DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-550/S-005

GlaxoSmithKline
Attention: Grace A. Pagano, MS
Assistant Director, Antiviral/Antibacterial Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Ms. Pagano:

Please refer to your supplemental new drug application dated September 30, 2002, received October 1, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Valtrex® (valacyclovir hydrochloride) 500 mg and 1 gram Caplets.

We acknowledge receipt of your submissions dated:

September 30, 2002	October 24, 2002	November 18, 2002	December 4, 2002
December 19, 2002	January 9, 2003 (2)	January 27, 2003	February 3, 2003
February 11, 2003	February 12, 2003	February 28, 2003	March 3, 2003
March 4, 2003 (2)	March 13, 2003	March 14, 2003	March 20, 2003 (2)
March 27, 2003			

Your submission of September 30, 2002 constituted a complete response to our March 18, 1998 action letter.

This supplemental new drug application provides for the use Valtrex® (valacyclovir hydrochloride) 500 mg Caplets for the suppression of recurrent genital herpes in HIV-infected individuals.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted March 20, 2003).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case 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 20-550/S-005." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments provided in your submission dated March 27, 2003. These commitments are listed below:

1. Evaluation of the safety and efficacy of valacyclovir for the suppression of recurrent genital herpes in HIV-infected patients with CD4 cell counts <100 cells/mm3.

   Final Report Submission: 4Q2006

2. Exploration of possible drug-interaction studies with renally-excreted HIV medications (i.e., tenofovir, didanosine, and stavudine).

   Final Report Submission: 3Q2004

3. Determine the effect of concurrent valacyclovir on the antiretroviral activity in vitro of abacavir, didanosine and tenofovir, and the effect of the antiretroviral drugs abacavir, didanosine and tenofovir on acyclovir antiviral activity in vitro.

   Final Report Submission: 4Q2003

4. Collect viral isolates in all future clinical studies of valacyclovir sponsored by GlaxoSmithKline, including the study described in Commitment 1 above.

   Final report of that study due: 4Q2006

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing

exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), 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

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Nitin Patel, R.Ph., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure: Package Insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Debra Birnkrant
4/1/03 11:27:52 AM
NDA 20-550