DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-671/S-009

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426-0989

Attention: Richard A. Swenson, Ph.D.
Director, U.S. Regulatory Affairs

Dear Dr. Swenson:

Please refer to your supplemental new drug application dated May 21, 2001, received May 22, 2001, and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hycamtin® (topotecan hydrochloride) for Injection, 4 mg.

This "Changes Being Effected" supplemental new drug application provides for changes to the PRECAUTIONS and DOSAGE AND ADMINISTRATION sections of the package insert. The changes add or strengthen a precaution and add or strengthen dosage and administration instructions that are intended to increase the safe use of Hycamtin.

We completed the review of this supplemental new drug application and concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the final printed labeling submitted on May 21, 2001. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

However, please note the following minor editorial revisions listed below. These changes should be made at the next printing or within six months, whichever comes first.

1. You should update the REFERENCES section, as needed, with the references that follow.

    1. ONS Clinical Practice Committee. Cancer Chemotherapy Guidelines and Recommendations for Practice. Pittsburgh, Pa: Oncology Nursing Society; 1999:32-41.

    2. Recommendations for the Safe Handling of Parenteral Antineoplastic Drugs. Washington, DC: Division of Safety, Clinical Center Pharmacy Department and Cancer Nursing Services, National Institutes of Health; 1992. US Dept of Health and Human Services, Public Health Service Publication NIH 92-2621.

3. AMA Council on Scientific Affairs. Guidelines for Handling Parenteral Antineoplastics. *JAMA*. 1985;253:1590-1591.

4. National Study Commission on Cytotoxic Exposure – Recommendations for Handling Cytotoxic Agents. 1987. Available from Louis P. Jeffrey, Sc.D., Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA 02115.

5. Clinical Oncological Society of Australia. Guidelines and Recommendations for Safe Handling of Antineoplastic Agents. *Med J Australia.* 1983;1:426-428.

6. Jones RB, Frank R, Mass T. Safe Handling of Chemotherapeutic Agents: A Report from the Mount Sinai Medical Center. CA-*A Cancer J for Clin*. 1983;33:258-263.

7. American Society of Hospital Pharmacists. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. *Am J Hosp Pharm.* 1990;47:1033-1049.

8. Controlling Occupational Exposure to Hazardous Drugs. (OSHA Work-Practice Guidelines). *Am J Health-Syst Pharm.* 1996;53-1669-1685.

2. You should move the "Rx only" statement to the TITLE section of the package insert.

   Currently, the "Rx only" statement immediately follows the REFERENCES section. This complies with Section 126 of FDAMA – Elimination of Certain Labeling Requirements. However, the *Guidance for Industry Implementation of Section 126 of the Food and Drug Administration Modernization Act of 1997 – Elimination of Certain Labeling Requirements* (revised July 1998) indicates, on pages 3-4, that the Agency "prefers" the Rx only statement "be placed in the TITLE section of the package insert."

We note that your package insert currently does not include a Geriatric Use subsection in the PRECAUTIONS section in accordance with the final rule published in the Federal Register on August 27, 2997 (62 FR 45313). Therefore, we suggest that you perform an analysis of existing clinical data and literature to evaluate any age differences in response and toxicity and submit this information as part of a Changes Being Effected, or prior approval, labeling supplement.

If significant differences in response and toxicity related to age cannot be determined, we recommend that you submit a Changes Being Effected Supplement which incorporates the following statement in a 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."

If you incorporate language in the Geriatric Use subsection that is different from the above, a prior approval supplement containing your proposed draft labeling should be submitted.

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, 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 21 CFR 314.80 and 314.81.

If you have any questions, call Dianne Spillman, Regulatory Project Manager, at (301) 594-5746.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Division Director
Division of Oncology Drug 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/

Richard Pazdur

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