



Food and Drug Administration  
Rockville, MD 20852

DEC 22 2004

Our STN: BL 125011/24

Corixa Corporation  
Attention: Monica S. Krieger, Ph.D.  
Vice President, Regulatory Affairs  
1900 9<sup>th</sup> Avenue, Suite 1100  
Seattle, WA 98101

Dear Dr. Krieger:

Your request to supplement your biologics license application for Tositumomab and Iodine I 131 Tositumomab to expand the indication to include patients with relapsed or refractory, low grade, follicular or transformed CD20 positive non-Hodgkin's lymphoma who have not received Rituximab has been approved.

As requested in your letter of July 1, 2004, marketing approval of this product is granted under the accelerated approval of biological products regulations, 21 CFR 601.40-46. These regulations permit the use of certain surrogate endpoints or an effect on a clinical endpoint other than survival or irreversible morbidity as bases for approvals of products intended for serious or life-threatening illnesses or conditions.

Approval under these regulations requires, among other things, that you conduct adequate and well-controlled studies to verify and describe the clinical benefit attributable to this product. Clinical benefit is evidenced by effects such as increased survival or improvement in disease-related symptoms. You are required to conduct such studies with due diligence. If postmarketing studies fail to verify that clinical benefit is conferred by Tositumomab and Iodine I 131 Tositumomab (BEXXAR<sup>®</sup>), or are not conducted with due diligence, the Agency may, following a hearing, withdraw or modify approval.

Granting of this approval, to expand the indication to include patients with relapsed or refractory, low grade, follicular or transformed CD20 positive non-Hodgkin's lymphoma who have not received Rituximab, is contingent upon completion of a clinical study to verify the clinical benefit of the BEXXAR<sup>®</sup> therapeutic regimen. Identified as postmarketing commitment (PMC) #1 in the June 27, 2003, approval letter for your biologics license application under STN 125011/0 and as outlined in your July 1, 2004, supplement submitted under STN 125011/24, this PMC is subject to the reporting requirements of 21 CFR 601.70 and is as follows:

- To conduct an open-label efficacy trial of Rituximab versus the Bexxar therapeutic regimen in patients with lymphoma who have received at least one, and no more than two, prior chemotherapy regimens, and who are appropriate candidates for systemic

therapy (Study CCBX001-049). The primary objective of this study is demonstration of a longer event-free survival in patients treated with the Bexxar therapeutic regimen as compared to those receiving Rituximab.

The final protocol will be submitted for special protocol assessment review by August 15, 2003, patient accrual will be initiated by January 2, 2004, patient accrual will be completed by March 3, 2006, the study will be completed by September 3, 2007, and the final study report will be submitted by May 9, 2008.

For administrative purposes, all submissions related to this postmarketing study commitment should be clearly designated “Subpart E Postmarketing Study Commitments.”

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 125011. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 125011. Please use the following designators to label prominently all submissions, including supplements, relating to this postmarketing study commitment as appropriate:

- **Postmarketing Study Protocol**
- **Postmarketing Study Final Report**
- **Postmarketing Study Correspondence**
- **Annual Report on Postmarketing Studies**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted),
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment), and
- a revised schedule if the study schedule has changed and an explanation of the basis for the revision.

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (<http://www.fda.gov/cder/pmc/default.htm>). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see <http://www.fda.gov/cber/gdlms/post040401.htm>) for further information.

As required by 21 CFR 601.45, please submit all promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement

with a cover letter requesting advisory comment. Send two copies of the promotional materials to The Division of Drug Marketing, Advertising and Communications, HFD-42, Food and Drug Administration, 5600 Fishers Lane, Rockville MD 20852. Please submit final promotional materials with FDA Form 2253 to the above address at the time of initial dissemination of the labeling or at the time of initial publication of the advertisement.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels).

Please refer to <http://www.fda.gov/cder/biologics/default.htm> for important information regarding therapeutic biological products, including the addresses for submissions. Effective October 4, 2004, the new address for all submissions to this application is:

CDER Therapeutic Biological Products Document Room  
Center for Drug Evaluation and Research  
Food and Drug Administration  
12229 Wilkins Avenue  
Rockville, Maryland 20852

This information will be included in your biologics license application file.

