020-839__ S.-016

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 20-839/S-016

Trade Name: Plavix Tablets

Generic Name(s): (clopidogrel bisulfate)

Sponsor: Sanofi-Synthelabo, Inc.
Agent:

Approval Date: July 19, 2001

Indication: Provides for CBE alternative packaging facility

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-839/S-016

7-19-01

Sanofi-Synthelabo, Inc.
Attention: Haley Zimmerman
90 Park Avenue
New York, NY 10016

Dear Mr. Zimmerman:

Please refer to your supplemental new drug application dated January 22, 2001, received January 23, 2001, 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 submission dated January 25, 2001.

This "Changes Being Effected in 30 days" supplemental new drug application provides for an alternative packaging facility, Sanofi-Synthelabo, Inc., St. Louis, Missouri to package the finished product in blisters.

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 Colleen LoCicero, RPh, Regulatory Health Project Manager, at (301) 594-5332.

Sincerely,

{See appended electronic signature page}

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

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/s/

Kasturi Srinivasachar
7/19/01 10:36:22 AM

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

1. Chemistry Review # 1

2. NDA # 20-839 S-016 (CBE-30)

3. Name & Address of Applicant
Sanofi-Synthelabo Inc
90 Park Avenue
New York, New York 10016
(212) 551-4261

Representative
John Purpura
Associate Director CMC
Drug Regulatory Affairs
(212) 551-4261

4. Supplement S-016

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 an alternative packaging facility, Sanofi-Synthelabo Inc., 6244 Lemay Ferry Road, St. Louis, MO 63129, to package the finished drug product in blisters.

10. Previous Documents: None

11. Submission Reviewed: Supplement dated Jan 22, 2001, received Jan 23, 2001
Amendment dated Jan 25, 2001, received Jan 26, 2001

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 $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ MWt base 321.83 MWt salt 419.9

19 Related / Supporting Documents: None

20 Status of Consults and Other Reviews:
CGMP Compliance Status: Overall acceptable on March 13, 2001 (See attached EES)

21 Comments:

(a) A stability study of bulk tablets in the shipping / storage container used to transport tablets from France to St Louis, MO showed acceptable appearance, dissolution, assay and impurities after storage for ——— at 25°C/60 % RH, 30°C/60% RH and 40°C/75% RH. These results confirm that the container closure system is acceptable.

(b) Sanofi-Synthelabo will add the first production lot of tablets packaged in blisters at the alternative site (St Louis, MO) and at least one lot annually thereafter to the long-term stability program using the approved Post-Approval Protocol. (Page 21). Results will be submitted in Annual Reports. (Stability testing is conducted by Bristol-Myers Squibb, New Brunswick, NJ)

(c) Packaging at the alternative site (St Louis, MO) will be done with the same equipment type, materials, labeling and packaging procedures used in the currently approved site (Bristol-Myers Squibb facility in Mayaguez, Puerto Rico).

(d) A categorical exclusion was submitted under 21 CFR § 25.31. The applicant states that extraordinary circumstances do not exist. There is no information that suggests that additional environmental information is needed.

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

23 Reviewer: Florian W Zielinski

24 Date Completed: July 16, 2000

25 Distribution:

Original NDA 20-839 S-016
HFD-110 Division File
HFD-110 Project Manager, Birdsong
HFD-110 Review Chemist, F Zielinski

Initialed by: K Srinivasachar

File name: NDA 20839 S-016, new packager.doc

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 20839/016
Stamp: 23-JAN-2001 Regulatory Due: 23-JUL-2001
Applicant: SANOFI SYNTHELABO
90 PARK AVE
NEW YORK, NY 100161389

Priority: 1P Org Code: 110
Action Goal: District Goal: 18-JUN-2001
Brand Name: PLAVIX (CLOPIDOGREL BISULFATE) 75MG TABS
Established Name:
Generic Name: CLOPIDOGREL BISULFATE
Dosage Form: TAB (TABLET)
Strength: 75 MG

FDA Contacts:
C. LOCICERO (HFD-110) 301-594-5300 , Project Manager
F. ZIELINSKI (HFD-110) 301-594-5348 , Review Chemist
K. SRINIVASACHAR (HFD-110) 301-594-5376 , Team Leader

Overall Recommendation:

ACCEPTABLE on 13-MAR-2001 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 1931809
SANOFI SYNTHELABO INC
6244 LEMAY FERRY RD
SAINT LOUIS, MO 63129

DMF No:
AADA No:

Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 13-MAR-2001
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE PACKAGER

APPEARS THIS WAY
ON ORIGINAL

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/s/

Florian Zielinski
7/16/01 12:03:48 PM
CHEMIST

Kasturi Srinivasachar
7/16/01 06:50:49 PM
CHEMIST