CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 19-898/S049

Trade Name: Pravacol Tablets

Generic Name: pravastatin sodium

Sponsor: Bristol Myers Squibb Company

Approval Date: January 14, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-898/S049

CONTENTS

Reviews / Information Included in this NDA Review.	
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Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-898/S049

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-049

Bristol-Myers Squibb Company
Attention: Mr. Richard J. Marciani
Associate Director, CMC Marketed Products
Global Regulatory Sciences
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Mr. Marciani:

Please refer to your supplemental new drug application dated July 19, 2001, received July 20, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pravachol (pravastatin sodium) Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application provides for three , sites for 10 mg, 20 mg and 40 mg tablets at

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.

If you have any questions, call Margaret Simoneau, R.Ph., Regulatory Project Manager, at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

Stephen K. Moore, Ph.D.
Chemistry Team Leader I, DNDC II for the
Division of Metabolic and Endocrine Drug Products,
(HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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

/s/

Stephen Moore
1/14/02 12:05:35 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-898/S049

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW

1. ORGANIZATION CDER/HFD-510 Division of Metabolism and Endocrine Drug Products	**2. NDA #** 19-898 Original NDA approved: 31-OCT-1991
3. NAME AND ADDRESS OF APPLICANT Bristol-Myers Squibb P.O. Box 4000 Princeton, NJ 08543-4000 (609)-252-4000	**4. SUPPLEMENT** SCM-049 19-JUL -2001 (Rec. 20-JUL -2001)
	5. Name of the Drug PRAVACHOL™
	6. Nonproprietary Name Pravastatin sodium
7. SUPPLEMENT PROVIDES for three [redacted] sites for 10 mg, 20 mg and 40 mg tablets at [redacted]	**8. AMENDMENT** --

9. PHARMACOLOGICAL CATEGORY Lipid-lowering agent	**10. HOW DISPENSED** Oral	**11. RELATED** -N. A. -
12. DOSAGE FORM Tablet	**13. POTENCY** 10 mg, 20 mg and 40 mg	

14. CHEMICAL NAME AND STRUCTURE

[1S-[1α(βS*,φS*)2α,6α,8β(R*),8α]]-1,2,6,7,8α-hexahydro-β,φ,6-trihydroxy-2-methyl-1-oxobutoxyl)-1-nephthaleneheptanoic acid, monosodium salt

15. COMMENTS This supplement is submitted as a CBE-30. EES report attached. Overall recommendation is Acceptable.

CONCLUSIONS AND RECOMMENDATIONS Satisfactory CMC information in NDA 19-898 SCM-049 is provided for the three [redacted] sites. All components of the [redacted] remain unchanged and are previously approved. A stability commitment for each facility is included. There are no deficiencies to be communicated to the sponsor. From the Chemistry viewpoint the application can be approved. Issue approval letter.

17. REVIEWER NAME (AND SIGNATURE) **DATE**

COMPLETED 07-JAN-2002

Sharon Kelly, PhD

filename: 19898#049 NDA

DISTRIBUTION: Original: sNDA 19-898 cc: HFD-510 Division File CSO Reviewer

AP

ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 19898/049
Stamp: 20-JUL-2001
Regulatory Due: 20-JAN-2002
Applicant: BRISTOL MYERS SQUIBB
RT 206 PROVINCE LINE RD
PRINCETON, NJ 085434000
Priority: 1S
Org Code:
FDA Contacts: S. KELLY (HFD-510) 301-827-6394 , Review Chemist
S. MOORE (HFD-510) 301-827-6430 , Team Leader

Action Goal:
District Goal: 16-DEC-2001
Brand Name: PRAVACHOL TABLETS
Estab. Name:
Generic Name:PRAVASTATIN SODIUM

Dosage Form:(TABLET)
Strength:80 MG

Overall Recommendation:ACCEPTABLEon 24-JUL-2001by EGASM
Establishment: [redacted]

DMF No:
Responsibilities: [redacted]
Profile: TCM
Estab. Comment:

AADA:

OAI Status: NONE

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	24-JUL-2001 KELLYS				
OC RECOMMENDATION	24-JUL-2001 DAMBROGIOJ			ACCEPTABLE BASED ON PROFILE	

Establishment: [redacted]

DMF No:
Responsibilities: [redacted]
Profile: TCM
Estab. Comment: THREE [redacted] PRAVACHOL TABLETS, 10MG, 20MG AND 40 MG IN [redacted]. ALL COMPONENTS OF [redacted] REMAIN UNCHANGED. (on 24-JUL-2001 by S. KELLY (HFD-510) 301-827-6394)

AADA:

