DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-221/S-015

MedImmune Oncology, Inc.
35 West Watkins Road
Gaithersburg, MD 20878

Attention: Hanne Johansen, Ph.D.
Senior Director, Worldwide Regulatory Affairs

Dear Ms. Johansen:

Please refer to your supplemental new drug application dated November 12, 2001, received November 13, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ethyol (amifostine) for Injection.

This "Changes Being Effected" supplemental new drug application provides for updated safety information in the sections **WARNINGS**, **PRECAUTIONS**, and **ADVERSE REACTIONS** to strengthen the information for hypotension, cardiac events, and allergic reactions. Additionally, the **ADVERSE REACTIONS** section has been reorganized to comply with new FDA Guidance on content and format of this section.

We have completed the review of this supplemental application 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 Final Printed Labeling submitted on November 12, 2001. Accordingly, the supplemental application is approved effective on the date of this letter.

However, we did note that the October 2001 package insert has the drug name with the applicant name and logo side-by-side in bold lettering at the top of the package insert. The inclusion of the applicant name and logo in such bold prominence and close proximity is confusing and inconsistent with the FDA's labeling policy. Please place the sponsor name and logo elsewhere and in smaller font at the next printing.

Additionally, during our review of the package insert dated 10/2001 (N-LB2022 PH) we noticed the absence of a ADVERSE REACTIONS *Geriatric Use* subsection. We request that you submit a Changes Being Effected (CBE-0) supplement and refer you to October, 2001 Guidance for Industry, Content and Format for Geriatric Labeling available on the Internet.

We request that the following changes in the labeling be made so as to furnish adequate information for the safe and effective use of the drug:

1. Delete lines 255-258, "Although clinical trials of ETHYOL included elderly patients, no clinical studies have been performed specifically evaluating the safety of ETHYOL in patients with preexisting cardiovascular or cerebrovascular conditions" from the ADVERSE REACTIONS section.

2. We suggest that you perform an analysis of existing clinical data and literature to evaluate any age differences in response and toxicity. If significant differences cannot be determined, we recommend that you insert the following statement in the new Geriatric Use subsection:

   "Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy in elderly patients."

Submit twenty copies of final printed labeling, ten of which are individually mounted on heavyweight paper or similar material, exactly as specified above as a "Supplement - Changes Being Effected." Incorporate all previous revisions as reflected in the most recently approved package insert. To facilitate review of your submission, provide a highlighted or marked-up copy that shows the changes that are being made.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" 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, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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

If you have any questions, call Maureen Pelosi, Project Manager, at (301) 594-5778.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
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/

Richard Pazdur

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