Roche

Pharmaceuticals

**PUBLIC COMMUNICATION**
**Health Canada Endorsed Safety Information on RITUXAN®**

November 10, 2006

**Subject: Reports of Bowel Obstruction and Perforation with RITUXAN® (rituximab)**

Hoffmann-La Roche Limited, in consultation with Health Canada, has informed Canadian health care professionals of important safety information concerning RITUXAN® (rituximab).

RITUXAN® has been authorized for use in Canada since 2000 and is used to treat non-Hodgkin's lymphoma (a cancer of the lymph nodes) and rheumatoid arthritis. Please note the following new safety information:

- **Bowel obstruction (blockage of the small or large intestine) and bowel perforation (development of a hole in the small or large intestine) have been observed in patients receiving RITUXAN®. Some deaths have occurred in non-Hodgkin's lymphoma patients who were receiving RITUXAN®.**
- **A relationship between RITUXAN® and these events has not been clearly established.**
- **The average time for RITUXAN® patients to develop bowel perforation was 6 days from the start of therapy.**
- **Patients who experience abdominal pain, especially early in treatment, should contact their physician immediately.**

Most of the reports of bowel obstruction and perforation associated with RITUXAN® use occurred in patients taking this drug for non-Hodgkin's lymphoma. In addition, it should be noted that most patients had other underlying medical conditions and were undergoing other treatments such as chemotherapy, steroids, and radiation therapy.

There have been 2 cases of bowel obstruction (1 death) and 2 cases of bowel perforation reported in Canada.

| **Signs and symptoms of bowel obstruction may include:** | **Signs and symptoms of gastrointestinal perforation include:** |
|---|---|
| • nausea<br>• vomiting<br>• abdominal swelling<br>• abdominal pain<br>• constipation or diarrhea | • sudden onset of abdominal pain, worsened by movement<br>• abdominal tenderness<br>• high fever, chills<br>• nausea<br>• vomiting |

Bowel obstruction and perforation are serious conditions that require immediate medical attention. Patients who experience the above symptoms or any other unusual symptoms should contact their physician immediately.

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The prescribing information for RITUXAN® has been revised to include this updated information, and can be found at the following link: http://www.rochecanada.com/pdf/rituxanHPE.pdf.

This advisory is in addition to a letter issued to health care professionals concerning this information. The letter can be accessed at Health Canada's website via the following link: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/index_e.html

Hoffmann-La Roche Limited continues to work closely with Health Canada to monitor adverse event reporting and to ensure that up-to-date information regarding the use of RITUXAN® is available. 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.

Serious or unexpected adverse reactions in patients receiving RITUXAN® should be reported to Hoffmann-La Roche Ltd. or Health Canada, at the following addresses:

Hoffmann-La Roche Limited
Drug Safety Department
2455 Meadowpine Boulevard
Mississauga, ON 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 incident can also be reported to:**
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
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
cadrmp@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: please refer to contact information.
**Marketed Health Products Directorate (MHPD)**
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Tel: (613) 954-6522
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Sincerely,

Lorenzo Biondi,
Vice President, Medical and Regulatory Affairs