020757__5005

NDA 20-757/S-005

SEP 3 1998

Sanofi Pharmaceuticals, Inc.
Attention: Gregory Torre, Ph.D., J.D.
90 Park Avenue
New York, NY 10016

Dear Dr. Torre:

Please refer to your March 17, 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.

We acknowledge receipt of your submission dated August 6, 1998.

The user fee goal date is September 18, 1998.

The supplemental application provides for an additional manufacturing site for the irbesartan drug substance, at Humacao, Puerto Rico.

We have completed the review of this supplemental application and it is approved with the understanding that you will submit stability data on drug product manufactured using irbesartan synthesized at Humacao, Puerto Rico, as soon as they are available.

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,

K. Srinivasan 9-3-98
Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

cc: NDA 20-759/S-005
HFD-110/ DIV FILE
HFD-110/ RMittal 09/03/98
HFD-110/ Project Manager/ K BONGIOVANNI
HFD-92
DISTRICT OFFICE
HFD-810/ CHoiberg
cg 09/03/98

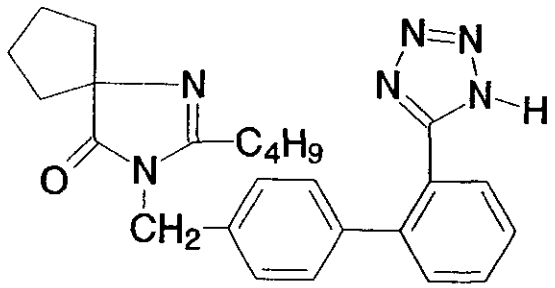
Approval Date: SEPTEMBER 30, 1997

APPROVAL

DF

FEB 23 2000

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

CHEMIST'S REVIEW	1. ORGANIZATION HFD - 110	2. NDA Number 20-757
3. Name and Address of Applicant (City & State) Bristol Myers Squibb Company P. O. Box 4000 Princeton, NJ 08543-4000		4. Supplement(s) Number(s) Date(s) S-005(SNC) 10/25/99
5. Drug Name Avapro	6. Nonproprietary Name Irbesartan	7. Amendments & Other (reports, etc) - Dates
7. Supplement Provides for: [ ] stability data for drug product manufactured at [ ] with drug substance from Puerto Rico.		
9. Pharmacological Category Angiotensin II Receptor Antagonist/Hypertension	10. How Dispensed /x/ RX /__/ OTC	11. Related IND(s)/ NDA(s)/DMF(s) 20-758
12. Dosage Form(s) Tablets	13. Potency(ies) 75 mg, 150mg, and 300 mg.	
14. Chemical Name and Structure 2-Butyl-3-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl) methyl]-1,3-diazaspiro[4.4]non-1-en-4-one. 		15. Records/Reports Current /x/ Yes /__/ No Reviewed /x/ Yes /__/ No
16. Comments: See review notes.		
17. Conclusions and Recommendations: Satisfactory and no reply is necessary.		
18. REVIEWER		
Name Ramsharan D. Mittal	Signature R D Mittal	Date Completed 01/06/00
19. Distribution: /__/ Original Jacket /__/ Reviewer /__/ Division File /__/ CSO		

R. Srinivasan
2-23-00

1 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEP 3 1998

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

NDA #: 20-757/SCM-005 **REVIEW DATE:** 20-AUG-98

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
SCM	17-MAR-98	18-MAR-98	19-MAR-98
SCM(BC)	06-AUG-98	07-AUG-98	07-AUG-98

NAME & ADDRESS OF APPLICANT

Bristol Myers Squibb Company
P. O. Box 4000
Princeton, NJ 08543-4000

SUPPLEMENT PROVIDES FOR:

The approval of Humacao, Puerto Rico facility as an additional manufacturing site for the irbesartan drug substance.

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/DESI/Patent Status:

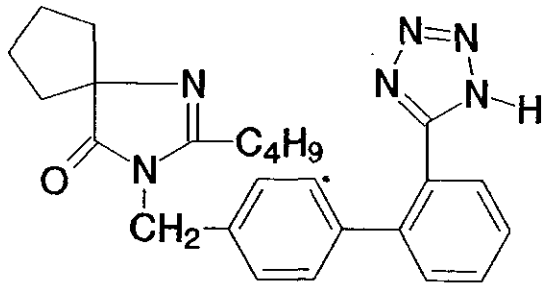
The U.S. Patent 5,270,317 held by Elf Sanofi was issued for irbesartan and is due to expire on March 2011.

PHARMACOL.CATEGORY/INDICATION: Angiotensin II Receptor Antagonist/Hypertension
DOSAGE 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** $C_{25}H_{28}N_6O$ **MOLECULAR WEIGHT** 428.5

STRUCTURAL FORMULA



SUPPORTING DOCUMENTS:

DMF# [redacted]

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

CONSULTS: None at present.

REMARKS/COMMENTS:

A request for inspection was submitted on April 08, 1998. As of April 9, 1998 EER status is acceptable and a copy of the EER report is attached at the end of this review.

The applicant has committed to submit [redacted] product stability data report after about a month or so.

CONCLUSIONS & RECOMMENDATIONS:

Satisfactory and approval is recommended.

cc:
HFD-110/Division File
HFD-110/Ram Mittal/date
HFD-110/CSO

R/D Init by: KSrinivasachar/
K. Srinivasachar
8-25-98

R.D. Mittal

Ramsharan D. Mittal Ph.D., Review Chemist
filename: C:\NDA\20757\20757SCM.005

4 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

for May 01, 1998

Application: **NDA 20757/005**
Stamp: **18-MAR-1998** Regulatory Due: **18-SEP-1998**
Applicant: **SANOFI PHARMS**
90 PARKE AVE
NEW YORK, NY 10016

Priority: **1S** Org Code: **110**
Action Goal: District Goal: **14-JUL-1998**
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)**	**301-594-5300**	**, Project Manager**
R. MITTAL	**(HFD-110)**	**301-594-5353**	**, Review Chemist**
J. SHORT	**(HFD-110)**	**301-594-5300**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 09-APR-1998 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: **2623458**
SQUIBB MANUFACTURING INC
STATE RD #3 KM775
HUMACAO, PR 00791

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **09-APR-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Appears This Way
On Original