Health Canada Endorsed Important Safety Information on ACTEMRA™ (tocilizumab)

September 16, 2010

Subject: **ACTEMRA™ (tocilizumab) and the Risk of Death Due to Severe Allergic Reaction**

Hoffmann-La Roche Limited, in consultation with Health Canada, has informed health care professionals of important new safety information regarding ACTEMRA™ (tocilizumab) and severe allergic reactions.

ACTEMRA is a drug that is used intravenously to treat adults with moderate to severe rheumatoid arthritis.

Roche would like to inform you of the following;

- A death from a severe allergic reaction has been reported in a patient with rheumatoid arthritis treated with ACTEMRA. No Canadian cases of anaphylactic reaction have been reported.
- As allergic reactions can occur with the administration of ACTEMRA, it is important that you are monitored closely throughout the infusion for signs and symptoms of any allergic reaction.
- ACTEMRA should not be given to patients who are allergic to tocilizumab or any non-medicinal ingredient in ACTEMRA.

A fatal case of a severe allergic reaction has been reported in an elderly patient with a prolonged history of rheumatoid arthritis who was treated with ACTEMRA. The patient also had prior treatment with other rheumatoid arthritis medication. This patient was also taking rheumatoid arthritis medications while taking ACTEMRA. This patient also suffered from high blood pressure for which the patient was being treated with blood pressure lowering medications.

During the fourth infusion of ACTEMRA, the patient experienced lightheadedness resulting in discontinuation of the infusion. A decrease in blood pressure was noted, and medical attention at the infusion center was followed by an emergency room evaluation. Two weeks later, the patient received a fifth infusion of ACTEMRA after first receiving steroids and antihistamines. Moments after the start of the infusion, the patient experienced dizziness and very low blood pressure. Even though medical attention was delivered promptly, unfortunately, the patient died within 24 hours after these events.

This is the first reported case of a death due to a suspected severe allergic reaction in a patient

treated with ACTEMRA. Allergic reactions associated with ACTEMRA and requiring treatment discontinuation have been reported in 13 of 3778 patients receiving tocilizumab in clinical trials. These reactions were generally observed during the second to fifth infusion of ACTEMRA.

In the event of an allergic reaction, ACTEMRA treatment should be stopped immediately. **Appropriate medical management should be initiated, and ACTEMRA should be permanently discontinued.**

Managing marketed health product related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious hypersensitivity reactions, anaphylactic reactions or other serious or unexpected adverse reactions in patients receiving ACTEMRA should be reported to Hoffmann-La Roche Limited, or Health Canada at the following addresses:

Hoffmann-La Roche Limited
Drug Safety Department
2455 Meadowpine Boulevard
Mississauga, Ontario, L5N 6L7
or call toll free at: 1-888-762-4388
or Fax at: 905-542-5864
or email to: mississauga.drug_safety@roche.com

Any suspected adverse reaction can also be reported to:
Canada Vigilance Program
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
Ottawa, Ontario, K1A 0K9
Tel: 613-957-0337 or Fax: 613-957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866-234-2345
Fax: 866-678-6789
CanadaVigilance@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*

http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2010-guid-dir_indust_hppc-cpsp/2010-temp-mod_dhcpl-aps_hp-ps-eng.php.

For other inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: MHPD_DPSC@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

Should you have any questions or require additional information regarding the use of ACTEMRA, please contact the Drug Information Department at Hoffmann-La Roche Limited at 1-888-762-4388 from 8:30 a.m. to 4:30 p.m. Monday to Friday Eastern Standard Time.

Sincerely,

original signed by

Lorenzo Biondi,
Vice President, Medical and Regulatory Affairs
Hoffmann-La Roche Limited