DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 14-691/S-020

Glaxo Wellcome, Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park, NC 27709

Attention: Kevin C. Fitzgerald, R.Ph.
Senior Assistant Director, Technical Regulatory Affairs

Dear Mr. Fitzgerald:

Please refer to your supplemental new drug application dated December 6, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ALKERAN (melphalan) Tablets.

This supplemental new drug application provides for manufacture of reformulated ALKERAN Tablets 2 mg at Glaxo Smith Kline Operations in Dartford, UK, dissolution test results, and results of a biocomparability study.

We have completed the review of this supplemental 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. Accordingly, the supplemental application is approved effective on the date of this letter.

We acknowledge your May 21 and 24, 2001 commitments to make the following change in the CLINICAL PHARMACOLOGY section:

> In a separate study in 18 patients given single oral doses of 0.2 to 0.25 mg/kg of ALKERAN, the mean dose adjusted (± SD) plasma C_{max} was 212 ± 74 ng/mL, the AUC was 498 ± 137 ng•h/mL, the $t_{1/2}$ was 1.12 ± 0.15 hours, and the t_{max} was 1.0 ± 0.5 hours.
>
> Should be changed to:
>
> In a separate study in 18 patients given single oral doses of 0.2 to 0.25 mg/kg of ALKERAN, C_{max} and AUC, when dose adjusted to a dose of 14 mg, were (mean **± SD)** 212 ± 74 ng/mL, and 498 ± 137 ng•h/mL, respectively. Elimination phase $t_{½}$ in these patients was approximately 1 hour and the median t_{max} was 1 hour.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted May 21, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 14-691/S-020." 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 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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