



NDA 20-550/S-019

GlaxoSmithKline  
Attention: Sherman N. Alfors  
Director, Antiviral/Antibacterial Regulatory Affairs  
Five Moore Drive  
P.O. Box 13398  
Research Triangle Park, NC 27709

Dear Mr. Alfors:

Please refer to your supplemental new drug application dated October 31, 2002, received November 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:

October 31, 2002	February 10, 2003	February 18, 2003	March 3, 2003
March 5, 2003	March 7, 2003	March 13, 2003	March 18, 2003
March 27, 2003	March 28, 2003	April 1, 2003	April 2, 2003
April 8, 2003	April 1, 2003	April 30, 2003	May 2, 2003
May 6, 2003	May 7, 2003 (2)	May 8, 2003	May 12, 2003 (2)
May 19, 2003	May 28, 2003	May 30, 2003	June 5, 2003
June 6, 2003	June 9, 2003	June 27, 2003 (4)	July 1, 2003
July 8, 2003	July 18, 2003 (3)	July 25, 2003	July 28, 2003
July 29, 2003	July 30, 2003	July 31, 2003	Aug 1, 2003
Aug 5, 2003 (2)	Aug 6, 2003 (2)	Aug 13, 2003 (2)	Aug 14, 2003
Aug 15, 2003	Aug 20, 2003	Aug 21, 2003	Aug 25, 2003
Aug 26, 2003	Aug 27, 2003	Aug 28, 2003 (2)	

This supplemental new drug application provides for the use Valtrex® (valacyclovir hydrochloride) 500 mg Caplets in combination with safer sex practices for the reduction of the risk of transmission of genital herpes during suppressive therapy of the source partner in a heterosexual couple.

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 enclosed labeling (package insert submitted August 6, 2003 and patient package insert submitted August 28, 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 15 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-019." Approval of this submission by FDA is not required before the labeling is used.

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

1. Collect and characterize appropriate viral isolates for resistance to acyclovir in the GSK-sponsored clinical study of suppressive therapy with valacyclovir in patients with HIV infection.  
Protocol Submission: Within 4 months of the date of this letter  
Study Start: Within 9 months of the date of this letter  
Final Report Submission: Within 40 months of the date of this letter
  
2. Collect and characterize appropriate viral isolates for resistance to acyclovir in a study of the efficacy and safety of suppressive therapy with Valtrex® in immunocompetent newly diagnosed patients.  
Protocol Submission: Within 7 months of the date of this letter  
Study Start: Within 13 months of the date of this letter  
Final Report Submission: Within 52 months of the date of this letter
  
3. Finalize a protocol and conduct a comprehension study of the patient brochure messages communicating safer sex practices when using suppressive therapy with Valtrex® to reduce the risk of transmission of genital herpes.  
Protocol Submission: Within 4 months of the date of this letter  
Study Start: Within 7 months of the date of this letter  
Final Report Submission: Within 16 months of the date of this letter

We also remind you of the Pediatric Written Request issued on January 22, 2003.

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."

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(s) 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, HFD-410  
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, please 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

Enclosures: Final Printed labeling (product package insert and patient 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  
8/29/03 10:29:20 AM  
NDA 20-550