

020839-S-007

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 20-839/S-007

Trade Name: Plavix Tablets

Generic Name(s): (clopidogrel bisulfate)

Sponsor: Sanofi-Synthelabo, Inc.

Agent:

Approval Date: July 10, 2000

Indication: Provides for new building

JUL 10 2000

NDA 20-839/S-007

Sanofi-Synthelabo, Inc.
Attention: John Purpura
90 Park Avenue
New York, NY 10016

Dear Mr. Purpura:

Please refer to your supplemental new drug application dated February 11, 2000, received February 14, 2000 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plavix (clopidogrel bisulfate) Tablets, 75 mg.

We acknowledge receipt of your submissions dated March 17 and June 13, 2000.

The supplemental application provides for manufacturing clopidogrel bisulfate $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_2\text{S}_2$ in a new building $\text{L} \quad \text{J}$ at Sanofie Chimie in Sisteron, France.

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.

Sincerely yours,

/s/

7-10-00

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products (HFD-110)
Office of New Drug Chemistry
Center for Drug Evaluation and Research

NDA 20-839/S-007-Page 2

cc:

Original NDA 20-839/S-007

HFD-110/DIVISION FILE

HFD-110/FZielinski

HFD-110/Project Manager/CLoCicero

HFD-95

DISTRICT OFFICE

HFD-810/JSimmons

Init: by KSrinivasachar

Draft by: TArcher 7/10/00

Approval Date: 11/17/97

APPROVAL

JUL 7 2000

REVIEW OF CHEMISTRY, MANUFACTURING AND CONTROLS
Division of Cardio Renal Drug Products (HFD-110)

1. Chemistry Review # 1
2. **NDA # 20-839 S-007 (CBE 30, new building)**
3. Name & Address of Applicant Representative
Sanofi-Synthelabo Inc John Purpura
90 Park Avenue Associate Director CMC
New York, New York 10016 Drug Regulatory Affairs
(212) 551-4261 (212) 551-4261
4. Supplement S-007
5. Proprietary Name: Plavix Tablets
6. Nonproprietary Name: Clopidogrel bisulfate
7. Code Name: SR 25990C
8. Chemical Type / Submission Priority: N/A
9. Supplement provides for manufacturing clopidogrel bisulfate in new
building — at Sanofie Chimie in Sisteron, France.
10. Previous Documents: None
11. Submissions Reviewed:
 (a) Supplement dated February 11, 2000
 (b) Amendment dated March 17, 2000
 (c) Amendment dated June 13, 2000
12. Pharmacological Category: Prevention of vascular ischemia
13. Rx / OTC: Rx
14. Dosage Form: Tablet (film coated) TCM
15. Strength / Potency: Equivalent to 75 mg base
16. Route of Administration: oral
17. Spots: NO
18. Chemical Name: Methyl (+)-(S)- α -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5 (4H)-
acetate sulfate (1:1)
CAS # 120202-66-6 C₁₆H₁₆ClNO₂S · H₂SO₄ MWt base 321.83 MWt salt 419.9

19 Related / Supporting Documents: None

20 Status of Consults and Other Reviews:

CGMP Inspection: Overall acceptable on March 2, 2000 (See attached EES)

21 Comments:

- (a) This CBE Supplement is submitted according to agreements reached between the applicant and Drs. Short & Srinivasachar on December 17, 1999.
- (b) The drug substance is manufactured in a new building, using similar equipment and processes is used in the new building. Batch size remains the same. (Reference: NDA 20-839 SCS-007, Cover Letter). There are no significant changes.
- (c) So far, only the was done in the new building to produce 3 batches of drug substance (Batch Numbers 9SS0001, 9SS0002 and 9SS0003). Analytical data for these 3 lots are attached. (Reference: Supplement, Attachment 1) All drug substance specifications are met. The 3 batches are not significantly different.
- (d) One Certificate of Analyses for the drug product (Batch 0353) prepared from a batch of drug substance manufactured in was provided in the Amendment dated March 17, 2000 and it is attached. This amendment satisfies the commitment made in Attachment # 5 of the supplement dated Feb. 11, 2000. All drug product specifications are met.
- (e) One batch (9SS0001) is entered into the 25C/60% RH stability testing protocol (A 2). Results will be reported in the Annual Report.
- (f) The original Supplement stated that 3 batches of drug substance will be entirely in between April 1 and May 31, 2000. Certificates of Analyses for these 3 batches were expected (A 3) prior to approval of the supplement. In a follow up telephone conversation on June 12, 2000, John Purpura stated that only one batch of drug substance was manufactured in using the . No other batches of this drug substance will be : entirely in . As a result, only one Certificate of Analyses can be provided. This C of A was submitted in the Amendment dated June 13, 2000. Please see attached. (Evaluation: acceptable)
- (g) The first and only batch of drug substance entirely in will be tested for stability at 25C/60% RH (A4). Results will be reported in the Annual Report.
- (h) The first batch of Plavix (drug product) prepared from the batch of drug substance manufactured entirely in will be tested for stability (A 6). Results will be reported in the Annual Report.

22 Conclusions and Recommendation: I recommend approval of the supplement.

23 Reviewer: Florian Zielinski

24 Date Completed: June 21, 2000

25 Distribution

Original NDA 20-839/S-007
HFD-110/Division File
HFD-110/Project Manager, Locicero
HFD-110/F Zielinski

Initialed by: K Srinivasachar

ISI

June 21, 2000

ISI

7-7-00

Redacted _____

4

page(s) of trade secret.

and/or confidential

commercial information

(b4)