "We're pleased that these patients will now have the option of Actemra as a subcutaneous injection or an IV infusion."

ACTEMRA, originally approved by the FDA as an IV medicine in 2010, is the first and only humanized interleukin-6 (IL-6) receptor-antagonist monoclonal antibody approved by the FDA for both SC and IV administration.

The approval is based on data from the phase III clinical trials SUMMACTA and BREVACTA. For ACTEMRA SC, the FDA recommended dosage is 162 mg administered subcutaneously every other week, followed by an increase to 162 mg every week based on clinical response for patients less than 100 kg (220 lbs) in weight. For patients at or above 100 kg (220 lbs), the dosing is 162 mg administered subcutaneously every week.

About SUMMACTA

SUMMACTA is a randomized, double-blind, active controlled, parallel group, multicenter study with a double-blind period of 24 weeks in 1,262 patients with moderately to severely active RA. SUMMACTA demonstrated comparable efficacy (non-inferiority) of the SC formulation of ACTEMRA162 mg given weekly plus DMARDs compared to 8 mg/kg of ACTEMRA given intravenously every four weeks plus DMARDs in patients with moderately to severely active RA in the DMARD-IR population (20 percent of whom had inadequate response to anti-tumor necrosis factor [anti-TNF] therapy). A similar proportion of RA patients in each group experienced at least a 20 percent improvement in tender and swollen joints (American College of Rheumatology [ACR] 20 response) at Week 24 (69 percent with ACTEMRA SC formulation vs. 73 percent with ACTEMRA IV).

Analysis of safety at Week 24 showed that the adverse event profile of the SC and IV groups were comparable, except for SC injection site reactions.

About BREVACTA

BREVACTA is a randomized, double-blind, parallel-group study of ACTEMRA SC versus placebo SC in combination with traditional DMARDs in patients with moderately to severely active RA, who had an inadequate response to DMARD therapy. In the study, 656 patients were randomly assigned in a 2:1 ratio to two treatment groups receiving ACTEMRA SC every two weeks administered with a pre-filled syringe and placebo SC every two weeks with a pre-filled syringe. All patients continued their background DMARD therapy.

Results from BREVACTA showed RA patients who received the SC formulation of ACTEMRA every two weeks plus DMARDs were significantly more likely to have achieved ACR20 response than those given placebo SC plus DMARDs at 24 weeks (61 percent vs. 32 percent, respectively). At Week 24, significantly less structural joint damage progression was observed in patients receiving ACTEMRA SC plus DMARDs compared to placebo plus DMARDs as assessed radiographically and expressed as a change from baseline in the van der Heijde modified total Sharp score (mTSS) (mean change from baseline in mTSS of 0.62 vs. 1.23, respectively, with an adjusted mean difference of -0.60 [-1.1, -0.1]). No new clinically meaningful safety signals for ACTEMRA, except SC injection site reactions, were observed in this study.

About rheumatoid arthritis

RA is an autoimmune disease estimated to affect up to 70 million people worldwide.[1] Joints become chronically inflamed, painful and swollen, and patients can become increasingly disabled as cartilage and bone is damaged.[2]

About ACTEMRA (tocilizumab)

ACTEMRA, known as RoACTEMRA outside the U.S., is the first humanised interleukin-6 (IL-6) receptor agonist approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have used one or more disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, that did not provide enough relief. The extensive ACTEMRA clinical development programme included five phase III clinical studies and enrolled more than 4,000 people with RA in 41 countries. In addition, the phase IV ADACTA study showed that monotherapy with ACTEMRA was superior to monotherapy with adalimumab in reducing signs and symptoms of RA in methotrexate-intolerant patients or patients for whom methotrexate treatment was considered ineffective or inappropriate.[3] The overall safety profile of both medications was consistent with previously reported data. [3]

ACTEMRA is also used as an IV formulation for patients with active polyarticular juvenile idiopathic arthritis (PJIA) or systemic juvenile idiopathic arthritis (SJIA) two years of age and older.

ACTEMRA is part of a co-development agreement with Chugai Pharmaceutical Co., Ltd. It has been approved in Japan since April 2005 for Castleman's disease, followed by approvals for RA, SJIA and PJIA in 2008. It is approved in the European Union, and several other countries, including the United States, China, India, Brazil, Switzerland and Australia.

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, infectious diseases, inflammation, metabolism and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a frontrunner 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 2012 Roche had over 82,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 45.5 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

References

1. World Health Organisation. Chronic rheumatic conditions. http://www.who.int/chp/topics/rheumatic/en/ (Last accessed Oct 2013).
2. Patient UK.Rheumatoid arthritis. http://www.patient.co.uk/health/rheumatoid-arthritis (Last accessed Oct 2013).
3. Gabay C, et al. The Lancet 2013. 381;9877:1541-1550