DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Elaine Fashana
Manager, Regulatory Affairs
Berlex Laboratories
15049 San Pablo Avenue
PO Box 4099
San Pablo, CA 94804-0099

RE: NDA # 20-038
Fludara® (fludarabine phosphate) for Injection
MACMIS # 10154

Dear Ms. Fashana:

This letter notifies Berlex Laboratories (Berlex) that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has identified promotional activities that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Specifically, Berlex promoted Fludara for the unapproved use of first-line therapy of chronic lymphocytic leukemia in the commercial exhibit hall of the 37th American Society of Clinical Oncology (ASCO) Annual Meeting held in San Francisco, California in May 2001.

Promotion of an Unapproved Use

In the commercial exhibit hall, Berlex's representatives told visitors to the exhibit booth that "findings demonstrate that in the initial treatment of CLL, fludarabine is superior to chlorambucil. The rate of complete remission and the overall rate of response (complete or partial remission), as well as the duration of the response and of progression-free survival, were significantly better among patients treated with fludarabine than among those given chlorambucil." Thus, the representative's statements show that Berlex intended Fludara to be used for the unapproved use of primary therapy for chronic lymphocytic leukemia. These statements are contrary to the PI, which states that Fludara is indicated for "the treatment of patients with B-cell chronic lymphocytic leukemia (CLL) who have not responded to or whose disease has progressed during treatment with at least one standard alkylating-agent containing regimen. The safety and effectiveness of Fludara for Injection in previously untreated or non-refractory patients with CLL have not been established."

Requested Actions

Berlex should immediately cease making such violative statements and should cease the distribution or use of any promotional materials for Fludara that contain the same or similar statements or presentations. Berlex should submit a written response to DDMAC on or before July 13, 2001, describing its intent and plans to comply with the above. In its letter to

DDMAC, Berlex should include the date on which this and other similarly violative materials were discontinued.

Berlex should direct its response to me by facsimile at (301) 594-6771 or by written communication at the Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. In all future correspondence regarding this matter, please refer to MACMIS ID # 10154 in addition to the NDA number. DDMAC reminds Berlex that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

Joseph A. Grillo, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joseph Grillo
6/28/01 08:25:08 AM