DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-326/S-015

MedImmune Oncology, Inc
ATTN: Hanne Johansen, Ph.D.
Senior Director, Worldwide Regulatory Affairs
One MedImmune Way
Gaithersburg, MD 20878

Dear Dr. Johansen:

Please refer to your supplemental new drug application dated July 15, 2005, received July 15, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Neutrexin® (trimetrexate glucuronate for injection), 25 mg and 200 mg.

This CBE-0 supplement provides for the following changes to the package insert (additions are indicated by a double underline and deletions are struck out):

1. The following changes were made to the **PRECAUTIONS/ General** subsection:

General

Neutrexin-associated myelosuppression, stomatitis, and gastrointestinal toxicities generally can be ameliorated by adjusting the dose of leucovorin. Mild elevations in transaminases and alkaline phosphatase have been observed with Neutrexin administration and are usually not cause for modification of Neutrexin therapy (see **DOSAGE AND ADMINISTRATION**). Seizures have been reported rarely (< 1%) in AIDS patients receiving Neutrexin; however, a causal relationship has not been established. Trimetrexate is a known inhibitor of histamine metabolism. Hypersensitivity/allergic type reactions including but not limited to rash, chills/rigors, fever, diaphoresis and dypsnea have occurred with trimetrexate primarily when it is administered as a bolus infusion or at doses higher than those recommended for PCP, and most frequently in combination with 5FU and leucovorin. In rare cases, anaphylactoid reactions, including acute hypotension and loss of consciousness have occurred. Neutrexin infusion should be permanently discontinued in all patients with severe hypersensitivity reactions. Epinephrine should be available for treatment of acute allergic symptoms.

2. The revision date and number were revised as follows below the **REFERENCES** section:

Revision Date ~~11/2000~~ 1/2005 N-LB3020 P~~G~~H

We have completed our review of this supplemental new drug 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 labeling text (enclosed). Accordingly, this supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (text for the package insert submitted July 15, 2005).

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format - NDAs (January 1999) and Providing Regulatory Submissions in Electronic Format – Content of Labeling (February 2004). The guidances specify that labeling is to be submitted in PDF format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, this submission should be designated "**FPL for approved supplement NDA 20-326/S-015."** Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MedWatch: The FDA Safety Information and Adverse Event Reporting Program
Office Of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Mail Stop 4447
Silver Spring, MD 20993-0002

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Brenda Marques, Pharm.D., Regulatory Project Manager at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial 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/

Renata Albrecht

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