

PUBLIC COMMUNICATION
Health Canada Endorsed Important Safety Information on
Erythropoiesis-Stimulating Agents (ESAs):
Aranesp® (darbepoetin alfa) and EPREX* (epoetin alfa)



JANSSEN-ORTHO

April 19, 2007

Subject: Important Safety Information and New Prescribing Information for the Erythropoiesis-Stimulating Agents, Aranesp® (darbepoetin alfa) and EPREX* (epoetin alfa)

The manufacturers of the erythropoiesis-stimulating agents (ESAs), in consultation with Health Canada, would like to inform you of updated safety information and pending label changes regarding treatment with ESAs. Two ESAs, Aranesp® and EPREX, are authorized for use in Canada. ESAs are drugs used to increase the production of red blood cells and decrease the need for red blood cell transfusion. These medicines may be used in patients with kidney failure or in patients with cancer where the anemia is associated with chemotherapy.

As a result of these updates, EPREX is no longer approved for use in patients with cancer who do not have anemia associated with chemotherapy. Therefore, none of the ESAs are approved for use in this patient population.

In consultation with Health Canada, the Canadian prescribing information for these medicines will be revised by the manufacturers to reflect the new safety information listed in the box below. Patients are advised to contact their doctor or pharmacist if they have any questions or concerns regarding their current treatment with these medicines.

- **ESAs are drugs used to increase the production of red blood cells and to decrease the need for red blood cell transfusion and the dose should be gradually adjusted to achieve this goal. Hemoglobin levels during ESA treatment should not be higher than 120 g/L. (May not be applicable to all surgery patients, see below).**
- **Patients treated with EPREX before elective surgery should receive antithrombotic treatment to avoid blood clots.**
- **In recent studies, a higher risk of death and serious cardiovascular adverse events, such as stroke, heart attack, heart failure and blood clots was seen in both cancer and chronic kidney disease patients receiving ESAs to maintain a target hemoglobin level higher than 120 g/L.**
- **A higher risk of death was seen in patients with cancer and anemia who were not receiving either radiation or chemotherapy and receiving ESAs to maintain a target hemoglobin level of 120 g/L. ESAs are not authorized for use in this patient population.**

- **Progression of tumour growth in patients with head and neck cancer receiving radiation therapy only, occurred sooner in patients who were also being treated with ESAs to a target hemoglobin level of greater than 120 g/L.**
- **Increased death was seen in patients with metastatic breast cancer receiving chemotherapy, who were also being treated with ESAs to a target hemoglobin level of greater than 120 g/L.**

Several new medical studies, have described new risks associated with the use of ESAs. These risks include cardiovascular problems, such as heart attack, heart failure, stroke, blood clots or death, as well as decreased survival in patients with cancer due to worsening of their cancer. ESAs are not authorized for use in patients with cancer who do not have anemia associated with chemotherapy. All patients should be monitored to ensure that their red blood cell levels do not exceed 120 g/L while on ESA therapy.

Signs and symptoms of serious cardiovascular events may include, but are not limited to:

- chest pain
- leg pain and swelling
- shortness of breath
- sudden weakness, numbing or tingling of face, arm or leg
- severe sudden headache, loss of vision, or loss of speech

Patients experiencing these signs or symptoms should contact their doctor immediately. Patients should NOT discontinue their medication without consulting their doctor first.

A copy of the Health Care Professional letter and this communication are available on the Health Canada website (http://hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/index_e.html). This information is also available at <http://www.janssen-ortho.com>

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 heart attack, heart failure, stroke or blood clots or other serious or unexpected adverse reactions in patients receiving Aranesp[®] or EPREX should be reported to Amgen Canada (for Aranesp[®]), Janssen-Ortho Inc (for EPREX) or Health Canada at the following addresses:

Aranesp®

Amgen Canada, Inc.
6755 Mississauga Road, Suite 400
Mississauga, Ontario L5N 7Y2
Tel: (866) 502-6436
Fax: (888) 264-3655
safetycanada@amgen.com

EPREX

Janssen-Ortho Inc.
19 Green Belt Drive
Toronto, ON M3C 1L9
Tel: (800) 567-3331
Fax: (866) 767-5865
dsscan@joica.jnj.com

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

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

Sincerely,



David N. Churchill, MD, FRCPC
Medical Director, Nephrology
AMGEN Canada Inc.



Cathy Lau, PhD.
Vice President
Regulatory and Quality
Janssen-Ortho Inc.

For media enquiries, please contact:

Natasha Bond, Amgen Canada Inc.,
(905) 285-3007

Suzanne Frost, Janssen Ortho Inc.,
(416) 449-9444

For Additional Information, please contact:

Amgen Canada Medical Information
Department
1-866-50AMGEN, from 9 a.m to 5 p.m Monday
to Friday, EST

Janssen-Ortho Medical Information
Department
1-800-567-3331, from 8:30 a.m. to 4:30 p.m.
Monday to Friday, EST

* All trademark rights used under license.