OAI Status: NONE

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	24-JUL-2001 KELLYS				
OC RECOMMENDATION	24-JUL-2001 EGASM			ACCEPTABLE BASED ON PROFILE	

Establishment: [redacted]

DMF No:
Responsibilities: [redacted]
Profile: TCM
Estab. Comment:

AADA:

OAI Status: NONE

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	24-JUL-2001 KELLYS				

ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

16-DEC-2001

20-JAN-2002
BRISTOL MYERS SQUIBB
1S
510
Priority:
Org Code:
Application Comment:

OC RECOMMENDATION	24-JUL-2001 DAMBROGIOJ		ACCEPTABLE BASED ON PROFILE

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/s/

Sharon Kelly
1/7/02 04:39:33 PM
CHEMIST

Stephen Moore
1/7/02 04:43:22 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-898/S049

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-049

CBE-30 SUPPLEMENT

Bristol-Myers Squibb Company
Attention: William J. Regan
Director, CMC Marketed Products
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Mr. Regan:

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: Pravachol (pravastatin sodium) Tablets

NDA Number: 19-898

Supplement Number: S-049

Date of Supplement: July 19, 2001

Date of Receipt: July 20, 2001

This supplemental application, submitted as a "Supplement - Changes Being Effected in 30 days" supplement, proposes to add three [redacted] sites to package the 10 mg, 20 mg, and 40 mg tablets in [redacted] These sites are [redacted]

Unless we notify you within 60 days of our 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 September 18, 2001, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 20, 2002.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

Margaret Simoneau, R.Ph.
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Margaret Simoneau
8/1/01 10:30:42 AM

Bristol-Myers Squibb
Pharmaceutical Research Institute

P.O. Box 5400 Princeton, NJ 08543-5400
609 818-4732 Fax: 609 818-5832

ORIGINAL

William J. Regan
Director, CMC
Regulatory Science and Outcomes Research

NDA NO 19898 REF. NO. 045
NDA SUPPL FOR SCM

Supplement -- Changes Being Effected in 30 Days

July 19, 2001

NDA 19-898
PRAVACHOL® (pravastatin sodium) Tablets

Dr. John Jenkins, M.D., Director
Division of Metabolism and Endocrine Drug Products (HFD-150)
Center of Drug Evaluation and Research
Food and Drug Administration
Department of Health & Human Services
5600 Fishers Lane
Rockville, MD 20857

Note 7/23/01 "Qualifies CBE-30 Qualifies phone conv. to S. Kelly for determination" SK 7/24/01

Attention: Document Control Room (14B-03)

Dear Dr. Jenkins:

Reference is made to our approved New Drug Application, NDA 19-898, for PRAVACHOL® (pravastatin sodium) Tablets, 10 mg, 20 mg, and 40 mg.

We are requesting to provide for three [redacted] sites. The sites are:

[redacted]

PRAVACHOL® (pravastatin sodium) 10 mg, 20 mg and 40 mg tablets will be packaged in [redacted] at the [redacted] sites. All components of the [redacted] remain unchanged and have been previously approved.

Included in this supplement are three letters, one from each facility stating compliance with cGMP and providing dates of the most recent FDA inspections. Also provided is Bristol-Myers Squibb's commitment to place product packaged at each facility into our marketed product stability program.

As recommended by the FDA Guidance for Industry titled, Changes to an Approved NDA or ANDA dated November 1999, we are submitting this as a *Changes Being Effected Supplement in 30 Days.* We cite section VI (C)(1)(c) of the guidance document, which provides for a "CBE" as the appropriate filing for this type of change. The effective date being 30 days after the date of this letter.

Bristol-Myers Squibb Company certifies that a field copy of this supplemental application has been provided to the North Brunswick office (120 North Center Drive, North Brunswick, NJ 08902) of the Food and Drug Administration. We further certify that the field copy is a true copy of this supplemental application.

Should you have any questions concerning this supplement, please contact me at (609) 818-4732.

Sincerely,

Richard J. Marciani
for

William J. Regan
Director
CMC - Marketed Products
Regulatory Sciences and Outcomes Research

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Randall D. Curtiss
Bristol-Myers Squibb Company
P.O. Box 5400
Princeton, NJ 08543

2. TELEPHONE NUMBER *(Include Area Code)*

(609) 818-5220

3. PRODUCT NAME
PRAVACHOL® (pravastatin sodium) Tablets

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____
(APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

6. LICENSE NUMBER / NDA NUMBER
NDA 19-898

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See Item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetics Act
(See Item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See Item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 20 2001
HFD-510

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO
(See reverse side if answered YES)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Richard Marcuan for WJR William J. Regan	Director – CMC Marketed Products Regulatory Sciences and Outcomes Research	July 19, 2001