020757—SO19
NDA 20-757/S-019

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 dated October 30, 2000, received October 31, 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.

This "Changes Being Effected in 30 days" supplemental new drug application provides for $L$ is an alternative manufacturer of the $L$ used in the synthesis of irbesartan.

We have completed the review of this supplemental application, and it is approved. Please note for future reference that $L$ in the synthesis of the drug substance, irbesartan, and not $L$ as stated in your supplemental application.

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 Edward Fromm, Regulatory Project Manager, at (301) 594-5313.

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

cc:
Sanofi-Synthelabo, Inc.
Attention: Gregory Torre, Ph.D., J.D.
90 Park Avenue
New York, NY 10016
/s/
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Kasturi Srinivasachar
3/6/01 05:16:45 PM
DIVISION OF CARDIO-renal DRUG PRODUCTS  
Review of Chemistry, Manufacturing, and Controls

<table>
<thead>
<tr>
<th>CHEMIST’S REVIEW</th>
<th>1. ORGANIZATION</th>
<th>2. NDA Number</th>
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<tbody>
<tr>
<td></td>
<td>HPD - 110</td>
<td>20-757</td>
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3. Name and Address of Applicant (City & State)

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<thead>
<tr>
<th>Bristol-Myers Squibb Company</th>
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<tr>
<td>P. O. Box 5400</td>
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<td>Princeton, NJ 08543-5400</td>
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4. Supplement(s)

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<tr>
<th>Number(s)</th>
<th>Date(s)</th>
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<tr>
<td>SCM-019</td>
<td>10/30/00</td>
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5. Drug Name

| Avapro       |

6. Nonproprietary Name

| Irbesartan   |

7. Supplement Provides for: CHANGES BEING EFFECTED IN 30 DAYS

\[
\text{as used in the synthesis of the irbesartan.}
\]

9. Pharmacological Category

| Angiotensin II Receptor Antagonist/Hypertension |

10. How Dispensed

| RX | CTC |

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

| Yes | No |


17. Conclusions and Recommendations:

The changes reported in the manufacturing process involve different site with no change in the synthesis route. Such supplements can be accepted as a CBE in 30 days and the supplement is recommended for approval.

18. REVIEWER

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<thead>
<tr>
<th>Name</th>
<th>Signature</th>
<th>Date Completed</th>
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<tbody>
<tr>
<td>Ramsharan D. Mittal</td>
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<td>03/2/01</td>
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19. Distribution:

/\ Original Jacket /\ Reviewer /\ Division File /\ CSO
2 Page(s) Withheld

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

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling
/s/
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Ramsharan Mittal
3/5/01 01:09:47 PM
CHEMIST

Kasturi Srinivasachar
3/5/01 06:04:30 PM
CHEMIST
NDA 20-757/S-019

Sanofi-Synthelabo, Inc.
c/o Bristol-Myers Squibb Pharmaceutical Research Institute
Attention: Ms. Melody A. Brown
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Ms. Brown:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Avapro (irbesartan) Tablets

NDA Number: 20-757

Supplement Number: S-019

Date of Supplement: October 30, 2000

Date of Receipt: October 31, 2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on December 30, 2000 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Office of Drug Evaluation I
Attention: Document Control Room 5002
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/signed/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products, HFD-110
Office of Drug Evaluation I
Center for Drug Evaluation and Research
SUPPLEMENT ACKNOWLEDGEMENT
/s/
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Natalia Morgenstern
12/14/00 05:56:24 PM