



**IMPORTANT LEUKINE SAFETY INFORMATION:**  
**US Market Withdrawal and Replacement Program for Liquid Leukine**

January 23, 2008

Dear U.S. Health Care Professional:

Bayer HealthCare Pharmaceuticals, in consultation with the FDA, has decided to withdraw the current liquid formulation of Leukine® from the supply system. This decision was made in light of an upward trend in spontaneous reports of adverse reactions, including syncope (fainting), which are temporally correlated with a change in the formulation of liquid Leukine to include EDTA (edetate disodium). We request that you immediately stop using liquid Leukine and return any unused vials.

Bayer will establish a special access program for the currently marketed lyophilized Leukine 250 mcg vial, which does not contain EDTA. It is important to note that the upward trend in reporting rates for certain adverse events is only associated with the current liquid Leukine containing EDTA. Bayer has not observed an upward trend in reporting rates in these adverse events with lyophilized Leukine and is taking this interim step to provide priority access to the limited inventory of lyophilized Leukine until we can increase supply of Leukine.

The special access program is designed to prioritize the supply of lyophilized Leukine for oncologists and hematologists who prescribe Leukine to treat patients following induction chemotherapy in acute myelogenous leukemia (AML) and bone marrow transplantation failure or engraftment delay. Leukine is the only myeloid growth factor approved to reduce the incidence of infections resulting in early death following induction chemotherapy in older adults with AML and to prolong survival of patients with bone marrow graft failure or engraftment delay, as compared to historical experience.

## **Spontaneous Adverse Reactions Reported with Liquid Leukine**

Bayer informed the FDA of an increase in reporting rates of syncope, with or without documented hypotension; these adverse reactions are listed in the enclosed Leukine prescribing information. The timing of increased reporting of these adverse events coincides with a change in the formulation of liquid Leukine to include EDTA.

## **Return of Liquid Leukine Inventories**

Bayer is withdrawing current stock and no longer accepting new orders for the current liquid Leukine formulation, and no existing orders will be shipped from our distribution centers. Bayer asks that all hospitals, clinics and offices having current supplies of liquid Leukine<sup>®</sup> 500 mcg vial be prepared to return those to Bayer. In the coming days, oncologists and hematologists will be contacted by a Bayer representative to work through the details of the return and file the appropriate paperwork to initiate reimbursement. If physicians, clinics or hospital pharmacies have questions regarding the return process they may call Bayer HealthCare Pharmaceuticals toll-free at 1-888-84Bayer (1-888-842-2937).

## **Special Access Program for Lyophilized Leukine**

While Bayer works to increase supplies of lyophilized Leukine and reformulate the liquid Leukine (to eliminate EDTA), there will be insufficient quantities of lyophilized Leukine to meet demand. Accordingly, during this transition, the lyophilized Leukine 250 mcg vial will be preferentially available to physicians for Leukine indications with benefits in life-threatening situations:

- patients following induction chemotherapy in AML, and
- patients with bone marrow transplantation engraftment failure or delay.

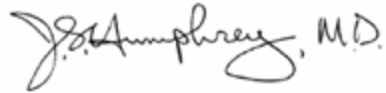
In addition, all patients currently on Leukine therapy in clinical studies will continue to have access to lyophilized Leukine through this special access program. Instructions for accessing priority supplies of lyophilized Leukine 250 mcg vial will be distributed in the next few days.

Bayer has posted this letter along with its enclosures on its websites today at [www.pharma.bayer.com](http://www.pharma.bayer.com), [www.bayeroncology.com](http://www.bayeroncology.com) and [www.leukine.com](http://www.leukine.com) and will be mailing it to U.S. oncologists and hematologists who prescribe and use Leukine for their patients. Leukine is presently marketed under the Berlex Laboratories name. Bayer acquired Berlex in 2006 to form Bayer HealthCare Pharmaceuticals.

Patient safety is Bayer's primary concern and we will continue to work closely with the FDA to address this issue.

We appreciate your patience and cooperation through this transition. If you wish to request further information, please contact Bayer HealthCare Pharmaceuticals toll-free at 1-888-84Bayer (1-888-842-2937).

Sincerely,

A handwritten signature in black ink that reads "J. Humphrey, M.D." The signature is written in a cursive style with a large, looping initial "J".

Jeff Humphrey, MD  
Vice President, U.S. Medical Sciences, Oncology

Enclosures: Leukine Background Information  
Leukine Prescribing Information



**Bayer HealthCare**  
Pharmaceuticals

## **About Leukine**

Leukine<sup>®</sup> (sargramostim) is a growth factor that helps fight infection and disease in appropriate patients by enhancing immune cell function. Leukine was approved in the United States in 1991, and is marketed by Bayer HealthCare Pharmaceuticals. Leukine is the only growth factor approved in the US for use following induction chemotherapy in older adults with acute myelogenous leukemia (AML) to shorten the time to neutrophil recovery and reduce the incidence of severe and life-threatening infections and infections resulting in death. Leukine also has been approved in the US for use in four additional indications: myeloid reconstitution following allogeneic and autologous bone marrow transplantation (BMT), peripheral blood stem cell (PBSC) mobilization and subsequent myeloid reconstitution in patients undergoing PBSC transplantation, and bone marrow transplantation failure or engraftment delay.

For full prescribing information, please visit [www.pharma.bayer.com](http://www.pharma.bayer.com), [www.bayeroncology.com](http://www.bayeroncology.com) and [www.leukine.com](http://www.leukine.com).