This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Tofacitinib citrate

August 22, 2019

Non-proprietary name

Tofacitinib citrate

Branded name (Marketing authorization holder)

Xeljanz Tablets 5 mg (Pfizer Japan Inc.)

Indications

Rheumatoid arthritis in patients who have not adequately responded to conventional treatments

Remission induction and maintenance therapy for moderate to severe ulcerative colitis (only for patients who have not adequately responded to conventional treatments)

Summary of revisions

1. “Venous thromboembolism” should be added to the Clinically Significant Adverse Reactions section.
2. Common to all indications, the necessity to consider alternative treatments when this drug is administered to patients with risk factors of cardiovascular events should be added in the PRECAUTIONS CONCERNING INDICATIONS section.
3. Language concerning patients with risk factors of cardiovascular events should be newly added in the PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS section as a precaution for development of signs and symptoms of venous thromboembolism and careful determination on the necessity of administration at a dose of 10 mg twice daily.

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Investigation results and background of the revision

In an ongoing overseas clinical study in patients aged 50 years or older with rheumatoid arthritis and risk factors of cardiovascular events (A3921133 Study), it was pointed out that the risks of pulmonary embolism and death tended to be higher in patients who received this drug at a dose of 10 mg twice daily than in patients who received TNF inhibitors. Based on the findings, MHLW/PMDA considered the necessity of taking measures. It was concluded that the following revision in the package insert was appropriate based on the results of the above clinical study, as a result of investigations and in consultation with expert advisors, although no cases for which a causal relationship between this drug and events cannot be ruled out have been identified among the cases involving venous thromboembolism reported in Japan after the launch.

- A precaution should be placed for venous thromboembolism as Clinically Significant Adverse Reaction because the incidence of deep vein thrombosis as well as pulmonary embolism also tended to be higher in patient who received this drug than those who received TNF inhibitors.
- Regarding patients with risk factors of cardiovascular events, a precaution concerning the necessity of considering alternative treatments, careful determination on the necessity of administration at a dose of 10 mg twice daily in particular, and development of signs and symptoms of venous thromboembolism should be stated, together with results of the A3921133 Study including the risk of death.

Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

A total of 6 cases involving venous thromboembolism have been reported to date. (A causal relationship between the drug and event could not be established for any of these cases.)
One patient mortality has been reported to date. (A causal relationship between the drug and death subsequent to the event could not be established for this case.)

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