7-15-98 Honorray Weikel HFD-120

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 15 1998

David E. Wheadon, M.D.
Vice President and Director, Regulatory Affairs
and Product Professional Services
SmithKline Beecham Pharmaceuticals
P.O. Box 7929
Philadelphia, PA 19101-7929

RE: Invoice for Application Fees for NDA 021-019,
Compazine (prochlorperazine maleate) Spansules (capsules)

Dear Dr. Wheadon:

This communication contains an invoice (Attachment A) for application fees for Fiscal Year (FY) 1998 for NDA 021-019, Compazine (prochlorperazine maleate) Spansules (capsules), under the Prescription Drug User Fee Act of 1992 as amended by the Food and Drug Administration Modernization Act of 1997.

The Division of Neuropharmacological Drug Products (DNDP) received a supplement to NDA 011-000 on October 1, 1997, for reformulation of the drug product as a replacement for the current product involving a change to a different release mechanism. SmithKline Beecham Pharmaceuticals submitted the supplement without payment of an application fee. During the course of the review, the DNDP determined that the supplement should have been submitted as a new drug application (NDA) in accordance with agency policy as expressed in the "Interim Guidance: Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees Under The Prescription Drug User Fee Act of 1992." The supplemental application was reclassified as NDA 021-019, Compazine (prochlorperazine maleate) Spansules (capsules), and received a not-approvable letter on February 19, 1998.

The enclosed invoice is for the entire FY 1998 application fee for NDA 021-019 which did not require clinical data for approval. **Payment is due within 30 days of the date of the invoice.** Instructions for payment are included in Attachment B.

If you have any questions concerning the invoice, please contact:

Mr. Michael Jones
Consumer Safety Officer
Center for Drug Evaluation and Research
Food and Drug Administration, HFD-5
5600 Fishers Lane
Rockville, MD 20857
(301) 594-2041
Internet addresses: JONESM@CDER.FDA.GOV

We appreciate your continued cooperation and thank you in advance for your prompt payment.

Sincerely yours,

/S/

Jim Donahue, Director
Office of Financial Management

Enclosures:

Attachment A - Action Invoice
Attachment B - Payment Instructions

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-019

Smithkline Beecham Pharmaceuticals
Attention: Dale E. Stockbower
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA 19426

JUN 18 1998

Dear Ms. Stockbower:

Please refer to your New Drug Application (NDA) dated September 29, 1997, received October 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Compazine[R] (prochlorperazine maleate) Spansule[R] Capsules

This application was originally submitted as supplemental application [redacted] to NDA 11-000 and provided for reformulation of the drug product as a replacement for the current product involving a change to a different release mechanism. Please note that we have reclassified the former supplemental application as an NDA as a result of the change to a different release mechanism and to conform to the July 12, 1993, 'Interim Guidance on Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees Under the Prescription Drug User Fee Act of 1992'. A copy of the Interim Guidance has been enclosed for your convenience. If you have any questions concerning the Interim Guidance, please contact Michael Jones, Program Manager, Center for Drug Evaluation and Research Office of Policy at (301) 594-2041.

Accordingly, we acknowledge receipt on May 4, 1998, of your April 30, 1998, resubmission to your new drug application for Compazine[R] (prochlorperazine maleate) Spansule[R] Capsules.

This resubmission contains additional information, including an additional bioequivalence study report, submitted in response to our February 19, 1998 action letter. We also note your minor amendment dated May 18, 1998.

We consider your May 4, 1998, resubmission a complete, class 2 response to our February 19, 1998, action letter. Therefore, the user fee goal date is November 4, 1998.

We apologize for any inconvenience due to this oversight. If you should have any questions, please contact Anna M. Homonnay-Weikel, R.Ph., Project Manager, at (301) 594-5535.

Sincerely yours,

/S/ 6/18/98

Paul Leber, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

attachment

APPEARS THIS WAY
ON ORIGINAL

3/4/99

Division of Neuropharmacological Drug Products

PROJECT MANAGER LABELING REVIEW

Application Number: 21-019

Name of Drug: Compazine® (prochlorperazine maleate)

Sponsor: SmithKline Beecham Pharmaceuticals (SKB)

Material Reviewed:
1) NDA 21-019 draft labeling dated 4/30/98 (attachment 1)
2) Current labeling from NDA 11-000 annual report Y-034 (1/30/96 - 1/29/97), CZ:L89 (rev 10/96) (deemed acceptable in a 6/3/97 FDA letter) (attachment 3).

