CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-776

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-776
Pharmacia Corporation
Attention: Susan Tegtmeyer
Manager, Global Regulatory Affairs
4901 Searle Parkway
Skokie, Il 60077

Dear Ms. Tegtmeyer:

Please refer to your New Drug Application (NDA) dated May 19, 1997, received May 20, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Daypro ALTA (oxaprozin potassium) 600 mg tablets and subsequent submissions dated April 21, 1998, March 9, 2000, June 11, 2001, April 19, June 14, October 1 and 11, 2002.

We also refer to the Approval Letter dated October 17, 2002, in which the Final Printed Label was inadvertently excluded. Please find attached below the Final Printed Label.

If you have any questions, call Nancy Halonen, Project Manager, at 301-827-2040.

Sincerely,

{See appended electronic signature page}

Carmen DeBellas, R.Ph.
Chief, Project Management Staff
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Attachment: Final Printed Label
cc: Original
HFD-550/Div. Files

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Eva Essig

From: Ms. Nancy M. Halonen

Fax: -847-982-8090

Fax: 301-827-2531

Phone: 847-982-8980

301-827-2019

Pages: (4)

Date: October 18, 2002.

Re: NDA 20-776 (Daypro ALTA) APPROVAL Letter

☐ Urgent For xReview Only ☐Please Comment ☐ Please Reply ☐ Please Recycle

Hello Eva,

Here is the APPROVAL Letter for NDA 20-776 (Daypro ALTA).

IF you have any concerns or questions, please call Nancy Halonen, Project Manager, at 301-827-2090.

Regards,
Nancy

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Susan Tegtmeyer	From: Ms. Nancy M. Halonen
Fax: 847-982-8811	Fax: 301-827-2531
Phone: 847-982-8090	Phone: 301-827-2019
Pages: (2)	Date: September 18, 2002.

Re: NDA 20-776 Daypro ALTA (oxaprozin potassium tablets) clinical comments to response letter.

☐ Urgent For ☐Review Only ☐Please Comment x Please Reply ☐ Please Recycle

Hello Susan,

Here are the comments from the medical reviewer. We encourage your prompt response. Our goal is to issue an approval letter.

Please call me with any concerns or questions.

Regards,

Nancy Halonen

The major comments are the following:

1. The statements in the Clinical Studies section should be revised as the following: "With respect to GI events, Daypro ALTA appeared to be less well tolerated than oxaprozin acid in this study. The rates for symptomatic ulcers (2.2%) and nausea (13%) for Daypro ALTA treated patients were higher than the rates observed with oxaprozin acid (0% and 6%, respectively)."

The findings reported as stated above are

2. The use of an is not considered acceptable. One of the major reasons for using NSAID template is the observed similarity between the drugs in the class in terms of their pharmacological activities. Safety database on oxaprozin potassium is very limited. The maximum exposures included a 24-week exposure to 1200mg in about 300 subjects (in the two 24-week OA trials; one with and one without controls), a 2-week exposure to 1800mg in 60 subjects, and any exposure to the drug in less than 1800 subjects. When the specific events listed in the NSAID's class labeling were less frequently or not reported in the studies of oxaprozin/oxaprozin potassium, it does not mean that the potential risks for patients taking oxaprozin products to have similar events are much smaller. Using GI ulcer (which is followed by a double asterisks in the 1 to 10% AE rate category) as an example, symptomatic/bleeding ulcer were reported in 0.8 to 2.2% of patients receiving oxaprozin potassium versus zero percent in the active control arms in the 4 controlled OA studies. The rate of asymptomatic ulcer could not be determined because patients were not followed by endoscopic evaluations in these studies. Another example is melena (which is followed by double asterisks in the <1% AE rate category). Melena was reported in 1% of about 300 patients on oxaprozin potassium in the 24-week controlled OA trial and in 2% of about 400 patients who were treated with oxaprozin for 4 to 8 weeks in 5 post-marketing clinical trials. Therefore, should be removed from the adverse event section.

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Susan Tegtmeyer, Pharmacia	**From:** Lori Gorski, Project Manager
Fax: 847-982-8152	**Fax:** 301-827-2531
Phone: 847-982-8811	**Phone:** 301-827-2521
Pages: 2 (including cover page)	**Date:** December 20, 2001

Re: NDA 20-776, Division response to submission dated June 11, 2001

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

• **Comments:** Ms. Tegtmeyer,

The following deficiencies and comments are regarding NDA 20-776, oxaprozin potassium. Items 1 & 2 are approvability issues, the remaining issues are comments. These issues will be discussed further at our teleconference this afternoon at 4:30 EST.

Please let me know if you need anything else.

Thanks
Lori Gorski

1. The following statements should be added to the end of the paragraph in the **CLINICAL STUDIES** section under **Osteoarthritis**:

2. The following statement should be inserted under the **PRECAUTIONS** section.

   "Photosensitivity: Oxaprozin has been associated with rash and/or mild photosensitivity in dermatologic testing. An increased incidence of rash on sun-exposed skin was seen in some patients in the clinical trials."

3. The dosage form "tablets" (which is missing from the established name in the proposed labeling) should be included as part of the established name (where ' — is not an official dosage form).

4. For the unit-dose label the prominence of the established name should be increased as per [§21 CFR 201.10 (g)(1) and (2)] and the dosage form (tablet) should be included.

5. For the container label and carton label:

   a. revise the net quantity statement to read as: "100 Caplets (capsule-shaped tablets)";
   b. revise the statement that "Each caplet contains..." to read as: "Each tablet contains oxaprozin potassium equivalent to 600 mg of oxaprozin";
   c. revise the Usual Adult Dosage statement to read as: "Take two tablets daily. See package insert", and
   d. the labels (color, design, etc.) for oxaprozin potassium should be distinctly different from Daypro to prevent medication errors between these two products.

6. The proposed proprietary name — is not acceptable because of the potential for the — to i... — The proprietary name Daypro — is not acceptable because of the — We recommend that you submit proprietary names for review.

7. Under the **DESCRIPTION** section it should be corrected to "structural formula" instead of "structured formula".

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

/s/

Lori Gorski
12/21/01 03:21:53 PM
CSO

PHARMACIA

Pharmacia Corporation
Global Regulatory Affairs
4901 Searle Parkway
Skokie, Illinois 60077

GENERAL CORRESPONDENCE:

December 19, 2001

Lee Simon, M.D., Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-776
oxaprozin potassium

Dear Dr. Lee:

This is to advise that G.D. Searle & Co., a Delaware corporation (the "Company"), holder of this NDA has changed its name (i.e., been converted into) G.D. Searle LLC. This conversion does not constitute a change in ownership, but rather, is a continuation of the existence of the Company in the form of a Delaware limited liability company. The LLC is for all purposes of the laws of the State of Delaware, deemed to be the same entity as the Company.

G.D. Searle LLC is now also a wholly owned subsidiary of Pharmacia Corporation. Pharmacia Corporation is the successor by merger between Monsanto Company and Pharmacia & Upjohn. This is to advise you that this NDA is still held in the name of G.D. Searle LLC; however correspondence for G.D. Searle LLC will be sent to FDA using Pharmacia Corporation letterhead.

If you have any questions concerning this correspondence, please do not hesitate to contact me.

Sincerely,

Ruben Diaz, B.S., Manager
Global Regulatory Affairs
(847) 982-7214
(847) 982-8090 fax

RD/ha
Enc.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Schmidt

Food and Drug Administration
Rockville MD 20857

JUL 25 2000

Edward B. Portnoy, M.D.
Westlake Medical Research
1250 La Venta Drive, Suite 101A
Westlake Village, California 91361

Dear Dr. Portnoy:

Between June 20 and 23, 2000, Mr. Ronald Koller, representing the Food and Drug Administration (FDA), met with you to review your conduct of a clinical study (protocol # N48-98-02-022) of the investigational drug Benilas (oxaprosin potassium 600 mg tablets), performed for G.D. Searle & Co. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report and the documents submitted with that report, we conclude that, except for not reporting an adverse drug event in the case report form for subject #409, you adhered to pertinent federal regulations and/or good clinical investigational practices governing your conduct of clinical investigations and the protection of human subjects.

We appreciate the cooperation shown Investigator Koller during the inspection. Should you have any questions or concerns about any aspect of the clinical testing of investigational drugs, please contact me by letter at the address given below.

Sincerely yours,

for Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

FEI: 3003949715

Field Classification: NAI
Headquarters Classification:
__ _1) NAI
_X _2)VAI-no response required
_____3)VAI-response requested

Deficiencies noted:
____ inadequate consent form
____ inadequate drug accountability records
____ failure to adhere to protocol
____ inadequate records
__X_ failure to report ADRS in the case report form
____ Other (specify)

cc:
HFA-224
HFD-550 Review Div. Dir.
HFD-550/ MO/Fang
HFD-550/ PM/Schmidt
HFD-550/Doc. Rm. NDA # 20-776
HFD-45 r/f
HFD-47 c/r/s GCP file# 10132
HFD-47/Carreras
HFD-47/Currier
HFR-PA250/Kozick
HFR-PA2565/Koller

O:\JAC\20-776.portnoy.doc

Note to Rev. Div. M.O.

This investigator enrolled 40 subjects in the study. Thirty subjects completed the study. The field investigator examined 20 records. Data audit revealed that one adverse event (muscle cramp) was not reported in the proper form of the case report form for subject # 409 and thus not captured in the data set. Otherwise the data collected from this site appears acceptable.

SEARLE

SEARLE

June 11, 2001

Jonca Bull, M.D., Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-776
Benilas™ -
oxaprozin potassium

Dear Dr. Bull:

In response to the July 21, 2000 Action Letter of NDA 20-776 (approvable for osteoarthritis and rheumatoid arthritis indications), and in reference to our letter of July 27, 2000 pursuant to 21 CRF 314.110(a)(1) stating our intention to file an amendment, we hereby amend NDA 20-776 with the following:

- Revised draft oxaprozin potassium labeling. Please note that we propose revisions to the text in the approvable oxaprozin potassium labeling provided by the Division as part of the July 21, 2000 Action Letter. Draft labeling is provided in both hard copy and electronic format (Word 6.0/95).

  -Copy of our proposed labeling (Attachment 1; Daypro XS label.doc)

  -Highlighted version - revisions to approvable text are highlighted in yellow, new proposed text is in red font (Attachment 2; Daypro XS proposed revisions.doc).

- Reference hard copy of oxaprozin potassium packaging components (Attachment 3):

  -hospital unit dose blister (hud.pdf)

  -carton label (carton.pdf)

  -100 count bottle label (bottle.pdf)

NDA 20-776 was amended pursuant to 21 CFR 314.50(d)(5)(iv)(b) in our submission of March 22, 2000. There are no additional safety data to report.

ORIGINAL

We request that the following new proposed tradenames for oxaprozin potassium be forwarded to the Office of Post-Marketing Risk Assessment for consideration:

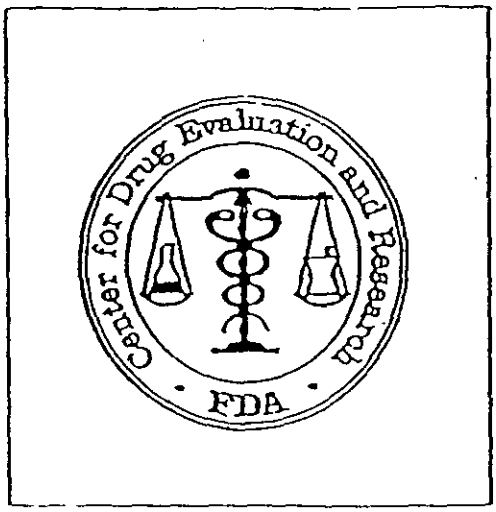
[redacted]

We look forward to hearing from the Division in regard to this amendment. Please feel free to contact me with any questions concerning this submission.

