



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-174/S-020

Wyeth Pharmaceuticals, Inc.
87 CambridgePark Drive
Cambridge, MA 02140

Attention: Jennie K. H. Allewell
Director, Worldwide Regulatory Affairs

Dear Ms. Allewell:

Please refer to your supplemental new drug application dated March 22, 2005, received March 23, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mylotarg (gemtuzumab ozogamicin) for Injection, 5 mg/20 mL.

This application is subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated August 2, 2005 and January 13, 2006.

This supplemental new drug application provides the interim analysis of the observational study entitled, "*Prospective Observational Study of Mylotarg® (gemtuzumab ozogamicin) in Usual Care*"; and the proposed draft labeling based upon this interim analysis.

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

The final printed labeling (FPL) must be identical to the submitted labeling package insert submitted January 13, 2006.

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 supplement NDA 21-174/S-020.**" Approval of this submission by FDA is not required before the labeling is used.

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitment made under 21 CFR 314.510:

2. In addition to the submission of the quarterly update reports for the Observational Study entitled "Prospective Observational Study of Mylotarg (gemtuzumab ozogamicin) in Usual Care (Protocol No. 0903X- 100847)", an interim analysis for this study and draft labeling changes based on this analysis is to be submitted.

We also remind you of your additional commitment under 21 CFR 314 Subpart H which is still pending:

1. A randomized controlled trial of gemtuzumab ozogamicin, daunorubicin and cytarabine versus daunorubicin and cytarabine as induction therapy in patients with *de novo* CD33-positive acute myeloid leukemia. This trial should be designed to demonstrate superior survival in the three-drug (gemtuzumab ozogamicin containing) group. Response rate results can be used as supportive evidence; responses should be defined as CR's or CRp's of at least 4 weeks duration. If the three-drug regimen cannot be designed with acceptable toxicity, a randomized controlled trial designed to show that survival in patients treated with gemtuzumab ozogamicin and cytarabine is not inferior to survival in patients given daunorubicin and cytarabine should be initiated following discussion with the division. Again, the definition of the supportive secondary end point, response (CR and CRp), should include a pre-specified minimum duration of response of 4 weeks.

We also remind you of your April 20 and 27, 2000 commitments to conduct the following post-marketing studies still pending:

1. Examine the pharmacokinetic data collected from all trials to explore the possibility that various patient characteristics (demographic, clinical status) affect total and unconjugated calicheamicin pharmacokinetics.
2. Analyze the pharmacokinetic data for total and unconjugated calicheamicin for study 203 and studies 201 and 202 providing a comparison of pharmacokinetics in patients under 60 years and patients 60 years of age or older.
3. Provide a detailed description of the test methods used for analyzing the strength and purity of (b) (4).
4. Develop a specification for assay of unconjugated antibody.

Although orphan drugs are exempt from the requirements of the pediatric rule, Wyeth-Ayerst initiated on March 11, 1999, a phase 1 study in pediatric patients in order to pursue a pediatric indication for the treatment of relapsed acute myeloid leukemia. A phase 2 pediatric study is planned to evaluate the safety and efficacy of gemtuzumab ozogamicin in pediatric patients with acute myeloid leukemia in first relapse.

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

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Sean Bradley, R.Ph., Regulatory Project Manager, at (301) 796-1332.

Sincerely,

{See appended electronic signature page}

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

**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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