Health Canada Endorsed Important Safety Information on RITUXAN® (rituximab)

June 2, 2011

Subject: RITUXAN® (rituximab) and Fatal Infusion Related Reactions in Patients with Rheumatoid Arthritis (RA)

Dear Health Care Professional,

Hoffmann-La Roche Limited, in consultation with Health Canada, would like to inform you of important new safety information regarding fatal infusion related reactions following the use of RITUXAN® (rituximab) in RA patients. Roche is issuing this letter to ensure that you have the most recent information available when considering RITUXAN as a treatment option in rheumatoid arthritis.

RITUXAN is a chimeric mouse/human monoclonal antibody that binds specifically to the transmembrane antigen CD20. It is authorized to reduce the signs and symptoms in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more tumour necrosis factor (TNF) inhibitor therapies**.**

- Post-marketing cases of fatal infusion related reactions have been reported in patients with RA treated with RITUXAN.
- If anaphylaxis or other serious hypersensitivity/infusion reaction occurs,
  - administration of RITUXAN should be stopped immediately, and
  - appropriate medical management should be initiated.
- Infusions should not be administered unless they are in a setting where resuscitation equipment is easily and immediately available.
- Pre-medication prior to infusion of RITUXAN for RA should always be administered (see below)
- Patients with pre-existing cardiac conditions and those who experienced prior cardiopulmonary adverse reactions need to be monitored closely following the RITUXAN infusion.

Among the patients with fatal reactions, it is not known if the patients had received the recommended premedication prior to the infusion of RITUXAN. Analgesic/anti-pyretic (*e.g. acetaminophen*) and an antihistaminic drug (*e.g. diphenhydramine*) should always be administered before each infusion of RITUXAN. Patients should receive 100 mg IV methylprednisolone 30 minutes prior to each RITUXAN infusion.

Health care professionals must be vigilant for signs of hypersensitivity or anaphylaxis in all patients experiencing an infusion reaction during or following RITUXAN administration.

Available details of the spontaneous post marketing reports of fatal infusion related reactions, none of them originating from Canada, are as follows:

- A patient, with a medical history of pericardial effusion and sleep apnoea syndrome, developed shortness of breath and weakness in his extremities after the fifth course of rituximab resulting in a cardiorespiratory arrest. CPR was unsuccessful..

- A patient, with a history of aortic valve incompetence, developed an anaphylactic reaction during the second infusion of the first course of rituximab. The patient was transferred to the ICU. After initial improvement, the patient's condition deteriorated resulting in death.

- Two other patients died on the same day as having received a rituximab infusion. Symptoms suggestive of an anaphylactic reaction were not reported for either patient: however, based on the temporal relationship between the infusion and death, infusion related reactions could not be ruled out.

Roche will be working with Health Canada to update the Product Monograph to reflect new safety information.

We encourage you to review this additional important safety information with your patients.

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 occurrence of serious and/or unexpected adverse reactions in patients receiving RITUXAN 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/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

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 RITUXAN, 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,

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