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APPLICATION NUMBER:

21-677

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-677
NDA 21-462/S-001

Eli Lilly and Company
Attention: John Worzalla
Research Scientist, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Mr. Worzalla:

Please refer to your new drug application (NDA) dated November 3, 2003, received November 4, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Alimta® (pemetrexed for injection).

We acknowledge receipt of your submissions dated December 4, 10 and 23, 2003; March 3, 15, 30, and 31; April 14 and 23; May 13 and 20; June 22, 29, and 30; July 12 and 13; and August 3, 5, 13, and 16, 2004. Finally, we acknowledge your August 12, 2004 supplement to NDA 21-462, which provides for updating the labeling in the "parent NDA."

This new drug application provides for the use of Alimta® (pemetrexed for injection) as a single-agent for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after prior chemotherapy.

We completed our review of this application, as amended and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text and required patient labeling. Accordingly, the application and relevant supplement are approved effective on the date of this letter. 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 and patient package insert). 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 21-677 and supplement NDA 21-462/S-001**." 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 submission dated August 3, 2004. These commitments, along with any completion dates agreed upon, are listed below.

1. H3E-MC-JMDB: Multicenter, Randomized Phase III Trial of ALIMTA® and Cisplatin Versus GEMZAR® and Cisplatin in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer

   Status: Recently began enrolling. There are approximately 3/1700 patients enrolled.
   Last patient visit: June 2008
   Final study report: November 2008

2.

Submit final study reports to NDA 21-462 as a supplemental application. For administrative purposes, all submissions relating to these postmarketing study commitments must be clearly designated "**Subpart H Postmarketing Study Commitments**."

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, we note your following postmarketing study commitments, specified in your submission dated August 3, 2004, that are not a condition of the accelerated approval. This commitment is listed below.

H3E-MC-JMGX: Multicenter, Randomized Phase III Trial of Alimta 500 mg/m2 versus 900 mg/m2 in Patients with Locally Advanced or Metastatic (Stage III or Stage IV) Non-Small Cell Lung Cancer Who Have Been Previously Treated With Chemotherapy

Status: Actively enrolling with approximately 22/1000 patients enrolled globally.
Last patient visit: December 2006
Final study report: May 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 21-462. In addition, under 21 CFR 314.81 (b)(2)(vii) and 314.82(b)(2)(viii), you should include a status summary of each commitment in your annual report to NDA 21-462. The status summary 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 Protocol", Postmarketing Study Final Report", or "Postmarketing Study Correspondence"**.

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:

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

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

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

All 15-day alert reports, periodic adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 21-462 for this drug product, not to this NDA. This includes the quarterly periodic adverse drug experience reports required by this new NDA. In the future, no submissions should be made to this NDA except for the 20 copies of the final printed labeling, as requested above.

If you have any questions, call Patty Garvey, Regulatory Project Manager, at (301) 594-5766.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure