CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020740/S002

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY FOR NDA # 20-740 SUPPL # 002

Trade Name Baycol Generic Name CERIVASTATIN Tablets

Applicant Name Bayer HFD # 510

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES /___/ NO /✓/

b) Is it an effectiveness supplement?

YES /✓/ NO /___/

If yes, what type? (SE1, SE2, etc.) SE2

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /✓/ NO /___/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

_____

_____

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

_____

_____

d) Did the applicant request exclusivity?

YES /___/ NO /✓/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

NO

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

NO

YES /___/ NO /✓/

If yes, NDA #_____. Drug Name _____.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /✓/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved.

Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /✓/ NO /___/

APPEARS THIS WAY ON ORIGINAL

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20-740 Bayco L .05mg, .1mg, .2mg + .3mg

NDA# _____ _____

NDA# _____ _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

N/A YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /✓/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /✓/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /✓/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /✓/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /✓/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

A. Protocol # D149 European Study

B. Protocol D96-008 U.S. Study

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Protocol # 0149 (European) [redacted]

D96-008 (US) [redacted]

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # [redacted] YES /✓/ ! NO /___/ Explain: _____

! _____

Investigation #2

IND # _____ YES /___/ ! NO /___/ Explain: _____

_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /✓/

If yes, explain: _____

_____

/S/ [redacted]
Signature
Title: _____

5/10/99
Date

/S/ [redacted]
Signature of Office/
Division Director

5/22/99
Date

cc: Original NDA Division File HFD-85 Mary Ann Holovac

APPEARS THIS WAY ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

A/BLA # 20-740 Supplement # 002 Circle one: SE1 (SE2) SE3 SE4 SE5 SE6

HFD 510 Trade and generic names/dosage form: Baycol (Cerivastatin) Action: (AP) AE NA

Applicant Bayer Therapeutic Class Lipid Altering Agents

Indication(s) previously approved ↓ of Elevated LDL cholesterol levels in pts w primary hypercholesterolemia + mixed dyslipidemia (Fred IIa + IIb).

Pediatric information in labeling of approved indication(s) is adequate ___ inadequate ✓

Proposed indication in this application none for peds

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? ✓ **Yes (Continue with questions)** ___ **No (Sign and return the form)**

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

___ Neonates (Birth-1month) ___ Infants (1month-2yrs) ___ Children (2-12yrs) ✓ Adolescents(12-16yrs)

___ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

___ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

✓ 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

___ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

___ c. The applicant has committed to doing such studies as will be required.

- ___ (1) Studies are ongoing.
- ___ (2) Protocols were submitted and approved.
- ___ (3) Protocols were submitted and are under review.
- ___ (4) If no protocol has been submitted, attach memo describing status of discussions.

✓ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

___ 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

___ 5. **If none of the above apply, attach an explanation, as necessary.**

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? ___ **Yes** ✓ **No**

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from Team Leader (e.g., medical review, medical officer, team leader)

/S/ [redacted]

Signature of Preparer and Title

5-20-99

Date

Orig NDA/BLA # 20/740-002

HFD 510 /Div File

NDA/BLA Action Package

HFD-006/ KRoberts

(revised 10/20/97)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-6 (ROBERTSK)

Debarment Certification

Bayer Inc. hereby certifies under Section 301(k) (1) of the act (21 USC 335 a (k) (1)) that it did not and will not use in any capacity the services of any person debarred under subsections (a) or (b) (section 306(a) or (b)), in connection with this NDA [redacted]

NDA 20-740/S002
Baycol (cerivastatin sodium) tablets
Bayer

Memo to the file: 5-7-99

The sponsor stated on the 5/6/99 Safety Update submission, " Since the cut-off date (July 16, 1998) for the Four Month Safety Update, submitted to FDA on November 13, 1998, no studies with Baycol 0.4 mg have completed." This Safety Update contained no additional information from the Four Month Safety Update which was included and reviewed in the Medical Officer's review dated 3/24/99.

/S/ [redacted]

S.W.Shen, M.D.
Medical Officer
HFD-510

5/7/99

/S/ [redacted]

5-14-99

APPEARS THIS WAY ON ORIGINAL

RECORD OF TELEPHONE CONVERSATION/MEETING	**Date:** April 22, 1999
Date: Thursday, April 22, 1999 Time: 10:15-10:30 AM FDA Attendees: Hae-Young Ahn Margaret Simoneau Bayer Attendees: Fred Sunderman Meeting Objective (Biopharm) T-Con was for clarification of Bayer's fax sent April 12, 1999, page 2 (enclosure 1). Discussion involved Q=[redacted] at [redacted] minutes. This was the proposed specification USP Apparatus 2(paddle) at [redacted] rpms pH 6.8 citrate/phosphate buffer This was originally accepted on an interim basis and was accepted as a final dissolution specification (enclosure 2). The April 12, 1999 fax that was sent discussed the shelflife requirements were fixed with Q=[redacted] Decisions: Mr. Sunderman would call Dr. Ahn back after he consults with the Biopharm team at Bayer. cc: Original NDA 20-740/S-002 Div File Margaret Simoneau /S/ [redacted]	**IND/NDA#:**NDA 20-740 S-002 **Telecon/Meeting initiated by:** ○ Applicant/Sponsor ● FDA **By:** Telephone **Product Name:** Baycol **Firm Name:** Bayer **Phone:** 203-812-5029

Bayer

Pharmaceutical
Division

William E. Maguire
Director
Clinical Quality Compliance

May 6, 1999

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research, Bldg. PKLN
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, Maryland 20857

Re: BAYCOL™ (cerivastatin sodium tablets)
NDA 20-740; S-002
Safety Update

Dear Dr. Sobel:

Pursuant to 21 CFR 314.50(d)(5)(vi)(b) and a request from Ms. Margaret Simoneau in a telephone conversation on Friday, April 30, 1999, Bayer Corporation Pharmaceutical Division submits the attached Safety Update to the subject NDA.

Since the cut-off date (July 16, 1998) for the Four Month Safety Update, submitted to FDA on November 13, 1998, no studies with Baycol 0.4-mg have completed; therefore, this Safety Update will contain only information from on-going US and Non-US studies received since that date. For reporting purposes we have established March 31, 1999 as the cut-off date for data to be included in this submission.

The Case Report Forms for deaths, discontinuations due to adverse events, and serious adverse events submitted to FDA as 7 or 15 Day Reports from these ongoing studies are being submitted as PDF files on the enclosed CD. These files have been bookmarked only with the study and patient number.

If there are any questions regarding this submission, please contact me at (203) 812-2435.

Sincerely,

William E. Maguire
Director, Clinical Quality Compliance

WEM/cac
Attachment

cc: Ms. Margaret Simoneau

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2435
Fax: 203 812-5029
E-mail: william.maguire.b@bayer.com

[redacted]

OI[illegible]AL

NDA [illegible] AMEND SE2-002 BM

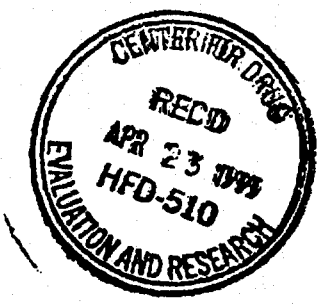
Bayer

Pharmaceutical
Division

William E. Maguire
Director
Clinical Quality Compliance

April 22, 1999

Ms. Margaret Simoneau
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857



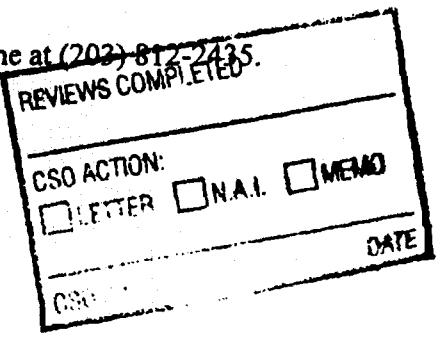
Dear Ms. Simoneau,

Re: NDA 20-740; S-002
BAYCOL™ (cerivastatin sodium tablets)
Response to FDA Request for Information

In response to our telephone conversation of today, April 22nd, I am enclosing a copy of the latest version of the Baycol™ Package Insert. This version displays in color the changes in the Clinical Studies section as agreed to during a teleconference between Bayer and Dr. Orloff and Dr. Shen on April 6, 1999. All previously suggested and agreed to changes have been incorporated into this document but are not displayed in color. These changes include those agreed to in telephone discussions with Dr. Orloff and Dr. Shen as well as those that resulted from our answer to comments from Dr. Steigerwalt which were sent to the Division on February 9, 1999.

We are still addressing the comment regarding AUC of parent and metabolite that we received from Dr. Steigerwalt via telephone call on March 10, 1999 and the follow-up FAX of March 25, 1999. It should be noted that in the telephone conversation Dr. Steigerwalt indicated that the current labeling could remain as is but that we should try to get the requested information as soon as possible.

If you have any further questions, do not hesitate to contact me at (203) 812-2435.



Sincerely,

William E. Maguire
Director, Regulatory Affairs

WEM/cac
attachment

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2435
Fax: 203 812-5029

ORIGINAL

RB

Bayer

5E2-002

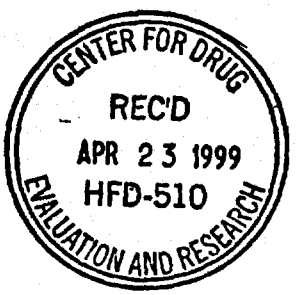
NI AMEND

Pharmaceutical Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

April 22, 1999

Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857



Re: NDA 20-740; S-002
BAYCOL® (cerivastatin sodium tablets)
Response to FDA Request for Information

Dear Dr. Sobel,

At the request of Dr. Hae-Young Ahn, Bayer Corporation is submitting the attached document "Proof of Dissolution of the Active Drug Substance (Cerivastatin 0.4 mg 2.40-01–19 Jun 98; Cerivastatin 0.05 – 0.3 mg: 2.40-01-29 APR 96) to the supplemental application to NDA 10-740.

If there are any questions regarding this submission please contact me at (203) 812-2435.

Sincerely,

William E Maguire

William E. Maguire
Director, Regulatory Affairs

/fks

Desk Copy: Hae-Young Ahn, Ph.D. (FDA)

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

ORIG NDA SUPP AMEND

Bayer

S-002 BM

Pharmaceutical Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

March 11, 1999

MAR 12 1999

HFD 510

Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-740; S002
BAYCOL® (cerivastatin sodium tablets)
Response to FDA Request for Information

Dear Dr. Sobel,

On March 5, 1999, representatives of the Bayer Corporation spoke with Dr. Shiao Wei Shen concerning the 0.4 mg efficacy supplement to NDA 20-740 BAYCOL® (cerivastatin sodium tablets). At this time Bayer is providing responses to each of Dr. Shen's questions. For ease of review, each of Dr. Shen's questions is repeated and followed by Bayer's response.

If there are any questions regarding this submission please contact me at (203) 812-2435.

Sincerely,

William E. Maguire
Director, Regulatory Affairs

/fks

Desk Copy: Dr. Shiao Wei Shen (FDA)

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
DATE
CSO INITIALS

ORIGINAL

Bayer

Pharmaceutical Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

March 3, 1999

Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-740; S002
BAYCOL® (cerivastatin sodium tablets)
Response to FDA Request for Information

Dear Dr. Sobel,

On February 19 and 23, and March 1, 1999, the Bayer Corporation received questions concerning the 0.4 mg efficacy supplement to NDA 20-740 BAYCOL® (cerivastatin sodium tablets) from Dr. Shiao Wei Shen. At this time Bayer is providing responses to each of Dr. Shen's questions. For ease of review, each of Dr. Shen's questions is repeated and followed by Bayer's response.

If there are any questions regarding this submission please contact me at (203) 812-2615.

Sincerely,

William Maguire
Director, Regulatory Affairs

/fks

Desk Copy: Dr. Shiao Wei Shen (FDA)

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

ORIGINAL

Bayer

NDA SUPP AMEND
S62-002 BP

Pharmaceutical
Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

February 9, 1999

Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-740; S-002
BAYCOL™ (cerivastatin sodium tablets)
Response to FDA Request for Information

Dear Dr. Sobel,

On January 15, 1999 the Bayer Corporation Pharmaceutical Division received comments from Dr. Ronald Steigerwalt, the pharmacology reviewer, regarding our submission noted above. At this time Bayer would like to respond to the comments made by Dr. Steigerwalt. Each of Dr. Stigerwalt's comments is repeated and followed by Bayer's response. Copies of pharma reports PH-27579 and PH24850, are included in this submission. These reports have been previously submitted and are included for ease of review of this submission.

We are aware that the information included in these responses will require changes to the package insert which was submitted with this sNDA. Bayer intends to address these issues during final labeling negotiations for this supplement.

If there are any questions regarding this submission please contact me at (203) 812-2435.

Sincerely,

William E. Maguire
Director, Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

Desk Copy: R. Steugerwalat (FDA)

/fks

DUPLICATE

Bayer

NDA SUPP AMEND
S02-002 BM

Pharmaceutical Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

January 27, 1999

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
Food and Drug Administration
Office of Drug Evaluation II (HFD-510)
CDER, Bldg. PKLN
ATTN: DOCUMENT CONTROL ROOM 14B-04
5600 Fishers Lane
Rockville, Maryland 20857

RE: Baycol (cerivastatin sodium tablets)
NDA 20-740, S-002 (SNDA 0.4 mg dosage)

Dear Dr. Sobel:

As discussed during a teleconference with Dr. Shen on Tuesday, January 26, 1999, he requested an additional compilation of specific laboratory data to assist in his review of the 0.4 mg supplemental NDA for Baycol (cerivastatin).

This submission contains the requested information, i.e. tabulations of elevations of CK, SGOT and SGPT in the 100 patients that completed 78 weeks of therapy with cerivastatin 0.4 mg.

Included are four sets of tables, each set containing the requested CK, SGOT and SGPT data. Table 1 displays the occurrence of elevations occurring at any time throughout the 78 weeks of therapy; Table 2 displays the occurrence of elevations occurring after 52 week of therapy. These two tables are similar to those presented for CK only in the December 7, 1998 submission. Two additional tables have been added: Table 3 displays the occurrence of elevations occurring through week 52 only, and Table 4 displays, in a cross-tabulation, the occurrence of elevations up through week 52 as compared with the occurrence of elevations after 52 weeks through 78 weeks.

If you need any clarification of this information, please do not hesitate to contact me at (203) 812-2435.

Sincerely,

William E. Maguire
Director, Clinical Quality Compliance
Regulatory Affairs

cc: Dr. Shiao Wei Shen - Medical Reviewer (Desk Copy)

012799.doc
WEM/lph

ORIGINAL

Baye

Pharmaceutica
Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 0
Phone: 203 812-2

DEC 22 1998

December 21, 1998

Solomon Sobel, MD, Director
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-04
5600 Fishers Lane
Rockville, MD 20857

NDA SUPP AMEND
SE2-002 3C

Re: NDA 20-740; S-002
BAYCOL™ (cerivastatin sodium tablets)
Additional Stability Data

Dear Dr. Sobel,

On June 21, 1998 Bayer Corporation Pharmaceutical Division submitted an efficacy supplement for 0.4 mg BAYCOL™ (cerivastatin sodium tablets). At this time Bayer is submitting a package containing updated stability information.

If there are any questions regarding this submission please contact me at (203) 812-2435.

Sincerely,

William E. Maguire
Director, Regulatory Affairs

/fks

Attachment

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

ORIGINAL

Bayer

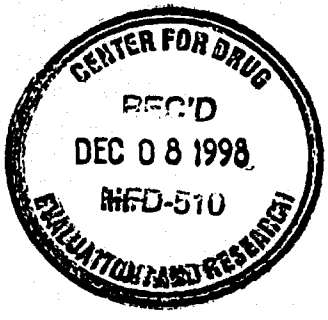
Pharmaceutical
Division

William E. Maguire
Director
Clinical Quality Compliance

NDA SUPP AMEND
SE2-002 BWI

December 7, 1998

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
Food and Drug Administration
Office of Drug Evaluation II (HFD-510)
CDER, Bldg. PKLN
ATTN: DOCUMENT CONTROL ROOM 14B-04
5600 Fishers Lane
Rockville, Maryland 20857



RE: Baycol (cerivastatin sodium tablets)
NDA 20-740, S-002 (SNDA 0.4 mg dosage)

Dear Dr. Sobel:

As discussed during a teleconference with Dr. Shen on Friday, December 4, 1998, he requested additional compilations of data to assist in the review of the 0.4mg supplemental NDA for Cerivastatin. Dr. Shen also requested a note, for the record, clarifying the meaning of VLDL in the tables of the sNDA.

This submission contains the requested information and is organized in five sections, each addressing a specific query:

Section 1
Baseline lipid parameters for all patients in each of the seven trials pooled for Figure 1 of the proposed package insert.

Section 2
Trend analysis of triglyceride values for all patients in the seven trials pooled for Figure 1 of the proposed package insert.

Section 3
Trend analysis of triglyceride values for patients who had baseline triglyceride values of $\geq$ 250 mg/dl in the seven trials pooled for Figure 1 of the proposed package insert.

Section 4
Tabulation of incidence of creatine kinase elevations in the 100 patients who completed 78 weeks of treatment (referred to in the table in section 1.8 of the 4-Month Safety Update) and the incidence after 52 weeks in the same 100 patients.

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2435
Fax: 203 812-5029
E-mail: william.maguire.b@bayer.com

Section 5
Statement of clarification that VLDL in the 0.4mg sNDA tables refers in fact to VLDL-C measurements performed by the Medical Research Laboratories of Highland Heights, Kentucky.

If you need any further clarification of this information, please do not hesitate to contact me at (203) 812-2435.

Sincerely,

William E. Maguire

William E. Maguire
Director, Clinical Quality Compliance
Regulatory Affairs

cc: Dr. Shiao Wei Shen - Medical Reviewer (Desk Copy)

120798.do
WEM/lph

APPEARS THIS WAY ON ORIGINAL

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

ORIGINAL

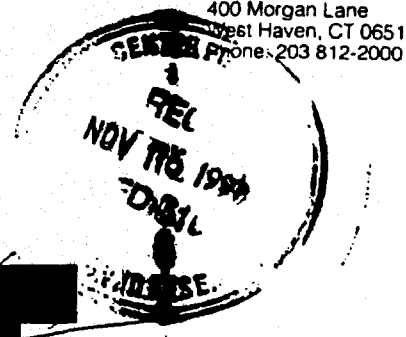
Bayer

Pharmaceutical
Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

November 13, 1998

NDA SUPP AMEND
SE2-002
SU



Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
Food and Drug Administration
Office of Drug Evaluation II (HFD-510)
CDER, Bldg. PKLN
ATTENTION: DOCUMENT CONTROL ROOM 14B-04
5600 Fishers Lane
Rockville, Maryland 20857

/S/ [redacted]
Wed
See Mail 3/24/99

Re: Baycol (cerivastatin sodium tablets)
NDA 20-740, S-002
Four Month Safety Update

Dear Dr. Sobel:

Pursuant to 21 CFR 314.50(d)(5)(vi)(b), Bayer Corporation Pharmaceutical Division submits the attached Four Month Safety Update to the subject NDA.

If there are any questions regarding this submission, please contact me at (203) 812-2615.

Sincerely,

Nancy C. Motola, PhD
Deputy Director, Regulatory Affairs

cc: Margaret Simoneau, RPh., CSO (cover letter)

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

SE2-002 BL

Bayer

Pharmaceutical Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

August 3, 1998

Shiao Wei Shen, MD,
Division of Metabolism and Endocrine Drug Products
Office of Drug Evaluation II HFD-510
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-740
BAYCOL™ (cerivastatin sodium tablets)
Copy of Package Insert

/S/ [redacted]
8/3/98

Dear Dr. Shen,

As you requested I am providing you with the package insert supplied with the 0.4 mg efficacy supplement which was submitted to this NDA (NDA 20-740, S-002). A copy of both the annotated and non-annotated versions are included. Also provided is a diskette with an electronic copy of these documents.

If there are any questions regarding this submission please contact me at (203) 812-2615.

Sincerely,

/S/ [redacted]
8-29-98

Nancy C. Motola, Ph.D.
Deputy Director, Regulatory Affairs

/fks

Attachment

cc RWStegmann 9/14/98

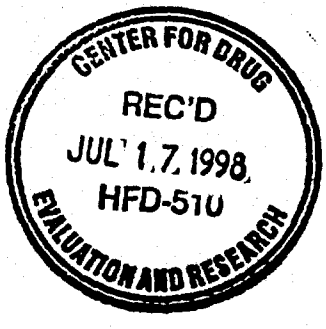
Bayer

Pharmaceutical
Division

Bayer Corporation
400 Morgan Lane
West Haven, CT 06516-4175
Phone: 203 812-2000

July 16, 1998

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
Food and Drug Administration
Office of Drug Evaluation II (HFD-510)
CDER, Bldg. PKLN
ATTENTION: DOCUMENT CONTROL ROOM 14B-04
5600 Fishers Lane
Rockville, Maryland 20857



Re: Baycol (cerivastatin sodium tablets)
NDA 20-740
Efficacy Supplement: 0.4 mg Dose

Dear Dr. Sobel:

Bayer Corporation, Pharmaceutical Division, files this Supplement in accordance with 21 CFR 314.71, to add a 0.4 mg dose to the subject NDA. The dosage form is a distinct 0.4 mg tablet. The product is currently marketed as 0.2 mg and 0.3 mg tablets, although 0.05 mg and 0.1 mg tablets were also approved but not marketed.

This NDA contains information from two pivotal clinical trials, as well as several other supportive short and long term studies, designed to demonstrate safety and efficacy of the 0.4 mg dose in hypercholesterolemia.

In order to facilitate review by the Division, some sections of this NDA are available in electronic format. Attachment #1 describes details of the electronic submission, which is provided with this NDA.

The User Fee for this original NDA (User Fee ID number [redacted] has been submitted on 6/9/98.

If there are any questions regarding this submission, please contact me at (203) 812-2615.

Sincerely,

Nancy C. Motola, PhD
Deputy Director, Regulatory Affairs

Attachment

cc: Margaret Simoneau, CSO (cover letter and attachment)