020757_5004
Bristol-Myers Squibb
Attention: Douglas B. Hay, Ph.D.
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Hay:

Please refer to your March 9, 1998 supplemental new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) Tablets, 75 mg, 150 mg and 300 mg.

The user fee goal date is September 10, 1998.

The supplemental application provides for the approval of an alternate manufacturer of irbesartan

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,

James H. Short, Ph.D.
Acting Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
cc: NDA 20-757/ S-004
HFD-110/ DIV FILE
HFD-110/ Rmittal 3/26/98
HFD-110/ Project Manager/ KBongiovanni
HFD-92
DISTRICT OFFICE
HFD-810/ CHoiberg
cg/03/27/98

Approval Date: September 30, 1997

APPROVAL
DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-757/SCM-S004
SUBMISSION TYPE: SCM-S004
DOCUMENT DATE: 09-MAR-98
REVIEW DATE: 23-MAR-98
CDER DATE: 10-MAR-98
ASSIGNED DATE: 11-MAR-98

NAME & ADDRESS OF APPLICANT
Bristol Myers Squibb Company
P. O. Box 4000
Princeton, NJ 08543-4000

SUPPLEMENT PROVIDES FOR:
The approval of facility as an alternative manufacturer of irbesartan in the synthesis of the irbesartan drug substance.

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

DRUG PRODUCT NAME
Established Name: Irbesartan
Proprietary: AVAPRO
Nonproprietary/USAN: Irbesartan
Code Name/#: SR 47,436, BMS-186295, BMS-186295-01
Chem. Type/Ther. Class: 1/S

AND Suitability Petition/DES/Patent Status:
The U.S. Patent 5,270,317 held by Elf Sanofi was issued for irbesartan and is due to expire on March 2011.

PHARMACOL. CATEGORY/INDICATION: Angiotensin II Receptor Antagonist/Hypertension
DOSE FORM: TABLETS
STRENGTH: 75 mg, 150 mg and 300 mg.
ROUTE OF ADMINISTRATION: ORAL
DISPENSED: Rx

CHEMICAL NAME: 2-Butyl-3-[(2'-{(1H-tetrazol-5-yl)biphenyl-4-yl}methyl)-1,3-diazaspiro[4.4]non-1-en-4-one.

CAS #: 138402-11-6
MOLECULAR FORMULA: C_{25}H_{28}N_{6}O
MOLECULAR WEIGHT: 428.5

STRUCTURAL FORMULA

![Structural Formula Image]
SUPPORTING DOCUMENTS:

DMF#1

RELATED DOCUMENTS (if applicable): NDA 20-758 Irbesartan/Hydrochlorothiazide

CONSULTS: None at present.

REMARKS/COMMENTS:

A request for inspection was submitted on March 23, 1998. As of March 24, 1998, the status of EER is acceptable and a copy of the EER report is attached at the end of this review.

CONCLUSIONS & RECOMMENDATIONS:

Satisfactory and approval is recommended.

CC:
HPD-110/Division File
HPD-110/Ram Mittal/date
HPD-110/CSO

R/D Init by: JShort/

Ramsharan D. Mittal Ph.D., Review Chemist
2 Page(s) Withheld

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

☐§ 552(b)(5) Deliberative Process

☐§ 552(b)(5) Draft Labeling
Application: NDA 20757/004
Stamp: 10-MAR-1998 Regulatory Due: 10-SEP-1998
Applicant: SANOFI PHARMS
90 PARKE AVE
NEW YORK, NY 10016

Priority: 1S
Brand Name: AVAPRO (IRBESARTAN) TABS
75/150/300 MG
Established Name:
Generic Name: IRBESARTAN TABS 75/150/300MG
Dosage Form: TAB (TABLET)
Strength: 75, 150, 300MG

FDA Contacts: K. BONGIOVANNI (HFD-110)
R. MITTAL (HFD-110)
J. SHORT (HFD-110)
301-594-5300, Project Manager
301-594-5353, Review Chemist
301-594-5300, Team Leader

Overall Recommendation:
ACCEPTABLE on 24-MAR-1998 by M. EGAS (HFD-322) 301-594-0095

Establishment:
DMF No:_____
AADA No:_____

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-MAR-1998
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Appears This Way
On Original