DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-205/SLR-021

GlaxoSmithKline
Attention: Martha Anne A. Moore, R.Ph.
Senior Director, Infectious Diseases U.S. Regulatory Affairs
P.O. Box 13398
Five Moore Drive
Research Triangle Park, NC 27709

Dear Ms. Moore:

Please refer to your August 11, 2008 supplemental new drug application, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRIZIVIR (abacavir sulfate, lamivudine, and zidovudine) Tablets.

This supplemental new drug application provides for revisions to the Medication Guide and the package insert's BLACK BOX WARNING, CONTRAINDICTIONS, and WARNINGS sections to include language regarding the association of the HLA-B*5701 allele with abacavir-related hypersensitivity reaction (HSR) and the recommendation for HLA-B*5701 testing prior to initiation of abacavir therapy. In addition, the Medication Guide and the PRECAUTIONS section of the package insert were revised to include information related to myocardial infarction.

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.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and Medication Guide). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 21-652/SLR-021.**"

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007

(FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that TRIZIVIR poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of TRIZIVIR. FDA has determined that TRIZIVIR is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, TRIZIVIR. In addition, patient labeling could help prevent serious adverse effects related to the use of the product. FDA previously approved a Medication Guide required for distribution with TRIZIVIR, but has become aware of new safety information since TRIZIVIR's approval indicating that patients who test positive for HLA-B*5701 carriage are at significantly increased risk of developing potentially fatal abacavir hypersensitivity. These patients should not initiate treatment with an abacavir-containing regimen except under exceptional circumstances when the potential benefit outweighs the risk and under close medical supervision. In addition, due to the potential increased risk for myocardial infarction with recent TRIZIVIR use, patients should inform their doctors if they smoke or have heart disease, high blood pressure, high cholesterol or diabetes.

Your proposed REMS, submitted on February 3, 2009 is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS that was included in your February 3, 2009 submission. The timetable you submitted is as follows

1st FDAAA assessment:	August 2010 (18 months from approval)
2nd FDAAA assessment:	February 2012 (3 years from approval)
3rd FDAAA assessment:	February 2016 (7 years from approval)

Information needed for assessment of the REMS will include but may not be limited to:

a. A survey of patients' understanding of the serious risks associated with the use of abacavir-containing products (Ziagen, Trizivir and Epzicom), particularly the increased risk of hypersensitivity reactions.

Use the following designators to prominently label all submissions, including supplements, relating to this REMS:

NDA 21-205 REMS Assessment
NDA 21-205 Proposed REMS Modification

Please note that:

- This Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- You are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24];

- The final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and

- You are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided [21 CFR 208.24(d)].

PROMOTIONAL MATERIALS

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 Products and two copies of both the promotional materials and the package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

HEALTHCARE PROFESSIONAL LETTER

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
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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 Robert G. Kosko, Jr., Pharm.D., M.P.H., Regulatory Project Manager, at (301) 796-3979.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Package Insert
Medication Guide

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

/s/

Kendall Marcus

3/9/2009 11:24:27 AM