

Summary of Investigation Results

Tocilizumab (genetical recombination) [including biosimilars]

Non-proprietary name Brand name	Non-proprietary name	Brand name (marketing authorization holder)
	Tocilizumab (genetical recombination) and biosimilars	Actemra for Intravenous Infusion 80mg, 200mg, 400mg, Actemra Syringes for Subcutaneous Injection 162mg, Actemra Auto-Injectors for Subcutaneous Injection 162mg (Chugai Pharmaceutical Co., Ltd.) and biosimilars
Japanese market launch	Actemra for Intravenous Infusion 200mg: June 2005 Actemra for Intravenous Infusion 80mg, 400mg: June 2008 Actemra Syringes for Subcutaneous Injection 162mg, Actemra Auto-Injectors for Subcutaneous Injection 162mg: May 2013	
Indications	〈Actemra for Intravenous Infusion 80mg, 200mg, 400mg〉 • Treatment of the following disease in patients who have had an inadequate response to conventional treatments: Rheumatoid arthritis (including the prevention of structural joint damage), Polyarticular juvenile idiopathic arthritis, Systemic juvenile idiopathic arthritis, Adult-onset Still's disease • Improvement of symptoms and laboratory findings associated with Castleman disease, including elevated C-reactive protein, elevated fibrinogen, increased erythrocyte sedimentation rate, decreased hemoglobin, decreased albumin, and general fatigue, in patients for whom lymph node excision is not indicated. • Cytokine release syndrome associated with antineoplastic therapy. • Pneumonia caused by SARS-CoV-2, limited to patients requiring oxygen therapy. 〈Actemra Syringes for Subcutaneous Injection 162mg, Actemra Auto-Injectors for Subcutaneous Injection 162mg〉 • Treatment of the following disease in patients who have had an inadequate response to conventional treatments: Rheumatoid arthritis (including prevention of structural joint damage), Takayasu arteritis, Giant cell arteritis	
Summary of revisions	“Drug-induced hypersensitivity syndrome” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.	
Investigation results and	Cases involving drug-induced hypersensitivity syndrome were evaluated. Cases in which a causal relationship between Tocilizumab (genetical recombination)	

background of the revision	and drug-induced hypersensitivity syndrome was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.	
Reference:	Japan	Overseas ^{*2}
Number of cases ^{*1} involving drug-induced hypersensitivity syndrome reported in Japan and overseas	A total of 3 cases have been reported to date (including 0 cases in which a causal relationship between the drug and the event was reasonably possible). No deaths have been reported to date.	A total of 4 cases have been reported to date (including 2 cases in which a causal relationship between the drug and the event was reasonably possible). A total of 2 deaths have been reported to date (including 0 cases in which a causal relationship between the drug and the death following the event was reasonably possible).

*1: Cases corresponding to MedDRA v28.1 PT “Drug reaction with eosinophilia and systemic symptoms” among those collected in PMDA's safety database for drugs.

*2: Cases meeting at least two elements of either of the following diagnostic criteria for drug-induced hypersensitivity syndrome (DIHS), among cases for which information on administration of the drug was available:

· Manuals for Management of Individual Serious Adverse Drug Reactions: Drug-induced Hypersensitivity Syndrome (DIHS)

· Shiohara T et al. (2007). A complex interaction between drug allergy and viral infection. Clinical Reviews in Allergy & Immunology 33:124-133.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).