

7/21/2008

**Re: Xigris® (drotrecogin alfa [activated])
Changes to preparation instructions**

Eli Lilly and Company would like to inform you of important new information related to the Preparation and Administration Instructions for Xigris (drotrecogin alfa [activated]), a biological therapeutic product indicated for the treatment of adult patients with severe sepsis who are at high risk of death.

The concentration of trace quantities of zinc ion in currently available Sodium Chloride Injection (USP) and the potential impact on the stability of Xigris have resulted in changes to these instructions and an update to the corresponding section (Dosage and Administration) of the U.S. Prescribing Information for Xigris.

Xigris stability in either an infusion bag or syringe pump depends on Xigris concentration, time, temperature, and zinc ion concentration. Recent analyses have shown that zinc ion concentration in Sodium Chloride Injection (USP) can vary by as much as 30-fold between manufacturers and between lots from the same manufacturer. In an effort to limit variability of these factors and ensure adequate potency of Xigris, the following changes to the package insert have been made:

- The final concentration of Xigris in an infusion bag and/or a syringe pump must be between 0.1 mg/mL and 0.2 mg/mL.
- The maximum in-use period of the room temperature infusion should not exceed 12 hours from the time of preparation.
- If not administered immediately, the intravenous solution in the infusion bag and/or the syringe pump should be refrigerated at 2° to 8° C (36° to 46° F) for up to 12 hours. The maximum time limit for use of the intravenous solution, including preparation, refrigeration, and administration, is 24 hours.

Enclosed is a copy of the updated U.S. Prescribing Information for Xigris. If you have questions or would like additional information, please contact The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979).

Lilly is committed to providing you with the most current information on all of our products. You can assist us with monitoring the safety of our products by reporting adverse events to the Lilly Answers Center at 1-800-LillyRx (1-800-545-5979). Alternatively, adverse events may be reported to the Food and Drug Administration (FDA) MedWatch reporting system (phone: 1-800-FDA-1088, facsimile: 1-800-FDA-0178, or website: www.fda.gov/medwatch).

Sincerely,



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Eli Lilly and Company