11 – April - 2019

Roche

Direct Healthcare Professional Communication

Actemra® (tocilizumab): A New Important Identified Risk: Hepatotoxicity

Dear Healthcare professional,

Roche Products Saudi Arabia L.L.C. in agreement with The Saudi Food and Drug Authority would like to inform you of the following:

Summary

- **Serious drug-induced liver injury, including acute liver failure, hepatitis and jaundice, in some cases requiring liver transplant, have been observed with the administration of Actemra® (tocilizumab). The frequency of serious hepatotoxicity is considered rare.**
- **The currently approved prescribing information states that tocilizumab should be discontinued in patients with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) above 5x upper limit of normal (ULN). Caution should continue to be exercised when considering initiation of tocilizumab treatment in patients with ALT or AST above 1.5x ULN.**
- **In patients with Rheumatoid Arthritis (RA), Giant Cell Arteritis (GCA), Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Systemic Juvenile Idiopathic Arthritis (sJIA), ALT and AST should now be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter.**
- **Recommended dose modifications (reduction, interruption or discontinuation) of tocilizumab due to liver enzyme abnormalities remain unchanged, refer to the guidance in the approved label.**

Background on the safety concern

Tocilizumab is indicated for treatment of:

- Rheumatoid Arthritis (RA) [IV and SC formulations]
- Giant Cell Arteritis (GCA) in adult patients [SC formulation only]
- Polyarticular Juvenile Idiopathic Arthritis (pJIA) [IV and SC formulations]

in patients 2 years of age and older.

- Systemic Juvenile Idiopathic Arthritis (sJIA) [IV and SC formulation]

Tocilizumab is known to cause transient or intermittent mild to moderate elevation of hepatic transaminases and, in particular with increased frequency when used in combination with potentially hepatotoxic drugs (e.g. methotrexate). A cumulative, comprehensive assessment of serious hepatic injury including hepatic failure reported with tocilizumab was performed across all available clinical and post marketing data sources including data from FDA Adverse Event Reporting System (FAERS) and Eudravigilance (EV) databases and from the literature.

The Marketing Authorization Holder (MAH) has identified eight cases of tocilizumab related moderate to severe drug-induced liver injury including acute liver failure, hepatitis and jaundice. These events occurred between 2 weeks to more than 5 years after initiation of tocilizumab with median latency of 98 days. In these eight cases, two cases of acute liver failure required liver transplantation. These events are considered rare and the benefit-risk profile of tocilizumab in the approved indications remains favorable.

To ensure adequate safety monitoring given this newly identified important risk, in RA, GCA, pJIA and sJIA patients, ALT and AST should now be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter.

Roche is working closely with health authorities to update the product label to reflect this identified risk of hepatotoxicity and to extend the frequency of monitoring of hepatic transaminases to sJIA and pJIA indications. Healthcare Professionals should follow the guidance including dose modification and tocilizumab discontinuation as per the approved label.

Call for reporting

Health care professionals should report any adverse events suspected to be associated with the use of Actemra® (tocilizumab) to:

Roche Products Saudi Arabia L.L.C.
Direct Tel. +966 12211 4618
Mobile : +966 5678 44 692
Email : jeddah.drug_safety@roche.com

Or:

The National Pharmacovigilance and Drug Safety Centre (NPC)

Land Line: 19999.
Website: https//:ade.sfda.gov.sa
Email : npc.drug@sfda.gov.sa
Fax: +96612057662.

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