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

October 21, 2009

Subject: **Association of RITUXAN® (rituximab) with Progressive Multifocal Leukoencephalopathy (PML)**

Hoffmann-La Roche Limited, in consultation with Health Canada, would like to inform patients of important new safety information regarding the use of RITUXAN® (rituximab) and Progressive Multifocal Leukoencephalopathy (PML).

RITUXAN is authorized in Canada for the treatment of non-Hodgkin's lymphoma (a cancer of the lymph nodes), chronic lymphocytic leukemia (a cancer of the white blood cells) and rheumatoid arthritis (RA; an inflammatory disease of the joints) in patients who have failed treatment with anti-tumour necrosis factor (anti-TNF) therapy.

- A new case of progressive multifocal leukoencephalopathy (PML) has been reported in a rheumatoid arthritis (RA) patient treated with RITUXAN.
- This is the first case of PML in a patient with rheumatoid arthritis receiving RITUXAN who has not previously received other potent medications that suppress the immune system (the body's system of defenses against disease).
- While the role of RITUXAN in the cause of PML is still unclear, a contributory role is possible. Patients with RA should consider that RITUXAN may increase the risk of developing PML.
- If you are taking RITUXAN and you develop new problems with your memory, ability to think, see, hear talk or walk, you should contact your doctor or healthcare professional immediately.

Previously, 2 fatal cases of confirmed PML were reported in RA patients treated with RITUXAN. These cases involved patients with possible risk factors for the development of PML prior to and during RITUXAN treatment.

Three cases of PML have now been reported in approximately 100,000 patients with RA receiving RITUXAN. While the role that RITUXAN plays in the development of PML is unclear, a contributory role is possible. Based on the information to date, physicians treating patients with RA should consider that RITUXAN may increase the risk of PML.

Progressive Multifocal Leukoencephalopathy
PML is a rare and sometimes fatal disorder, caused by a virus which causes progressive damage or inflammation of the brain. It occurs almost exclusively in people with severe immune deficiency, who are more susceptible to disease. There are no known interventions that can reliably prevent or adequately treat PML.

Some examples of signs and symptoms of PML are:

- progressive weakness on one side of the body or clumsiness of limbs
- disturbance of vision
- changes in thinking, memory and orientation leading to confusion
- personality changes

If you develop any of the above or any other unusual signs or symptoms, please contact your doctor or healthcare professional immediately. Your doctor may refer you to a neurologist for further testing. If you are diagnosed with PML your treatment with RITUXAN will be discontinued.

Managing marketed health product-related adverse reactions depends on healthcare 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 PML or other serious or unexpected adverse reactions in patients receiving RITUXAN should be reported to Hoffmann-La Roche 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: 1-866-234-2345
Fax: 1-866-678-6789
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