



Chugai's Actemra Intravenous Infusion Receives Approval for Additional Indication and Dosing for Cytokine Release Syndrome

- The first approved treatment in Japan for cytokine release syndrome induced by CAR-T cell therapy

TOKYO, March 26, 2019 -- [Chugai Pharmaceutical Co., Ltd.](#) (TOKYO: 4519) announced today that it has obtained regulatory approval for the humanized anti-human IL-6 receptor monoclonal antibody, “Actemra® Intravenous Infusion 80 mg, 200 mg, and 400 mg” [generic name: tocilizumab (genetical recombination)] from the Ministry of Health, Labour and Welfare (MHLW) for an additional indication of “cytokine release syndrome induced by tumor-specific T cell infusion therapy” and an additional dosing regimen for cytokine release syndrome (CRS). CRS is an adverse reaction associated with chimeric antigen receptor (CAR)-T cell therapy. It is caused by overactive immune response, leading to death if aggravated. CAR-T cell therapy is a type of tumor-specific T cell infusion therapies.

“We are very pleased to gain additional approval which enables us to provide Actemra as the first approved treatment in Japan for the treatment of CRS induced by CAR-T cell therapy,” said Dr. Yasushi Ito, Chugai’s Executive Vice President, Co-Head of Project & Lifecycle Management Unit. “We will continue our efforts for safety information collection and prompt information provision to healthcare providers so that they can use the drug for their patients with confidence.”

The approval is based on the results of two global phase II studies conducted by Novartis, to investigate efficacy and safety of tisagenlecleucel as CAR-T cell therapy in patients with blood cancers (B-cell acute lymphoblastic leukemia and diffuse large B-cell lymphoma). Actemra was administered as monotherapy or combination therapy with corticosteroids or other treatments to patients with severe CRS.

Prescribing Information *The underlined parts were newly added.

[Indications]

- The following diseases that have not responded sufficiently to existing therapies: rheumatoid arthritis (including inhibition of structural joint damage), polyarticular-course juvenile idiopathic arthritis, and systemic juvenile idiopathic arthritis
- Improvement of symptoms and laboratory findings associated with Castleman's disease (high C-reactive protein, high fibrinogen, elevated erythrocyte sedimentation rate, low hemoglobin, low albumin, and general malaise), excluding those for whom lymphadenectomy is indicated.
- Cytokine release syndrome induced by tumor-specific T cell infusion therapy

[Dosage and Administration]

- Rheumatoid arthritis and polyarticular-course juvenile idiopathic arthritis
The recommended dose of tocilizumab (genetical recombination) is 8 mg/kg as a single intravenous

injection administered at 4-week intervals.

- Systemic juvenile idiopathic arthritis and Castleman's disease

The recommended dose of tocilizumab (genetical recombination) is 8 mg/kg as a single intravenous injection administered at 2-week intervals. The dosing interval can be shortened to a minimum of 1 week depending on patients' disease symptoms.

- Cytokine release syndrome

The recommended dose of tocilizumab (genetical recombination) is 8 mg/kg in patients weighing at least 30 kg and 12 mg/kg in patients weighing less than 30 kg, as a single intravenous injection.

About Tumor-Specific T Cell Infusion Therapy

Tumor-specific T cell infusion therapy is an immunotherapy to enhance immune response to target tumor cells and to inject extracorporeally amplified T-cells expressing a specific receptor to recognize cancer cells. Tumor-specific T cell infusion therapies currently in development are chimeric antigen receptor (CAR)-T cell therapy and T cell receptor (TCR)-T cell therapy.

About Cytokine Release Syndrome

CRS is induced by the release of a large amount of cytokines in association with excessive immune response, and results in an extreme elevation of cytokine concentration in the blood.* CRS is an adverse reaction relatively common in CAR-T cell therapy, and many patients show mild to moderate influenza-like symptoms (pyrexia, nausea and chills, myalgia, etc.). However, severe hypotension, tachycardia, dyspnea, and others may be induced in some patients, and the symptoms may progress rapidly and may lead to death.

* Lee DW, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10; 124(2): 188-95.

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