Health Canada Endorsed Important Safety Information on HUMIRA (Adalimumab)

Abbott Laboratories, Limited

February 2, 2005

Subject: **Updated safety information on hematologic events associated with HUMIRA and the risk of infections associated with the concurrent use of HUMIRA and anakinra**

Dear Health Care Professional,

Abbott Laboratories, Limited, in consultation with Health Canada, would like to inform you of updated safety information for HUMIRA (adalimumab). This information has been submitted for inclusion in a revised Canadian Product Monograph.

HUMIRA (adalimumab) is a human IgG monoclonal antibody known as a Biological Response Modifier that is directed against tumor necrosis factor-α or TNFα. It is indicated for reducing the signs and symptoms, and inhibiting the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).

- **Serious hematologic events associated with HUMIRA have been reported, including medically significant cytopenias such as thrombocytopenia, leukopenia, and pancytopenia. A causal relationship between HUMIRA and these events is not clear.**
- **The use of HUMIRA in combination with anakinra (an interleukin-1 antagonist) is not recommended because of the risk of severe infections.**

Hematologic Events
Rare reports of pancytopenia including aplastic anemia have been reported with TNF-blocking agents. Adverse events of the hematologic system, including medically significant cytopenia (e.g. thrombocytopenia, leukopenia) have been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear. All patients should be advised to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g. persistent fever, bruising, bleeding, pallor) while on HUMIRA. Discontinuation of HUMIRA therapy should be considered in patients with confirmed significant hematologic abnormalities.

Use with Anakinra
Serious infections were seen in clinical studies with concurrent use of anakinra (an interleukin-1 antagonist) and another TNF-blocking agent, with no added benefit. Because of the nature of the adverse events seen with this combination therapy, similar toxicities may also result from the combination of anakinra and other TNF-blocking agents, including HUMIRA. Therefore, the combination of HUMIRA and anakinra is not recommended.

Use of HUMIRA in Canada
There have been no reports in Canada of hematologic abnormalities associated with HUMIRA or infections associated with the concurrent use of HUMIRA and anakinra based on limited post-market experience.

Clinical Trials
Approximately 13,500 patients have been treated with HUMIRA worldwide in clinical trials as of August 2004.

Post-Approval Use
Cumulatively, the estimated worldwide patient exposure for HUMIRA is approximately 50,860 patient-years as of November 30, 2004. This estimate is calculated based on the number of syringes sold globally and the estimated number of syringes administered to a person over a one-year period.

The Canadian Product Monograph for HUMIRA will be revised to include the above updated safety data.

Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse drug reaction reporting programmes. Any occurrences of serious and/or unexpected adverse reactions in patients receiving HUMIRA (adalimumab) should be reported to Abbott Laboratories, Limited or the Marketed Health Products Directorate at the following addresses:

Abbott Laboratories, Limited
Medical Information Department
8401 Trans-Canada Highway
Saint-Laurent, Quebec H4S 1Z1
Tel : 1-800-567-2226
Fax : (514) 832-7824

Any suspected adverse reaction 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

For other inquiries: please refer to contact information:
Marketed Health Products Directorate
Email: mhpd_dpsc@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

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/hpfb-dgpsa/tpd-dpt/adverse_e.html
http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html

Your professional commitment in this regard has an important role in protecting the well being of your patients by contributing to early signal detection and informed drug use. A copy of this letter is also available on the Health Canada website: http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_e.html

Sincerely Yours,

original signed by

Mauricio Ede, MD, PhD
Medical Director
Abbott Laboratories, Limited