

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-205/S-006

ADMINISTRATIVE AND CORRESPONDENCE
DOCUMENTS



Memorandum of Project Manager's Review: Final Printed Labeling

NDA: 21-205/S-006 Trizivir®
(abacavir sulfate, lamivudine, and zidovudine) Tablets

Date submitted: July 17, 2002
Date received: July 18, 2002
Date completed: August 3, 2002

Sponsor: GlaxoSmithKline
One Franklin Plaza
P.O.Box 7929
Philadelphia, PA 19101

*Approval letter should be sent to GSK office in Research Triangle Park, NC

Product: Trizivir® (abacavir sulfate, lamivudine, and zidovudine) Tablets

Materials Reviewed:

Labeling Supplement-Changes Being Effected (package insert and Medication Guide) dated July 17, 2002, was compared to the last approved package insert and Medication Guide (NDA 21-205, approved June 4, 2002).

Background:

This Labeling Supplement-Changes Being Effected provides for the following revisions to the package insert and patient package insert, as requested by the Division of Antiviral Drug Products (DAVDP):

- The addition of language regarding fat redistribution, as requested by a July 25, 2001 letter and by telephone facsimile correspondence on June 13, 2002.

Review Summary:

Fat Redistribution

Package Insert (PI):

The following was added to the **PRECAUTIONS** section of the package insert:

"Fat Redistribution: Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance"

have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown. A causal relationship has not been established.”

The following was added to the **PRECAUTIONS: Information for Patients** section of the package insert:

“Patients should be informed that redistribution or accumulation of body fat may occur in patients receiving antiretroviral therapy and that the cause and long-term health effects of these conditions are not known at this time.”

The following section was added to the **ADVERSE REACTIONS: Observed During Clinical Practice** section of the package insert:

“*Abacavir, Lamivudine, and Zidovudine: Body as a Whole*: Redistribution/accumulation of body fat (see PRECAUTIONS: Fat Redistribution).”

Medication Guide: Language added under “**What are the possible side effects of Trizivir?**”

“Changes in body fat have been seen in some patients taking antiretroviral therapy. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these conditions are not known at this time.”

Minor revisions

1. In the package insert, “current recommended dose” was changed to “currently recommended dose” under **CLINICAL PHARMACOLOGY: Drug Interactions: *Abacavir*** and under **PRECAUTIONS: Drug Interactions: *Abacavir***.

Conclusions/Recommendations:

This Special Supplement-Changes Being Effected, submitted on July 17, 2002, is acceptable. Please see the Medical Officer and Medical Team Leader concurrences. An approval letter should be sent to the applicant.

Virginia L. Yoerg
Regulatory Health Project Manager
Division of Antiviral Drug Products
FDA

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/s/

Virginia Yoerg
8/9/02 03:02:46 PM
CSO

Tony DeCicco
8/21/02 11:59:34 AM
CSO

**APPEARS THIS WAY
ON ORIGINAL**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-205

CBE-0 SUPPLEMENT

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

Dear Ms. Moore:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Trizivir® (abacavir sulfate, lamivudine, and zidovudine) Tablets

NDA Numbers: 21-205

Supplement numbers: S-006

Date of supplement: July 17, 2002

Date of receipt: July 18, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected." The appropriateness of reporting the proposed change(s) as changes being effected is under review.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 16, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Antiviral Drug Products, HFD-530
Attention: Division Document Room, N115
5600 Fishers Lane
Rockville, Maryland 20857

NDA-20-977S-008

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Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products, HFD-530
Attention: Document Room N115
9201 Corporate Boulevard
Rockville, Maryland 20850

If you have any question, call Virginia L. Yoerg, Regulatory Health Project Manager, at (301) 827-2335.

Sincerely yours,

{See appended electronic signature page}

Anthony W. DeCicco, R.Ph.
Chief, Project Management Staff
Division of Antiviral Drug Products
Office of Drug Evaluation 4
Center for Drug Evaluation and Research

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/s/

Tony DeCicco
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