CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-205 / S-005

Trade Name: Trizivir

Generic Name: (abacavir, sulfate, lamivudine, and zidovudine)

Sponsor: GlaxoSmithKline

Approval Date: July 24, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-205 / S-005

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Not Approvable Letter(s)	
Final Printed Labeling	
Medical Review(s)	
Chemistry Review(s)	**X**
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative and Correspondence Document(s)	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-205 / S-005

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-205/S-005

GlaxoSmithKline
Attention: Kevin A. Miller, R.Ph., RAC
Assistant Director, CMC Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Miller:

Please refer to your supplemental new drug application dated March 20, 2002, received March 21, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRIZIVIR® (abacavir sulfate, lamivudine, and zidovudine) Tablets, 300 mg of abacavir as abacavir sulfate, 150 mg of lamivudine, and 300 mg of zidovudine per tablet.

This "Changes Being Effected in 30 days" supplemental new drug application provides for approval of Glaxo Wellcome Manufacturing, Jurong, Singapore, as an alternate manufacturing site for [redacted] This site will also be used for quality control testing for the intermediate GR109714L and for quality control and stability testing for lamivudine drug substance. This submission also includes alternate analytical methods for [redacted] for GR109714L and lamivudine.

We have completed the review of this supplemental application, and it is approved.

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 Virginia Yoerg, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Chemistry Team Leader for the
Division of Antiviral Drug Products, (HFD-530)
DNDC III, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Stephen Paul Miller
7/24/02 09:52:13 AM
NDA 21-205 S-005 is approved

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-205 / S-005

CHEMISTRY REVIEW(S)

SUPPLEMENTAL NDA CHEMIST'S REVIEW	DUE DATE 09/21/02	1. ORGANIZATION HFD-530	2. NDA NUMBER 21-205

3. NAME AND ADDRESS OF APPLICANT
SmithKline Beecham Corporation d/b/a GlaxoSmithKline
Attn: Kevin A. Miller, R.Ph., RAC
One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101
Phone: 919-483-5784

4. TYPE OF SUPPLEMENT
CBE-30

5. DOCUMENT(S)

NUMBER	DATED	RECEIVED
SCM-005	3/20/02	3/21/02

6. NAME OF DRUG
Trizivir®

7. NONPROPRIETARY NAME
Abacavir sulfate, lamivudine, and zidovudine

8. SUPPLEMENT PROVIDES FOR: approval of Glaxo Wellcome Manufacturing, Jurong, Singapore, as an alternate manufacturing site for [redacted] of lamivudine drug substance. This site will also be used for quality control testing for the intermediate GR109714L and for quality control and stability testing for lamivudine [redacted]. This submission also includes alternate analytical methods [redacted] for GR109714L and lamivudine.

9. AMENDMENTS/DATES

10. PHARMACOLOGICAL CATEGORY
Antiviral

11. HOW DISPENSED
|X| Rx || OTC

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM(S)
Capsule-shaped, film-coated, tablet

14. POTENCY (CIES)
300 mg of abacavir as abacavir sulfate, 150 mg of lamivudine, and 300 mg of zidovudine per tablet

15. CHEMICAL NAME
a) Abacavir sulfate: [(1S,4R)-4-(2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl)-2-cyclopentene-1-methanol sulfate
b) Lamivudine: (-) 2',3'-dideoxy-3'-thiacytidine
c) Zidovudine: 3'-Azido-3'-deoxythymidine

16. **MEMORANDA**

17. COMMENTS

According to the CMC review of 20-564/SCM-017, the data provided by the Applicant is adequate and acceptable. On 7/8/02, J.D. Ambrogio (HFD-324, DMPQ, OC) issued an Acceptable Overall Recommendation for the Glaxo Wellcome Manufacturing facility in Jurong, Singapore. See Appendix for a copy of the EER summary report.

In conclusion, the Applicant provided adequate information for the approval of this supplement #SCM-005.

18. CONCLUSIONS AND RECOMMENDATIONS

The Supplement #SCM-005 to the NDA #21-205 is recommended for approval.

19. REVIEWER

NAME	SIGNATURE	DATE OF DRAFT REVIEW
Rao V. Kambhampati, Ph.D. Senior Regulatory Review Scientist	*[signed electronically in DFS]*	07/19/02

20. CONCURRENCE: HFD-530/SMiller *[signed electronically in DFS]*

DFS CC LIST											
L = Action Letter		L	RKambhampati		L	Med:			PharmTox
R = Review	R	L	SMiller	R	L	VYoerg			Micro
				R	L				

APPENDIX

08-JUL-2002 FDA CDER EES Page 1 of 1

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application : NDA 21205/005
Org Code : 530
Priority : 3P

Sponsor: GLAXOSMITHKLINE
5 MOORE DR
RESEARCH TRIANGLE PARK, NC 277093398

Stamp Date : 21-MAR-2002
PDUFA Date : 21-SEP-2002
Action Goal :
District Goal: 17-AUG-2002

Brand Name : TRIZIVIR
Estab. Name:
Generic Name: ABACAVIR SULFATE; LAMIVUDINE; ZIDOVUDINE
Dosage Form: (TABLET)
Strength : 300/150/300 MG PER TABL

FDA Contacts:			
V. YOERG	Project Manager	(HFD-530)	301-827-2419
R. KAMBHAMPATI	Review Chemist	(HFD-530)	301-827-2423
S. MILLER	Team Leader	(HFD-530)	301-827-2392

Overall Recommendation: ACCEPTABLE on 08-JUL-2002by J. D AMBROGIO(HFD-324) 301-827-0062

Establishment : [redacted]
GLAXO WELLCOME
2262
JURONG, , SN

DMF No: AADA:

Responsibilities: [redacted]

Profile : CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 08-JUL-02
Decision : ACCEPTABLE
Reason : BASED ON PROFILE

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/s/

Rao Kambhampati
7/22/02 09:23:24 AM
CHEMIST

Please sign off and file into DFS.

Stephen Paul Miller
7/23/02 10:54:02 AM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-205 / S-005

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-205/S-005

CBE-30 SUPPLEMENT

GlaxoSmithKline
Attention: Kevin A. Miller, R.Ph., RAC
Assistant Director, CMC Post-Approval Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Mr. Miller:

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/zidovudine) Tablets
NDA Number:	21-205
Supplement number:	S-005
Date of supplement:	March 20, 2002
Date of receipt:	March 21, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected in 30 days." The appropriateness of reporting the proposed change(s) as changes being effected in 30 days 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 May 20, 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: Document Control
5600 Fishers Lane
Rockville, Maryland 20857

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

If you have any question, please call Karen A. Young, RN, Regulatory Project Manager, at (301) 827-2376.

Sincerely yours,

Anthony DeCicco, R.Ph.
Chief, Project Manger
Division of Antiviral Drug Products, HFD-530
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Tony DeCicco
5/13/02 01:12:45 PM