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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-757/S-011
NDA 20-758/S-013

Sanofi-Synthelabo Pharmaceuticals Inc.
c/o Bristol-Myers Squibb
Attn: Ms. Grace D. Heckman
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Ms. Heckman:

Please refer to your supplemental new drug applications dated August 27, 1999, received August 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) 75, 150 and 300 mg Tablets and Avalide (irbesartan and hydrochlorothiazide) 75/12.5, 150/12.5 and 300/12.5 mg Tablets.

We acknowledge receipt of your submissions dated August 24, 2001 that constituted a complete response to our September 20, 2000 approvable letter.

These supplemental new drug applications provide for final printed labeling revised as follows:

Under PRECAUTIONS, the Geriatric Use subsections have been revised to read as follows:

NDA 20-757/S-011 Avapro (irbesartan) Tablets

> Of the 1965 subjects in controlled clinical studies of AVAPRO (irbesartan) for hypertension, 15% were age 65 and over, but few were over age 75. No striking differences in antihypertensive effect or in adverse events appear to be present in this database, but there were insufficient numbers of aged subjects to enable detection of less than striking differences. Greater or lesser sensitivity of some older individuals cannot be ruled out. (see Pharmacokinetics, Special Populations, and Clinical Studies).

NDA 20-758/S-013 Avalide (irbesartan and hydrochlorothiazide) Tablets

> Clinical studies of AVALIDE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the submitted final printed labeling (package insert included in your submissions of August 24, 2001). Accordingly, these supplemental applications are approved effective on the date of this letter.

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, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

/S/

{See appended electronic signature page}

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Raymond Lipicky
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

7/12/01

NDA 20-757/S-011

Sanofi-Synthelabo Pharmaceuticals, Inc.
c/o Bristol-Myers Squibb
Attention: Mary E. Norvitch, Ph.D.
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Norvitch:

Please refer to your August 27, 1999 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) Tablets.

We also refer to our letter of September 20, 2000 notifying you that your supplemental application was approvable.

We have no record that you have filed an amendment fully responsive to our September 20, 1999 letter. Since a year and six months have passed we will consider this supplemental application withdrawn under 21 CFR 314.110(a)(2) unless you file such an amendment within thirty (30) days. Alternatively, you may wish to withdraw the supplemental NDA under 21 CFR 314.65. Withdrawal would not prejudice any future resubmission of the supplemental application. You may request that the information in the withdrawn supplemental application be considered in conjunction with any resubmission.

If you have any questions, please contact:

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

Sincerely yours,

/S/

Natalia A. Morgenstern
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/

Natalia Morgenstern
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