Health Canada Endorsed Important Safety Information on EXJADE* (deferasirox)

NOVARTIS

March 9, 2007

Dear Health Care Professional:

Subject: Acute renal failure associated with EXJADE* (deferasirox)
Reports of cytopenias with EXJADE* (deferasirox)

Following discussions with Health Canada, Novartis wishes to provide you with updated safety information regarding reports of acute renal failure and peripheral blood cytopenias with EXJADE*.

EXJADE* (deferasirox) is indicated in the management of chronic iron overload in patients with transfusion-dependent anemias aged 6 years or older. EXJADE* is also indicated in the management of chronic iron overload in patients with transfusion-dependent anemias aged two to five who cannot be adequately treated with deferoxamine.

Therapy with EXJADE* should be initiated and maintained by physicians experienced in the treatment of chronic iron overload due to blood transfusions.

- **Cases of acute renal failure (some with fatal outcome) have been reported following the post-marketing use of EXJADE*. For the fatal cases, it is impossible to completely exclude a contributory role of EXJADE* to the renal impairment, although the fatalities in these critically ill patients could be attributable to other underlying diseases. The fact that there was an improvement after stopping the treatment in most of the cases with non-fatal acute renal failure is suggestive of a contributory role of EXJADE* to these cases.**
- **Serum creatinine should be assessed twice before initiating therapy. Weekly monitoring of serum creatinine is recommended in the first month after initiation or modification of therapy, and monthly thereafter. Tests for proteinuria should be performed monthly. Care should be taken to maintain adequate hydration in patients.**
- **There have been post-marketing reports (both spontaneous and from clinical trials) of cytopenias in patients treated with EXJADE*. Most of these patients had pre-existing hematologic disorders that are frequently associated with bone marrow failure. The relationship of these episodes to treatment with EXJADE* is unknown.**

EXJADE* has not been studied in patients with renal impairment. EXJADE-treated patients experienced dose-dependent increases in serum creatinine. Increases in creatinine that were > 33% at ≥ 2 consecutive post baseline visits occurred at a greater frequency in EXJADE-treated patients compared to deferoxamine-treated patients (38% vs. 14%, respectively) in a clinical trial. In clinical trials, under the dose adjustment instructions, dose reduction was required in one third of patients showing serum creatinine increase. In most patients undergoing dose reductions serum creatinine levels did not return to baseline; in 60% of patients undergoing dose reduction, serum creatinine remained elevated at > 33% without progression.

In line with standard clinical management of cytopenias, blood counts should be monitored regularly. Interruption of treatment with EXJADE* should be considered in patients who develop unexplained cytopenia.

Managing marketed health product related adverse reactions depends on health care professionals and consumers reporting them, in addition to reports collected from clinical trials. 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 serious or unexpected adverse events in patients receiving EXJADE* should be reported to Novartis or Health Canada at the following addresses:

Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, (QC) H9S 1A9
Phone:1-800-363-8883 (Medical information)

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

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.

Should you have medical enquiries regarding EXJADE*, please contact our Medical Information Department at 1-800-363-8883.

For more information please consult the EXJADE* Prescribing Information and Consumer Information on our Website (http://www.novartis.ca).

Sincerely,

original signed by

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*EXJADE is a registered trademark.