Sincerely,

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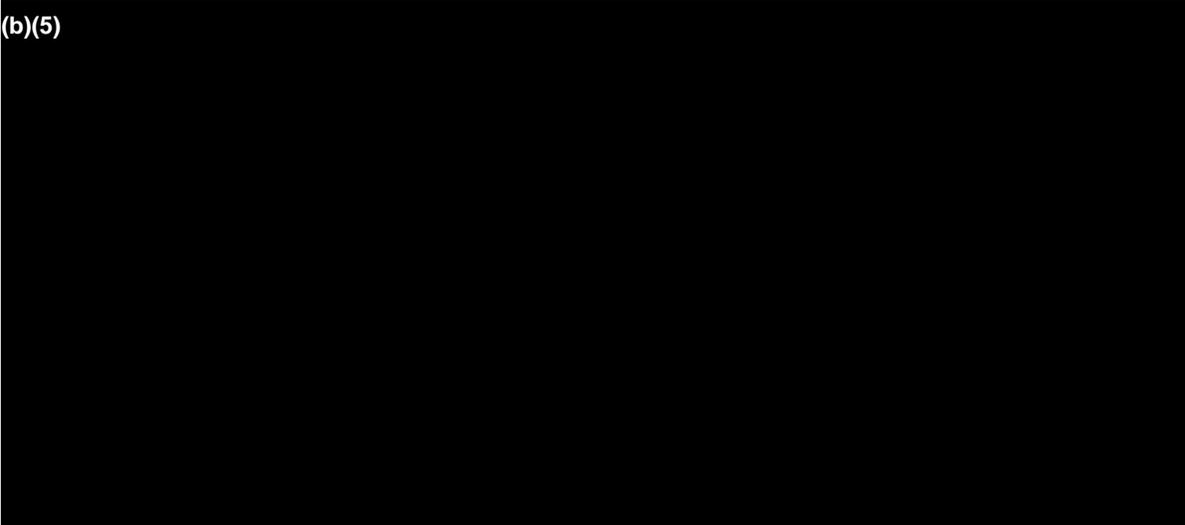
Patricia Keegan, M.D.  
Director  
Division of Therapeutic Biological Oncology Products  
Office of Drug Evaluation VI  
Center for Drug Evaluation and Research

**CONCURRENCE PAGE**

Letter Type: LETTER: Approval (AP)

Summary Text: Clinical Supplmt. Efficacy - New/Expanded Indication;  
Accelerated Approval

(b)(5)



cc: Attached label is sent to everyone

HFD-107/K. Shastri  
HFD-107/M. Andrich  
HFD-109/D. Slavin  
HFD-107/A. Rajpal  
HFD-711/M Rothmann  
HFD-711/A. Chakravarty  
HFD-711/S. Misra  
HFD-711/K. Koti  
HFD-430/R. Pratt  
HFD-328/J. Li  
HFD-106/K. Weiss  
HFD-106/G. Jones  
HFD-123 /Keith Webber  
HFM-110/RIMS/R. Eastep  
HFD-020/John Jenkins  
HFD-005/Mike Jones  
HFD-400/ODS M. Dempsey  
HFD-006/Exec sec P. Guinn  
HFD-013/FOI D. Taub  
HFD-013/FOI H. Brubaker  
HFD-240/OTCOM/ B. Poole  
HFI-20/Press/ L. Gelb  
HFI-20/Press/ J. Brodsky

HFD-230/OTCOM/CDER WebMaster  
HFD-001/B. Duvall-Miller (if PMC commitments)  
HFD-42/DDMAC/M. Kiester  
HFD-410/ODS/DSRCS/ Karen Young  
HFD-950/OCTAP/T. Crescenzi  
HFD-960/OCTAP/G. Carmouze  
HFD-320/DMPQ/ J. Famulare  
HFD-322/IPCB/ E. Rivera-Martinez  
HFM-555/DMA/ S. Kozlowski  
HFM-535/DTP/ A. Rosenberg  
HFM-570/DTBOP/ P. Keegan  
HFM-570/DTBIMP/ M. Walton  
HFD-328/TFRB Blue File/Mike Smedley  
HFD-430/ODS/DDRE (hard copy)  
HFD-410/CDER Medwatch Safety Labeling (hard copy)  
DRMP BLA file (hard copy)

History: Slavin: 12-1-04; Slavin 12.20.04; Slavin 12-21-04

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