

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-273

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-273

Antisoma
Attention: J. Kris Piper
300 Technology Square
Cambridge, MA 02139

Dear Mr. Piper:

Please refer to your new drug application (NDA) dated November 15, 2007, received November 19, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for fludarabine phosphate 10 mg tablets for oral use.

We acknowledge receipt of your submissions dated November 15, December 20, February 5, February 19, February 22, February 28, March 7, March 13 (2), March 21, April 21, June 4, June 20 (2), July 3, July 23, July 31, August 7, August 18, August 25 (2), August 28, August 29, September 2 (2), September 4, September 8, September 9, September 17 (2), September 25, December 2, December 5, December 9, and December 18, 2008.

This new drug application provides for the use of fludarabine phosphate 10 mg tablets for the treatment of adult patients with B-cell chronic lymphocytic leukemia (CLL) whose disease has not responded to or has progressed during or after treatment with at least one standard alkylating-agent containing regimen.

We completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.510), effective on the date of this letter, for use as recommended in the enclosed labeling text and required patient labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

ACCELERATED APPROVAL

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled trials to verify and describe clinical benefit. We remind you of your post marketing requirements specified in your submission dated September 8, 2008. This requirement is listed below:

1. To conduct a multicenter, randomized active control trial of oral fludarabine phosphate monotherapy versus chlorambucil monotherapy in patients with previously untreated progressive CLL. The primary endpoint of the trial will be progression-free survival.

Protocol Submission: by March 31, 2009
Trial Start: by September 30, 2009
Final Report Submission: by July 30, 2014

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirement.**"

PEDIATRIC RESEARCH EQUITY ACT (PREA)

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

CONTENT OF LABELING

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 package insert, text for patient 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 22-273.**"

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the submitted 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 22-273.**" 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.

PROPRIETARY NAME

If you choose to use a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

PROMOTIONAL MATERIALS

As required by 21 CFR 314.550, submit all promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of all promotional materials directly 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

Immediately submit all promotional materials (both promotional labeling and advertisements) to be used within the first 120 days after approval. Send one copy to this Division and two copies of the promotional materials and the package insert directly 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

In addition, as required by 21 CFR 314.550, submit all subsequent promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of the promotional materials and the package insert to the address above.

In addition, we request that you submit one copy of the introductory promotional materials you propose to use for this product to this division.

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

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

LETTERS TO HEALTH CARE PROFESSIONALS

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
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call James M. Saunders, Regulatory Project Manager, at (301) 796-0621.

Sincerely,

{See appended electronic signature page}

Ann Farrell, M.D.
Deputy Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure :

Package Insert
Patient Package Insert
Carton and Container labels

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

/s/

Ann Farrell

12/18/2008 03:18:27 PM