

**NOTICE TO HOSPITALS**  
**Health Canada Endorsed Important New Benefit-Risk Information on**  
**PrXIGRIS® [drotrecogin alfa (activated)]**



October 28, 2011

**[Please distribute to relevant Departments [Surgery, Pharmacy, Emergency Medicine, Anaesthesia, Intensive Care and/or other Departments as required], and other involved professional staff and post this Notice in your institution.]**

**Subject: Worldwide Withdrawal of XIGRIS® [drotrecogin alfa (activated)]**

Eli Lilly and Company is undertaking a worldwide withdrawal of Xigris® [drotrecogin alfa (activated)] due to new clinical trial findings of lack of efficacy which calls into question the benefit-risk profile of the product.

The withdrawal is effective immediately and will be completed as expeditiously as possible.

- Xigris treatment should not be initiated for new patients. Patients currently receiving treatment with Xigris should have their Xigris treatment discontinued.
- This action is based on results from the PROWESS-SHOCK trial which showed no 28-day survival benefit of Xigris in septic shock patients.
- The lack of efficacy seen in this trial calls into question the benefit-risk profile of Xigris for the indicated patient population.

Xigris was originally authorized in 2003 in Canada for treatment of severe sepsis based on the results of the PROWESS study, in which Xigris showed significant improvement in 28-day all-cause mortality. The PROWESS-SHOCK study showed a 26.4% 28-day mortality rate in patients receiving Xigris versus 24.2% in those who did not (RR 1.09 [0.92, 1.28]). The reasons for the unexpected results of PROWESS-SHOCK are not known; however, a contributing factor may be advances achieved in the standard of care for patients with sepsis and septic shock in the 10 years since completion of the original PROWESS trial. This is suggested by the fact that the mortality rate in placebo-treated patients in PROWESS-SHOCK was considerably lower than predicted.

Check your inventory for Xigris. All strengths and package sizes are subject to this withdrawal. If Xigris is found, return the product to the supplier (wholesaler/distributor) from whom it was purchased. Your supplier will return the product to Eli Lilly Canada Inc. For any additional questions about Xigris, please contact the Lilly Canada Customer Response Centre at 1-888-545-5972.

A copy of the letter can be accessed at Health Canada's website <http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/index-eng.php> and on [www.lilly.ca](http://www.lilly.ca).

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-market adverse reactions are generally presumed to underestimate the risks associated with health product treatments.

Eli Lilly Canada Inc.  
Toronto, Ontario  
1-888-545-5972

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)
- Call toll-free at 1-866-234-2345
- Complete a Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program  
Health Canada  
Postal Locator 0701E  
Ottawa, Ontario K1A 0K9

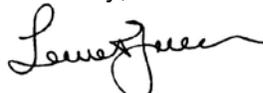
The Reporting Forms, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) section (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>). The Reporting Form is also in the *Canadian Compendium of Pharmaceuticals and Specialties*.

**For other health product inquiries related to this communication, please contact Health Canada at:**

Lead Directorate: **Marketed Health Products Directorate**  
E-mail: **MHPD\_DPSC@hc-sc.gc.ca**  
Telephone: **613-954-6522**  
Fax: **613-952-7738**

**To change your mailing address or fax number, contact the Market Authorization Holder (Industry).**

Sincerely,



Loren D. Grossman, MD, FRCPC, FACP  
Vice-President, Research and Development  
Eli Lilly Canada Inc.