CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-387

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-387

Bristol-Myers Squibb Company
Attention: Porter P. Layne, Ph.D.
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Layne:

Please refer to your new drug application (NDA) dated June 22, 2001, withdrawn on March 28, 2002, and resubmitted May 8, 2002, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Pravagard PAC (co-packaged 20, 40 or 80 mg pravastatin sodium and 81 or 325 mg buffered aspirin) Tablets.

We acknowledge receipt of your submissions dated March 13, April 18, May 20, 21 and 30 (two) and June 3, 2003

The May 30 and June 3, 2003 submissions constituted a complete response to our March 7, 2003 action letter.

This new drug application provides for the use of Pravagard PAC (co-packaged pravastatin sodium and buffered aspirin) to reduce the occurrence of cardiovascular events, including death, myocardial infarction or stroke, in patients who have clinical evidence of cardiovascular and/or cerebrovascular disease.

We have completed the review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the electronic final printed package insert, patient package insert and the immediate container and carton labels submitted on May 30, 2003.

At the time of the next printing, please make the following revisions to the labeling:

1. Change "hydroxypropyl methylcellulose" to "hypromellose" in the last sentence of the **DESCRIPTION/Buffered Aspirin** subsection.
2. Add "PAC" after "Pravagard" in the places throughout the labeling where it is currently absent.
3. Reduce the header font size of each subsection to be appropriate relative to the size of each section, e.g., **DESCRIPTION**(section)/PRAVACHOL(subsection).
4. Under the **INDICATIONS AND USAGE/PRAVIGARD** subsection, insert a comma after "stroke" in the second sentence.
5. Under the **INDICATIONS AND USAGE/PRAVACHOL/Hypercholesterolemia** subsection, add "LDL-C" after "Total-C" in the first sentence of the second paragraph.

We note that you have already submitted your proposed introductory promotional materials to the Division of Drug Marketing, Advertising, and Communications.

Please submit one market package of the drug product when it is available.

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

If you have any questions, please call Ms. Meg Pease-Fye, Regulatory Health Project Manager, at (301) 594-5312.

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Attachment

This is a representation of an electronic record that was signed electronically and **this page is the manifestation of the electronic signature.**

/s/

Robert Temple
6/24/03 02:48:15 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-387

Approvable Letter (S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-387

Bristol-Myers Squibb Company
Attention: Porter P. Layne, Ph.D.
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Layne:

Please refer to your new drug application (NDA) dated June 22, 2001, withdrawn on March 28, 2002 and resubmitted May 8, 2002, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pravagard PAC (pravastatin sodium/buffered aspirin) 20, 40 or 80 mg pravastatin sodium and 81 or 325 mg buffered aspirin Tablets.

We acknowledge receipt of your submissions dated August 20, October 30, November 29, and December 3, 11, 14, 18 and 21, 2001; January 14, February 7 and 14 (two), March 13, April 19, May 24 and 28, June 7 and 12, August 9 and 22, September 6 and October 25, 2002; February 27 and March 3, 2003.

We have completed the review of this application, as submitted with electronic final printed labeling (package insert, patient package insert, immediate container and carton labels submitted on February 27, 2003), and it is approvable. At the time of printing, please remove the Renal Toxicity/buffered aspirin sub-section under the Drug Interactions section.

During recent inspections of the manufacturing facilities for your NDA, a number of deficiencies were noted and conveyed to you or your suppliers by the investigator. Satisfactory inspections will be required before this application may be approved.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please call Ms. Zelda McDonald, Chief, Project Management Staff at (301) 594-5328.

Sincerely,

/S/

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Attachment: Final printed package insert
and patient package insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert Temple
3/7/03 03:16:55 PM

37 pages redacted from this section of the approval package consisted of draft labeling