DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 09-053/S-020

SmithKlineBeecham dba GlaxoSmithKline
1250 S. Collegeville Road
P.O. Box 5089
Collegeville, PA 19425-0989

Attention: Matthew Whitman
Manager, Regulatory Affairs

Dear Mr. Whitman:

Please refer to your supplemental new drug application dated October 5, 2001, received October 9, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Purinethol (mercaptopurine) 50 mg tablets.

We acknowledge receipt of your October 18, 2001 submission.

This "Changes Being Effected" supplemental new drug application provides for updated safety information in the package insert. The insert has been revised under CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, OVERDOSAGE, and DOSAGE AND ADMINISTRATION.

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 submitted final printed labeling (package insert submitted October 5, 2001). Accordingly, the supplemental application is approved effective on the date of this letter.

However, at the next printing or within 6 months, whichever comes first, we request that you make the following changes and include them in your next annual report:

Please update your REFERENCES section to comply with Division policy to include only the following references:

REFERENCES:

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, National Institutes of Health; 1983. US Dept of Health and Human Services, Public Health Service publication NIH 83-2621.
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, 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-SystPharm.* 1996;53-1669-1685

Please revise your proposed labeling change #3 as written below, i.e., separating the two sentences into two paragraphs:

> Inhibition of the anticoagulant effect of warfarin, when given with mercaptopurine, has been reported.
>
> As there is in vitro evidence that aminosalicylate derivatives (e.g., olsalazine, mesalazine, or sulphasalazine) inhibit the TPMT enzyme, they should be administered with caution to patients receiving concurrent mercaptopurine therapy (see WARNINGS).

Please delete your proposed labeling change #5 as the submitted support for this addition is not considered to be adequate:

> Hematologic toxicity is likely to be more profound with chronic over dosage than with a single ingestion of PURINETHOL.

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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