Roche

Dublin, 2nd of December 2010

Direct Healthcare Professional Communication on the association of tocilizumab (RoActemra®) with anaphylaxis

Dear Healthcare Professional:

Summary

- A case of fatal anaphylaxis has been reported in a patient treated with tocilizumab (RoActemra®)
- Healthcare professionals must be vigilant for signs of hypersensitivity or anaphylaxis in all patients receiving tocilizumab, both during and following its administration.
- Appropriate treatment should be available for immediate use in the event of an anaphylactic reaction during treatment with RoActemra.
- If anaphylaxis or any other serious hypersensitivity/infusion reaction occurs,
    - administration of tocilizumab should be stopped immediately.
    - appropriate medical management should be initiated, and
    - tocilizumab should be permanently discontinued.

Further information on the safety concern

A post-licensing case of fatal anaphylaxis has been reported in an adult patient with rheumatoid arthritis who was treated with tocilizumab (RoActemra®) infusion. The patient was also taking prednisone and leflunomide. During the fourth infusion of tocilizumab the patient experienced lightheadedness and a decreased systolic blood pressure. The infusion was discontinued. The next infusion of tocilizumab was given after pre-medication with steroids and antihistamines. Moments after the start of the infusion, the patient experienced dizziness and hypotension. Despite prompt medical intervention, the patient became apneic and unresponsive. The patient died within 24 hours of the anaphylactic event.

Clinically significant hypersensitivity reactions/serious infusion reactions associated with tocilizumab and requiring treatment discontinuation have been reported in 0.3% of all patients receiving tocilizumab in clinical trials.

The information in this letter to healthcare professionals has been agreed with the European Medicines Agency (EMA).

The Summary of Product Characteristics for RoActemra® has been updated to amend the information on hypersensitivity reactions as follows:

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Section 4.4 (Special warnings and precautions for use)

Hypersensitivity reactions

Serious hypersensitivity reactions have been reported in association with infusion of RoActemra (see section 4.8). Such reactions may be more severe, and potentially fatal in patients who have experienced hypersensitivity reactions during previous infusions even if they have received premedication with steroids and antihistamines. Appropriate treatment should be available for immediate use in the event of an anaphylactic reaction during treatment with RoActemra. If an anaphylactic reaction or other serious hypersensitivity / serious infusion related reaction occurs, administration of RoActemra should be stopped immediately and RoActemra should be permanently discontinued.

Section 4.8 (Undesirable effects)

The rate of anaphylactic reactions (occurring in a total of 6/3,778 patients, 0.2%) was several fold higher with the 4 mg/kg dose, compared to the 8 mg/kg dose. Clinically significant hypersensitivity reactions associated with tocilizumab and requiring treatment discontinuation were reported in a total of 13 out of 3,778 patients (0.3%) treated with tocilizumab during the controlled and open label clinical studies. These reactions were generally observed during the second to fifth infusions of tocilizumab (see section 4.4). Fatal anaphylaxis has been reported after marketing authorization during treatment with tocilizumab (see section 4.4).

Call for Reporting

Please report any suspected adverse events occurring with the use of tocilizumab to the Drug Surveillance Centre at Roche (either by mail, telephone [01 4690700], fax [01 4690793] or e-mail [Ireland.drug_surveillance_centre@roche.com]). Alternatively, suspected adverse events may be reported to the pharmacovigilance section of the IMB in the usual manner.

Should you have any questions or require additional information regarding anaphylactic or serious hypersensitivity reactions associated with the use of tocilizumab, please contact Medical Information at Roche (either by mail, telephone [01 4690700], fax [01 4690791] or e-mail [Ireland.druginfo@roche.com]).

Yours sincerely,

Michelle Rockingham

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