Sincerely,

Susan Tegtmeyer
Regulatory ~~Associate~~ manager
Global Regulatory Affairs
(847) 982-8811
(847) 982-8090 (fax)

FACSIMILE TRANSMISSION
RECORD



From: Sharon A. Schmidt

Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550

Direct Line: 827-2536
Phone 301-827-2040
Fax 301-827-2531

Date: Aug 9, 2000

To:

Name Daryl DeKarske
Company Searle
City Skokie State IL
Phone # 847-982-8606

FAX # 847-982-8152

Number of Pages (INCLUDING COVER PAGE) 3

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:
RE: NDA 20-776

Daryl,
Here are the minutes for our July 21, 2000 telecon.

Sharon A. Schmidt
Project Manager

cc: NDA 20-776
Div File
HFD-550/S.Schmidt

TELECON MINUTES

Meeting Date: 7-21-00 Time: 3:00 Location: S300

FDA requested meeting

NDA 20-776
DRUG: Benilas (oxaprozin potassium) tablets, 600mg
SPONSOR: G.D. Searle

Type of Meeting: Advice

FDA PARTICIPANTS:
Karen Midthun - Director DAAODP, HFD-550
Sharon Schmidt - Project Manager
Christina Fang - Medical Officer

INDUSTRY PARTICIPANTS:

Daryl DeKarske - Regulatory Affairs
Sheila Tallwalker - Statistics
Richard Spivey – Sr. V.P. Global Reg. Affairs
David Recker – Sr. Medical Dir. in Clin. Research

Meeting Objective:

To inform the sponsor that their January 21, 2000, submission did not provide sufficient evidence in support of

Background: The sponsor had been sent an approvable letter on May 20, 1998. This letter pointed out that this NDA was approvable for the osteoarthritis (OA) and rheumatoid arthritis (RA) indications; however insufficient information had been provided for the ——————— In response to the approvable letter, Searle sent in an amendment to the NDA on January 21, 2000 for review.

Discussion:

The sponsor was advised that there is inadequate information as submitted in the January 21, 2000, amendment to support the proposed ——— indication.

FDA noted that the action letter would be issued shortly, and that the sponsor could request a follow-up meeting to discuss the issues regarding what would be needed in support of the pain indication.

The sponsor requested Dr. Delap attends this meeting and the division concurred.

Action Items:

1. FDA will provide meeting minutes within 30 days.

8/9/2000

Sharon O. Schmidt
Sharon Schmidt, Project Manager

Concurrence Chair: 8-9-00
Dr. Karen Midthun, Div. Dir.

cc: NDA 20-776
Div. File
HFD-550/C. Fang/K.Midthun/S. Schmidt/S.Lin/L.Lu

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Daryl DeKarske, M.P.H.
Sr. Regulatory Affairs Associate
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

TELEPHONE: (847) 982-8351
FAX NUMBER: (847) 982-8152

DATE: June 6, 2000

	Name:	Location:	Fax Number:
TO:	Sharon Schmidt	FDA	(301) 827-2531
CC:			

NO. OF PAGES: 2
(Including Cover Page)

MESSAGE: Sharon-
I have attached a copy of the fax that Leslie had sent on June 1, 2000 with regard to the Medical Reviewers request for additional analyses for study -022 for your reference. Please contact me with any questions.

Sincerely,

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Daryl DeKarske, M.P.H.
Sr. Regulatory Affairs Associate
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

TELEPHONE: (847) 982-8351
FAX NUMBER: (847) 982-8152

DATE: June 6, 2000

	Name:	Location:	Fax Number:
TO:	Sharon Schmidt Project Manager	FDA	(301) 827-2531
CC:	Dr. Chrisitina Fang		
	Dr. Laura Lu		

NO. OF PAGES: 5
(Including Cover Page)

MESSAGE: Sharon-
Attached please find a copy of the analyses requested by the Medical Reviewer for Benilas (NDA 20-776) as detailed by Leslie Vaccari in a June 1, 2000 fax, with a copy of the accompanying cover letter for the official submission.. The official submission (hard copy as well as an electronic copy of the analyses tables to be used as a review aid) was sent today for arrival tomorrow at the Division. Please feel free to contact me with any questions.

