DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-025

NDA APPROVAL

Alba BioPharm Advisors, Inc.
Attention: Dr. William McCulloch
President/US Agent, TopoTarget A/S
12109 Betts Lane
Raleigh, NC 27614

Dear Dr. McCulloch:

Please refer to your new drug application (NDA) dated January 31, 2006, received February 1, 2006, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Totect™ 500 mg (dexrazoxane for injection).

We acknowledge receipt of your submissions dated March 16, March 17, March 29, and March 31; May 25 and May 31; June 5, June 9, and June 14; July 5, July 6, July 14, July 24(2), July 25; September 14 and November 22, 2006; January 24, March 19, March 21, March 22 and March 26, 2007; May 18, June 1, June 18, and July 3, 2007. The June 18, 2007 submission constituted a complete response to our May 24, 2007 action letter.

This new drug application provides for the use of Totect™ 500 mg (dexrazoxane for injection) for the treatment of extravasation resulting from IV anthracycline chemotherapy.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling text for the package insert. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 22-025."

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-025**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

An expiration dating period of 18 months is granted for the product when stored at 25º C/60% Relative Humidity. Upon accrual of adequate real time stability data, the shelf life may be extended in an annual report.

We remind you of your postmarketing study commitment in your submission dated March 9, 2007. This commitment is listed below.

You have agreed to complete and submit to the FDA the population pharmacokinetic analysis you have previously agreed to. This analysis will compare the population parameter estimates, including inter-individual variabilities, to the literature values for dexrazoxane. As is standard practice, the initial models should group all of the data for each patient (i.e., n = 6, not n = 18). Models incorporating inter-occasion variability should then be investigated. The relationship between dexrazoxane concentrations and clinical outcomes (extravasation-related and toxicity-related) should also be explored. The FDA will review these analyses and make a determination as to whether further pharmacokinetic data acquisition is needed. FDA has previously indicated that n=6 subjects (the current dataset) may be sufficient. If n=6 is not sufficient, n=15 subjects is very likely to be sufficient.

Protocol Submission:	03/29/2006
Study Start:	07/06/2006
Final Report Submission:	09/2007

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of this commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

Please submit one market package of the drug product when it is available.

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Brenda Atkins, Regulatory Project Manager, at (301) 796-1324.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Robert Justice

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