Background and Summary Description:
This NDA existed previously as supplements 11-000[redacted] however, were converted to NDA 21-019 per the 'Bundling Guidance'. It provides for a reformulation of the current Compazine® Spansules® involving a new mechanism of controlled release and a new manufacturing facility (the current formulation of Compazine® Spansules® is covered by NDA 11-000) . The initial submission of 9/29/97 provided for changes to the 'Description', and 'How Supplied' sections of the package insert to reflect these changes to the Spansule® dosage form (attachment 2).

Subsequently, in a 2/29/98 FDA action letter, SKB was requested to add the chemical name and chemical structure of prochlorperazine to the 'Description' section of the package insert. SKB submitted revised draft labeling in a 4/30/98 amendment with these requested changes added (attachment 1). The labeling changes were deemed approvable by Dr. Lostritto pursuant to Chemistry Review #1 dated 10/26/98 (p.6).

Review:
A side-by-side comparison between the most current labeling, CZ:L89 (Rev 10/96)(attachment 3), and the submitted marked-up draft labeling CZ:L90 (Rev 2/97)(attachment 1) revealed the following additional changes (in addition to the proposed marked-up revisions presented in this submission). The additional changes below were effected through annual report Y-035 (1/30/97 - 1/29/98) for NDA 11-000 (see notes in attachment 3 and 4):

1. Deleted [redacted] under 'Description' 5 mg and 10 mg Tablets and added [redacted]
2. Deleted 'NOTE: Compazine 5 mg and 10 mg tablets....remains unchanged.'
3. Under Spansule® sustained release capsules, added [redacted]

4. Under 'storage information' added [redacted]

The revisions (see #3) concerning the Spansule® dosage form have been superceded by this submission for the new Spansule® formulation. The other changes (#1, #2, #4) have been deemed acceptable by the chemist upon routine review of the annual report.

Additional Changes Requested:

During this resubmission, the following additional labeling changes have been requested in the Biopharmaceutics and Chemistry reviews, respectively:

> In the 2/17/99 Biopharmaceutics Review, Dr. Baweja requested that the package insert state that [redacted]
>
> Dr. Lostritto prefers that the storage statement for all dosage forms of Compazine® except for the injectable remain uniform between 15° - 30° C, as previously, pending approval of the CDER Stability Guidance.

In an attempt to accomplish an approval for this application, I had a conversation with Dale Stockbower in order to obtain SKB's agreement to the above requested labeling changes which I had intended to include in an approval letter. However, she indicated that SKB did not agree with the wording of the 'food effect statement' above.

Conclusion:
An approvable letter should request FPL with the revisions listed below:

1. Addition of the statement [redacted]
2. The storage statement should remain unchanged for all dosage forms of Compazine® except for the injectable.

/S/

Anna M. Homonnay-Weikel, R.Ph.
Project Manager 3/3/99

Supervisory Comment/Concurrence:

/S/ 3/4/99

20 pages
Redacted
DRAFT
LABELING

3. The 'Description' section of the package insert should be revised to include the chemical name and chemical structure of prochlorperazine maleate.

4. The [redacted] for the drug product [redacted] of the method. The [redacted] shows a [redacted]

BIOPHARMACEUTICS ISSUES:

1. Consideration should be given to conducting future bioequivalence studies with the highest capsule strength, i.e., 15 mg, rather than a lower strength.

2. Please be reminded that dissolution data (both mean and individual data) should be provided for the complete sampling time points to be included in the proposed specification. Further, this data should be provided for all capsule strengths that you propose to reformulate.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the supplemental application. Any amendments should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact Anna Marie Weikel, R.Ph., Project Manager, at (301) 594-5536.

Sincerely yours,

/S/ 2/18/98

Paul Leber, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 11-000
HFD-120/Div. files
HFD-810/ONDC Division Director
DISTRICT OFFICE
HFD-92/DDM-DIAB
HFD-120/Leber /S/ 2-18-98
HFD-120/Laughren/2.13.98
HFD-120/Guzewska/2.6.98/Zarifa/2.4.98 2.17.98 /S/ 2/17/98
HFD-860/Baweja/2.12.98 /S/ 2/17/98.
HFD-120/A.Weikel /S/ 2/17/98

drafted by: AMW/2.5.98
final: AMW/2.17.98

C:\WPFILES\NDA\SUPPS\11000[redacted]

NOT APPROVABLE (NA)