Sincerely,

8 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Daryl DeKarske, M.P.H.
Sr. Regulatory Affairs Associate
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

TELEPHONE: (847) 982-8351
FAX NUMBER: (847) 982-8152

DATE: April 20, 2000

	Name:	Location:	Fax Number:
TO:	Sharon Schmidt	FDA	(310) 827-2531
CC:	Dr. Laura Lu		

NO. OF PAGES: 2
(Including Cover Page)

MESSAGE: Sharon-

/

for Dr. Lu (see attached correspondence for your reference). I also intend to contact her directly regarding some additional questions she posed in our recent discussion. Hopefully you have now received the additional draft Benilas package labeling for use in OPDRAs review (please feel free to contact me if these have not been received). I would appreciate it if I could follow-up with you in the next couple of weeks to find out if you have received any feedback from OPDRA concerning the acceptability of the Benilas tradename in addition to checking on whether there are any issues/questions in regard to the review of the Benilas amendment that we might be able to provide you some clarification. Thank you for your continued assistance in this matter.

Sincerely,

SEARLE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

April 20, 2000

Karen Midthun, M.D.
Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
Benilas
(oxaprozin potassium)

Dear Dr. Midthun:

Please refer to our March 9, 2000 submission amending NDA 20-776 in which we provided SAS transport files, SAS data sets and annotated CRFs for study N48-98-02-022. Pursuant to a reviewer aid request from Dr. Laura Lu regarding electronic copies (in an editable format) of Tables 7-13 from clinical study report N48-99-06-022, attached please find a CD-ROM containing the SAS programs responsible for generating Tables 7-13. Also incorporated in the CD-ROM are instructions (READ ME FIRST.TXT) for utilizing these SAS programs in conjunction with the previously provided SAS data sets, specifically those relevant to the Tables mentioned above.

Although we are not able to provide the requested Tables in an editable electronic format (only images), the enclosed programs will allow for the modification of these tables.

Please feel free to contact me with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Enclosure

SEARLE

March 24, 2000

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

Sharon A. Schmidt
Project Manager
Room N362
Corporate 2
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: Benilas
(oxaprozin potassium)

Dear Ms. Schmidt:

Please refer to our March 9, 2000 letter in which we had submitted 4 alternative tradenames for oxaprozin potassium to be reviewed by OPDRA in addition to the preferred tradename, Benilas. With respect to a recent conversation with Leslie Vaccari in which she had clarified that only two proposed tradenames are officially provided to OPDRA per requested review, we would ask that Benilas, as the preferred tradename. be the primary name to be reviewed in addition to the alternative proposed tradename selection.

Thank you for your assistance in this matter. Please feel free to contact me with any questions or concerns.

Sincerely,

Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

SEARLE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

March 9, 2000

Leslie Vaccari
Supervisory Project Manager
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: Benilas
(oxaprozin potassium)

Dear Leslie:

Per your request, attached please find ten (10) desk copies of volume 1 of our January 21, 2000 amendment to NDA 20-776 for your reference.

Please feel free to contact me with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Enclosures

SEARLE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

March 9, 2000

NDA ORIG AMENDMENT

Karen Midthun, M.D.
Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

BM

Re: NDA 20-776
Benilas
(oxaprozin potassium)

Dear Dr. Midthun:

Please refer to our January 21, 2000 submission amending NDA 20-776. As requested by the Division and submitted in accordance with 21 CFR 314.110 (a)(1), we hereby further amend NDA 20-776 with the following:

- SAS transport files. SAS data sets and annotated CRFs for study N48-98-02-022 provided electronically in a CD-ROM format as well as a hard copy of the annotated CRFs for that study.

Please feel free to contact me with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Enclosures

HFD-550
S. Schmidt

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Daryl DeKarske	**From:** Leslie Vaccari
Fax: 847-982-8152	**Fax:** 301-827-2531
Phone: 847-982-8351	**Phone:** 301-827-2538
Pages: 1	**Date:** February 7, 2000

Re: FDA request for information NDA 20-776

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ■ **Please Reply** ☐ **Please Recycle**

• **Comments:**

The Medical Officer has the following request for information:

/

Please respond at your earliest convenience and let us know immediately if you need clarification about this request.

