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S025+



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-025
NDA 20-758/S-024

Sanofi-Synthelabo
C/o Bristol-Myers Squibb Company
Attention: George Zapf
P. O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Zapf:

Please refer to your supplemental new drug applications dated November 21, 2002, received November 25, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) Tablets, 75 mg, 150 mg and 300 mg. (NDA 20-757) and Avalide (irbesartan/hydrochlorothiazide) Tablets, 75/12.5 mg, 150/12.5 mg and 300/12.5 mg (NDA 20-758).

These supplemental new drug applications provide for $\square$
for irbesartan drug substance. J

We have completed our review of these supplemental applications, and they are approved.

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any question, please call Edward Fromm, Regulatory Health Project Manager, at (301) 594-5332.

Sincerely,

A handwritten signature in dark ink, appearing to read "KS", is written over the word "Sincerely,".

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
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-024

Sanofi-Synthelabo
c/o Bristol-Myers Squibb Company
Attention: Mr. George Zapf
Associate Director, Global Regulatory Sciences, CMC
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Zapf:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Avapro (irbesartan) 75, 150 and 300 mg Tablets

NDA Number: 20-757

Supplement number: 024

Date of supplement: October 31, 2002

Date of receipt: November 4, 2002

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on January 3, 2003 in accordance with 21 CFR 314.101(a). The user fee goal date will be May 4, 2003.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products,
HFD-110
Attention: Division Document Room, 5002
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products
HFD-110
Attention: Document Room 5002
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

/S/

Zelda McDonald
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Zelda McDonald
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-025

Sanofi-Synthelabo
c/o Bristol-Myers Squibb Co.
Attention: Mr. George Zapf
Associate Director, Global Regulatory Sciences, CMC
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Zapf:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Avapro (irbesartan) 75, 150 and 300 mg Tablets

NDA Number: 20-757

Supplement number: 025

Date of supplement: November 21, 2002

Date of receipt: November 25, 2002

This supplement application, submitted as a "Changes Being Effectuated"/"Changes Being Effectuated in 30 days" supplement, proposes to

1. irbesartan drug substance

Changes of this kind cannot be put into effect prior to approval of a supplement. An approved supplement is required for the proposed change prior to distributing drug product made with this change.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on January 24, 2003 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room, 5002
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Document Room 5002
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

/S/

Zelda McDonald
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Zelda McDonald
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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) SCS-024 10/31/02
5. Drug Name Avapro	6. Nonproprietary Name Irbesartan	7. Amendments & Other (reports, etc) - Dates SCS-024 (BC) 12/11/02
7. Supplement Provides for: CHANGES BEING EFFECTED the inclusion of ☒ irbesartan produced by Sanofi Chimie and ☐		
9. Pharmacological Category Angiotensin II Receptor Antagonist/Hypertension	10. How Dispensed ☒ RX ☐ 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.	DMF DMF
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 ☒ Yes ☐ No Reviewed ☒ Yes ☐ No
16. Comments: A CBE Supplement as per Changes to An Approved NDA or ANDA.		
17. Conclusions and Recommendations: The update of ☐ ☒ irbesartan produced by Sanofi and ☐ ☒ is satisfactory and increases assurance of the quality of the ☐ ☒ irbesartan. Similar supplement has been approved for other suppliers of irbesartan. The supplement may be approved for the irbesartan suppliers Sanofi Chimie and ☐ ☒		
18. REVIEWER Name Ramsharan D. Mittal		

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

 § 552(b)(5) Deliberative Process

 § 552(b)(5) Draft Labeling

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/s/

Ramsharan Mittal
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CHEMIST

Kasturi Srinivasachar
5/1/03 03:46:19 PM
CHEMIST