DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-478/S-003

GlaxoSmithKline
Kevin A. Miller, R.Ph., RAC
Associate Director, CMC Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709-3398

Dear Mr. Miller:

Please refer to your supplemental new drug application dated July 24, 2003, received July 25, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZOVIRAX® (acyclovir) Cream, 5%.

We acknowledge receipt of your submissions dated December 22, 2003, and January 19, 2004.

This "Changes Being Effected in 30 days" supplemental new drug application provides for a 0.9g foil sachet sample presentation of ZOVIRAX® Cream 5%.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted labeling (immediate container and display tray submitted July 24, 2003; revised folder submitted January 19, 2004).

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. 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 directly to:

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

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Nitin Patel, R.Ph., 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
1/23/04 10:35:05 AM
NDA 21-478 / S-003 is approved

SUPPLEMENTAL NDA CHEMIST'S REVIEW	DUE DATE 1/25/04	1. ORGANIZATION HFD-530	2. NDA NUMBER 21-478

3. NAME AND ADDRESS OF APPLICANT
GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709-3398
Attn: Kevin A. Miller, Tel: (919) 483-5784
Associate Director, CMC Regulatory Affairs

4. TYPE OF SUPPLEMENT
CBE-30

5. DOCUMENT(S)

NUMBERS	DATED	RECEIVED
SCP003	7/24/03	7/25/03

6. NAME OF DRUG
ZOVIRAX® Cream 5%

7. NONPROPRIETARY NAME
Acyclovir

8. SUPPLEMENT PROVIDES FOR:
A 0.9g foil sachet sample presentation of ZOVIRAX® Cream 5%

9. AMENDMENTS/DATES
SCP-003(BL)/Dec. 22, 2003
Amendment/Jan. 19, 2004

10. PHARMACOLOGICAL CATEGORY
Antiviral

11. HOW DISPENSED
|X| Rx | | OTC

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM(S)
Cream

14. POTENCY (CIES)
5%

15. CHEMICAL NAME AND STRUCTURE
9-[(2-Hydroxyethoxy)methyl]guanine

16. MEMORANDA

17. COMMENTS

This supplement, changes being effected in 30 days, provides for 0.9g foil sachet sample presentation of ZOVIRAX® Cream 5%. This sachet presentation will replace the 0.8g reduced fill tube sample presentation that was approved in the original NDA.

GSK Mississauga facility in Canada is currently approved site (acceptable CGMP compliance on May 14, 2002) for manufacturing, packaging, quality control, and stability testing for 0.8g reduced fill tube sample presentation of ZOVIRAX® Cream 5%. The container closure system used for the 0.9g foil sachet sample presentation is the same as previously approved for 0.9g foil sachet presentation of Zovirax ointment 5% in NDA 18-604.

[redacted] which conforms to CFR 21 Part 177.1330 for its use as food contact surface. The container, folder, and tray artwork for the foil sachet presentation were reviewed by DDMAC and medical reviewer and the comments had been conveyed to the firm on December 3, 2003 (see review notes for detail).

One batch (#C03L249) of release data for ZOVIRAX® Cream 5% packaged into 0.9g foil sachet is provided. The test results conform to previously approved specification. Three-month stability data at both 30°C/60%RH and 40°C/75%RH is provided. The results from all time point tested conform to the specification with no significant change observed.

Based on the information provided and the nature of this product, it is judged that introduction of the 0.9g foil sachet sample presentation of ZOVIRAX® Cream 5% is not expected to have a potential adverse effect on drug product quality. Therefore, the proposed storage condition at or below 25°C with excursions permitted to 15-30°C (see USP Controlled Room Temperature) and shelf life of 12 months are acceptable.

18. CONCLUSIONS AND RECOMMENDATIONS

Information provided is judged to be adequate to support the introduction of 0.9g foil sachet sample presentation ZOVIRAX® Cream 5% proposed in this submission. Therefore, this supplement is recommended for approval.