Leslie Vaccari /S/
Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products

cc: Orig NDA 20-776
HFD-550/Div File
S. Schmidt

SEARLE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

February 7, 2000

Sharon A. Schmidt, Consumer Safety Officer
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
Corporate II, Room N362
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: Benilas
(oxaprozin potassium)
NDA 20-776

Dear Sharon:

Per your request, attached please find four (4) copies of our January 21, 2000 amendment of the Benilas NDA 20-776 to be distributed as desk copies to Dr. Midthun, the assigned medical and statistical reviewers and yourself. Please feel free to contact me with any questions or concerns.

Sincerely,

for Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Enclosures
DD/jr

4 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEARLE

January 21, 2000

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077

Karen Midthun, M.D.
Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
Benilas
(oxaprozin potassium)

Dear Dr. Midthun:

Please refer to our May 26, 1998 letter in which, pursuant to 21 CFR 314.110 (a)(1), we had formally notified of our intention to file an amendment to NDA 20-776. We hereby submit the following clinical study report in order to address the Division's request for additional information by which to support the

labeling containing language consistent with this proposal is enclosed for the Division's review in both hard copy and electronic format (Word 7.0, both annotated and unannotated versions). Please note that proposed revisions to specific text are highlighted in the enclosed approvable Benilas labeling that had been previously provided by the Division as part of the May 20, 1998 Benilas Action Letter.

We look forward to hearing from the Division in regard to this amendment.

Please feel free to contact me with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Sr. Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Enclosures
DD/jr.

LUTWAK
550

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE CONFERENCE

IND: 47, 340

DATE: January 22, 1999

DRUG: Benilas™(oxaprozin potassium) 600mg Tablets

SPONSOR: G.D. Searle & Co.

Representatives of Searle
Dr. Tomas Bocanegra
Daryle DeKarske
Dr. Susan Rush
Dr. Richard Spivey
Dr. Sheila Tawalker

Representatives of FDA
Robert DeLap, M.D., Ph.D., Director, ODEV
Christina Fang, M.D., Medical Officer
John Hyde, Ph.D., M.D., Deputy Director, DAAODP
Anthony M. Zeccola, Supervisory Regulatory Management Officer

---

BACKGROUND: Telecon to convey FDA comments for protocol M98-836 (serial number 66), dated November 24, 1998.

DISCUSSION: After introductory statements, the following items were discussed:

Original IND 47,340

CONCURRENCE: 1/25/1999
HFD-105\Delap /S/
HFD-550\Fang /S/
HFD-550\Hyde /S/
HFD-550\Zeccolã /S/

CC:
Division File 47,340
HFD-550\Fang
HFD-550\Lutwak

Record of Telecon

SEARLE

October 26, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982 4701

Robert DeLap, M.D., Ph.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
Benilas
(oxaprozin potassium)

Dear Dr. DeLap:

Enclosed please find the minutes of the October 2, 1998 teleconference that was conducted in order to discuss the Agency's issues with regard to the proposed Benilas ——— as well as an appropriate strategy for addressing these issues.

We look forward to receiving FDA minutes from the aforementioned teleconference, and also from the previous teleconference on May 28, 1998 and meeting on June 12, 1998.

Please contact me with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Regulatory Associate
Worldwide Regulatory Affairs
(847) 982-8351
(847) 982-8152

Enclosure

5 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Daryl DeKarske, M.P.H.
Regulatory Affairs Associate
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

TELEPHONE: (847) 982-8351
FAX NUMBER: (847) 982-8152

DATE: 8 June 98

	Name:	Location:	Fax Number:
TO:	Vickey Lutwak	Div. Anti-Inflammatory	(301) 827-2531
CC:			

NO. OF PAGES: 2
(Including Cover Page)

MESSAGE: Vickey-
Attached please find an amended Table 3 for the document that was sent by fax to you on 4 June 98 in regard to the meeting to be held on 12 June 98 concerning Benilas. I will also be sending a copy of the revised Table 3 to you by overnight mail today. Please feel free to contact me with any questions or concerns.

Kind regards,

PLEASE NOTIFY SENDER OF ANY PROBLEMS WITH TRANSMISSION

SEARLE

June 4, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Michael Weintraub, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Reference is made to a May 20, 1990 letter regarding our pending NDA 20-776 for Benilas™ (oxaprozin potassium) Tablets. This letter states that the application is approvable for the osteoarthritis and rheumatoid arthritis indications. However, the letter further states "there is inadequate information to support the [redacted] indication...".

