

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20757/S16

APPROVAL LETTER

MAY 10 2000

NDA 20-757/S-016

Bristol-Myers Squibb Company
Attention: Melody A. Brown
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Ms. Brown:

Please refer to your supplemental new drug application (NDA) dated April 21, 2000, received April 24, 2000, 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 supplemental application provides for an alternative packaging site, Bristol-Myers Co., Mount Vernon, IN for Avapro tablets 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.

Sincerely,

jsl

5-10-00

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

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

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CHEMISTRY REVIEW(S)

MAY 4 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 5400 Princeton, NJ 08543-5400		4. Supplement(s) Number(s) Date(s) SCM-016 4/21/00	
5. Drug Name Avapro	6. Nonproprietary Name Irbesartan		7. Amendments & Other (reports, etc) - Dates
7. Supplement Provides for: CHANGES BEING EFFECTED IN 30 DAYS an alternative packaging site, Bristol-Myers Squibb Co., Mount Vernon, Indiana for Avapro tablets in blisters.			
9. Pharmacological Category Angiotensin II Receptor Antagonist/Hypertension		10. How Dispensed <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC	11. Related IND(s)/NDA(s)/DMF(s) NDA 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 <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No Reviewed <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
16. Comments: As of April 26, 2000, facility status is acceptable.			
17. Conclusions and Recommendations: Satisfactory and recommended for approval.			
18. REVIEWER			
Name Ramsharan D. Mittal	Signature 		Date Completed 04/26/00
19. Distribution: <input type="checkbox"/> Original Jacket <input type="checkbox"/> Reviewer <input type="checkbox"/> Division File <input type="checkbox"/> CSO			

IS!
5-4-00

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ADMINISTRATIVE DOCUMENTS

CSO Review of Final Printed Labeling

MAY 9 2000

Application: NDA 20-757/S-015⁴
NDA 20-758/S-016

Applicant: Bristol-Myers Squibb

Document Dates: February 23, 2000 (S-015 & S-016)

Receipt Dates: February 28, 2000 (S-015 & S-016)

Product Names: Avapro (irbesartan) Tablets, 75, 150, 300 mg
Avalide (irbesartan/hydrochlorothiazide) Tablets, 75/12.5, 150/12.5, 300/12.5 mg

Background: These supplemental applications were submitted as "Changes Being Effected" in response to our supplement request letter of August 23, 1999 that asked the sponsor to add hyperkalemia to the list of adverse reactions associated with irbesartan use.

Review: The sponsor has submitted final printed labeling (for both supplements) revised as follows:

1. Under **ADVERSE REACTIONS**, the *Post-Marketing Experience* subsection has been changed from:

[Redacted]

L

to:

The following adverse reactions have been reported in post-marketing experience: Rare cases of urticaria and angioedema (involving swelling of the face, lips, pharynx, and/or tongue); hyperkalemia.

2. The address information has been changed to reflect a new logo.

There are no other changes from the last approved package inserts.

Comments/Recommendations: An approval letter should issue for these supplements as set forth under 21 CFR 314.70 (c)(i) [To add or strengthen a contraindication, warning, precaution, or adverse reaction].



Edward Fromm
Consumer Safety Officer

Ef/4-11-2000