



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. H3E-MC-JMEN: Multicenter, Randomized Phase III Study of Maintenance Therapy with Single-Agent Alimta versus Best Supportive Care after Treatment with Gemcitabine plus Carboplatin in Chemo-naïve Patients with Advanced Non-Small Cell Lung Cancer

Status: Protocol is presently under special protocol assessment at DODP with Protocol approval planned for December 2004.

Planned number of patients enrolled: 660

First patient visit: March 2005

Last patient visit: May 2008

Final study report: November 2008

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

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/s/

Richard Pazdur
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