



NDA 20-564/S-015
NDA 20-596/S-016

GlaxoSmithKline Inc.
Attention: Robert Watson
Senior Director
Antiviral/Antibacterial Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC
27709

Dear Mr. Watson:

Please refer to your supplemental new drug applications dated August 30, 2001, received August 31, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Epivir[®] (lamivudine), 150mg tablets and oral solution.

We acknowledge receipt of your submissions dated:

August 30, 2001	February 4, 2002	March 29, 2002	June 10, 2002
November 6, 2001	February 13, 2002	April 10, 2002	June 11, 2002
November 9, 2001	February 15, 2002	April 15, 2002	June 13, 2002
November 16, 2001	February 25, 2002	April 22, 2002	June 14, 2002
December 18, 2001	February 27, 2002	May 15, 2002	
January 18, 2002	March 15, 2002	June 6, 2002	

These supplemental new drug applications provide for the use of Epivir[®] (lamivudine) once daily for the treatment of HIV infection in combination with other antiretroviral agents. In addition, N 20-564 supplement S-015 provides for a new higher strength 300 mg tablet.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted June 14, 2002).

Please submit the copies of final printed labeling (FPL) electronically to each application 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 heavyweight paper or similar material. For administrative purposes, these submissions should be designated "FPL

for approved supplement NDA 20-564/S-015, 20-596/S-016." In addition, please submit a Microsoft word version of the label. Approval of these submissions by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated June 6, 2002. These commitments are listed below.

1. Submit an "Information Amendment: Clinical" to (b)(4)----- to provide DAVDP with the results of genotypic and phenotypic analyses on HIV-1 viral isolates from patients who are protocol-defined virologic failures in the treatment group receiving lamivudine 300 mg once daily (with abacavir 300 mg twice daily plus efavirenz 600 mg once daily) in study CNA30021. This Information Amendment is expected to be available for submission in December 2003.
2. Submit an "Information Amendment: Clinical" to (b)(4)----- to provide DAVDP with the results of a non-US, non-IND PENTA study of the pharmacokinetic properties of lamivudine 8 mg/kg once daily compared with lamivudine 4 mg/kg twice daily in pediatric patients with HIV infection. This Information Amendment is expected to be available for submission in December 2003.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to these NDAs. 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 these NDAs. 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**."

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). The label currently includes information for pediatric use in ages greater than three months. However, additional information to determine the appropriate dosage of EPIVIR for treatment of neonates and infants younger than three months of age is needed. We will defer any requirements for submission of this information until December 31, 2005.

In addition, please submit three copies of the introductory promotional materials that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package inserts directly to:

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

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

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

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 Christine Lincoln, RN, MS, MBA, 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

ATTACHMENT-Labeling

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

/s/

Jeffrey Murray
6/24/02 01:28:50 PM
for D. Birnkrant