19. REVIEWER

NAME	SIGNATURE	DATE OF DRAFT REVIEW
Zi-Qiang Gu, Ph.D.	*[signed electronically in DFS]*	1/14/2004

20. CONCURRENCE: HFD-530/S. Miller, Ph.D. *[signed electronically in DFS]*

DFS CC LIST										
L = Action Letter	R	L	Zi-Qiang Gu		L	Med:			PharmTox	
R = Review	R	L	Steve Miller	R	L	PM			Micro	
						Biopharm				

5 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 1

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/s/

Zi-Qiang Gu
1/21/04 03:12:10 PM
CHEMIST

Chemistry review

Stephen Paul Miller
1/23/04 09:31:33 AM
CHEMIST

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: December 3, 2003

Sponsor: Glaxo Smith Kline
Five Moore Drive
Research Triangle Park, NC 27709

NDA: 21-478

Drug: ZOVIRAX ® (acyclovir) Cream 5%

To: Kevin A. Miller, R.Ph., RAC
Associate Director, CMC Regulatory Affairs

From: Nitin Patel, R.Ph., Regulatory Project Manager, DAVDP

Through: Zi-Qiang Gu, Ph.D., Chemist, DAVDP
Stephen P. Miller, Ph.D., Chemistry Team Leader, DAVDP
Kimberly A. Struble, Pharm.D., Senior Clinical Analyst, DAVDP
Kendall Marcus, M.D., Medical Team Leader, DAVDP

Subject: Comment regarding carton labeling for 0.9g foil sachets

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Please refer to your Supplement-Changes Being Effected in 30 Days (CBE-30) to NDA 21-478 dated July 24, 2003. The carton labeling pieces submitted include:

- Foil 0.9g sample
- Folder 0.9g sample
- Display Tray 0.9g sample

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has evaluated the carton labeling pieces and we would like to convey the following comment regarding the Folder 0.9g sample:

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

Nitin Patel, R.Ph.
Regulatory Project Manager
Division of Antiviral Drug Products

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/s/

Nitin Patel
12/3/03 11:40:13 AM
CSO

Comment from DDMAC regarding carton labeling for 0.9g foil sample sachets

Kendall Marcus
12/9/03 10:06:29 AM
MEDICAL OFFICER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: Sonny Saini, Pharm. D.
Regulatory Review Officer
HFD-42
OMP/DDMAC

FROM: Nitin Patel, R.Ph., Regulatory Project Manager,
Division of Antiviral Drug Products, HFD-530

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
September 29, 2003		21-478	Carton label of sample foil sachets	July 24, 2003

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
ZOVIRAX® (acyclovir) Cream 5%	N/A	Antiherpetic Topical	October 27, 2003

NAME OF FIRM: GlaxoSmithKline

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

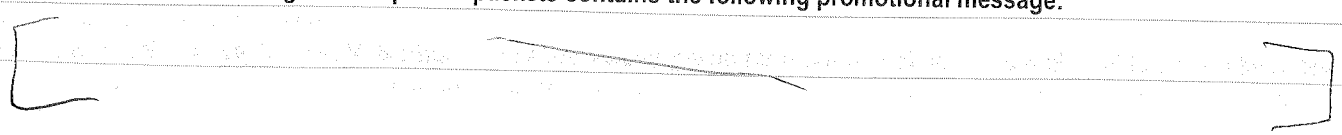
- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

The product carton for 0.9 gram sample foil packets contains the following promotional message:



The carton label is being sent to you via inter-office mail. Please evaluate this promotional message.
Background information: The 0.9 g sample foil sachet will replace the 0.8 g sample reduced fill tube that was approved in the original NDA. This label was submitted with the 'Changes Being Effected in 30 Days, CMC' supplement on July 24, 2003.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Nitin Patel, R.Ph., Regulatory Project Manager	☒ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Nitin Patel
9/29/03 03:24:24 PM