

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-877

APPROVAL LETTER(S)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-877

GlaxoSmithKline
2301 Renaissance Boulevard
P.O. Box 61540
King of Prussia, PA 19406-2772

Attention: Ellen S. Cutler
Senior Director, Regulatory Affairs

Dear Ms. Cutler:

Please refer to your new drug application (NDA) dated April 29, 2005, received April 29, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ARRANON® (nelarabine) Injection.

We acknowledge receipt of your submissions dated December 17, 2004; April 14, 2005; May 12 and 19, 2005; July 12, 22, 27, and 29, 2005; August 2, 11, 12, and 29, 2005; September 26 and 30, 2005; October 3, 4, 12, 25, and 26, 2005.

This new drug application provides for the use of ARRANON® (nelarabine) Injection for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.

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.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format - NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "FPL for approved NDA 21-877." Approval of this submission by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your post marketing study commitments specified in your submissions dated September 26 and October 25, 2005. This commitment, along with any completion dates agreed upon, are listed below.

1. Submit the results of the proposed phase III trial (AALL0434) to be conducted by the Children's Oncology Group to demonstrate nelarabine's clinical benefit.

First patient enrolled: April 2006

End of safety phase: 4Q 2009

Complete accrual: 4Q 2012

Complete 3-year follow-up: 4Q 2015

Availability of study report: 4Q 2016

A request for a Special Protocol Assessment should be submitted prior to initiation of the study.

Submit final study reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing study commitment must be clearly designated "Subpart H Postmarketing Study Commitments."

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:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857

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.

We also have the following comments:

1. We note that this approval provides for 15 month expiration dating for the drug product.
2. Adenosine deaminase (ADA) activity is required for the formation of the active species of nelarabine. (b) (4) of adenosine deaminase may reduce the effectiveness of this drug in some patients. Please correlate the pharmacokinetic results of the phase 1 studies with the results of the ADA genetic screening and submit this report to the FDA.

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

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

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 Nicholette Hemingway, Regulatory Project Manager, at (301) 796-1365.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
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/

Richard Pazdur
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