



NDA 20-977/S-012
NDA 20-978/S-014

GlaxoSmithKline
Attention: Martha Anne A. Moore, R.Ph.
Antiviral/Antibacterial US Regulatory Affairs
PO Box 13398
Five Moore Drive
Research Triangle Park, NC 27709

Dear Ms. Moore:

Please refer to your supplemental new drug applications dated October 2, 2003, received October 3, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZIAGEN® (abacavir sulfate) tablets and oral solution.

We acknowledge receipt of your submissions dated:

October 30, 2003	June 08, 2004	July 06, 2004
November 14, 2003	June 14, 2004 (2)	July 08, 2004
January 19, 2004	June 16, 2004	July 14, 2004
February 27, 2004	June 17, 2004	July 22, 2004
March 02, 2004	June 24, 2004	July 29, 2004
April 19, 2004	June 25, 2004 (2)	July 30, 2004
April 30, 2004	June 30, 2004 (3)	August 2, 2004.
May 07, 2004	July 02, 2004	

Specifically, these supplemental new drug applications provide for the use of ZIAGEN® (abacavir sulfate, 600 mg) tablets and oral solution once daily in combination with other antiretroviral agents for the treatment of HIV-1 infection.

We have completed the review of these applications, 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 agreed upon labeling text. Accordingly, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide and text for the Warning Card). Marketing the products with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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, these submissions should be designated "FPL for approved supplement NDA 20-977/S-012 and NDA 20-978/S-014." Approval of these submissions by FDA is not required before the labeling is used.

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. We are waiving the pediatric study requirement for ages less than three months and deferring pediatric studies for ages three months to 17 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing pediatric study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric patients ages 3 months to 17 years.

Final Report Submission: December 31, 2007.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

In addition, we remind you of your postmarketing study commitments in your submission dated July 27, 2004, which are listed below.

2. Provide human pharmacokinetic information on plasma abacavir concentrations and intracellular carbovir triphosphate [CBV-TP] concentrations following administration of abacavir 600mg once daily. Provide this information from collaborative study COL101665 following successful completion of quality assurance activity. Alternatively, if study COL101665 can not be delivered, provide this human pharmacokinetic information from a new study.

Timeline: If study COL101665 is completed, submit to FDA no later than March 31, 2005. If a new study must be done, this new study report should be submitted to FDA within 24 months of receiving feedback from FDA on the proposed study design.

2. Assess baseline and failure RT resistance mutations and failure phenotypes of HIV-1 isolates from patients who experience virologic failure in clinical study CAL30001, a study comparing 600 mg once daily abacavir vs. 300 mg twice daily abacavir (in combination with other drugs). Submit an analysis of genotypic and phenotypic results of study CAL30001.

Timeline: Submit results of these assessments within 12 months of the date of this letter.

3. Assess the frequency and severity of hypersensitivity to abacavir (given 600mg once daily or 300mg twice daily) in combination with other antiretroviral drugs in study ESS101822. This

randomized, open-label, multicenter, parallel group study is designed to assess 900 abacavir-naive patients.

Timeline: Submit the results within 18 months of the date of this letter.

4. Provide additional safety information from GSK-sponsored clinical trials utilizing abacavir plus stavudine (with other antiretroviral drugs). Specifically, provide a report of 96-week results of study ESS40001 (an open-label, randomized study comparing the safety and efficacy of ABC/d4T/3TC versus ABC/3TC/EFV versus ABC/3TC/908/RTV in therapy-naive patients) and a summary of deaths, dropouts, and serious adverse events from other GSK-sponsored clinical studies utilizing abacavir plus stavudine.

Timeline: Submit results by February 28, 2005.

5. Determine the *in vitro* combination antiretroviral activity relationships of abacavir with tenofovir, abacavir with efavirenz, and abacavir with emtricitabine.

Timeline: Results for ABC/TDF, ABC/EFV and ABC/FTC will be submitted to FDA by November 30 2004.

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 these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Antiviral Drug Products 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

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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 contact Tanim Sinha, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely yours,

{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: Approved Draft Labeling (Package Insert, Medication Guide and Warning Card)

**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
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