The purpose of this submission is to respond to your comments on the [redacted] and to confirm our requested meeting with you and members of the Division. This meeting will take place on Friday June 12, 1998 from 11:30-12:30 in the Division's Corporate Boulevard office. Attendees from Searle include:

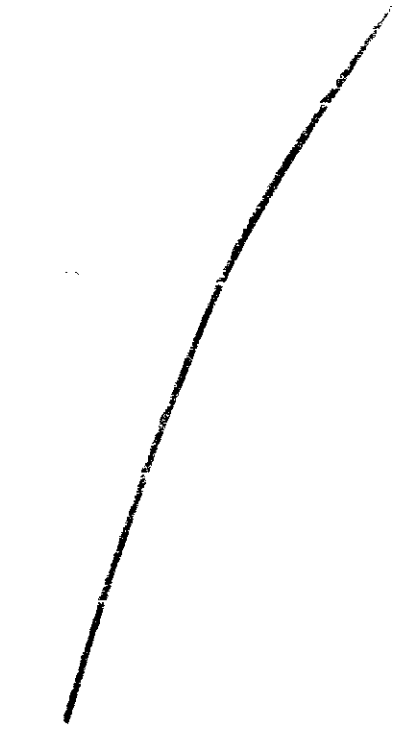
Mr. Daryl DeKarske	Regulatory Affairs
Dr. Richard Spivey	Regulatory Affairs
Dr. Tomas Bocanegra	Clinical Research
Mr. Mike Kuss	Clinical Research
Dr. Sheela Talwalker	Statistician

3 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling



We are appreciative of the timely response to our request for a meeting with the Division. This submission will serve as a background document and be the basis for our discussion regarding the ⟶ . Should you have any questions prior to our meeting, please contact Daryl DeKarske at (847) 982-8351.

Sincerely,

Richard N. Spivey, Pharm.D., Ph.D.
Vice President
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556 fax

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Daryl DeKarske, M.P.H.
Regulatory Affairs Associate
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

TELEPHONE: (847) 982-8351
FAX NUMBER: (847) 982-8152

DATE: 3 June 98

	Name:	Location:	Fax Number:
TO:	Vickey Lutwak	Div. Anti-Inflam.	(301) 827-2531
CC:			

NO. OF PAGES: 2 (11 pages on previous document)
(Including Cover Page)

MESSAGE: Vickey-
As per our discussion, could you please substitute the attached Table 1 document with the Table 1 document that was included in the letter that I had previously sent. Please don't hesitate to contact me with any questions. I hope I'm not contributing to another late evening for you!

Kind regards,

6 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Table 3. Incidence of Adverse Events by Treatment and Study [N (%)]

Event	Oxaprozin Potassium 1800 mg Study 007 (N=19)*	Oxaprozin Acid 1800 mg Study 007 (N=7)*	Oxaprozin Acid 1800 mg Study 028 (N=25)**
nausea	5 (26)	0 (0)	6 (24)
dizziness	2 (11)	1 (14)	2 (8)
injection site inflammation	2 (11)	1 (14)	0 (0)
dyspepsia	2 (11)	0 (0)	0 (0)
pharyngitis	2 (11)	0 (0)	5 (20)
headache	1 (5)	2 (29)	10 (40)
constipation	1 (5)	0 (0)	0 (0)
diarrhea	1 (5)	0 (0)	3 (12)
paresthesia	1 (5)	0 (0)	0 (0)
skin cold clammy	1 (5)	0 (0)	0 (0)
syncope	1 (5)	0 (0)	0 (0)
abdominal pain	0 (0)	1 (14)	0 (0)
vomiting	0 (0)	0 (0)	2 (8)
asthenia	0 (0)	0 (0)	1 (4)
flatulence	0 (0)	0 (0)	1 (4)
hot flushes	0 (0)	0 (0)	1 (4)
palpitations	0 (0)	0 (0)	1 (4)
hyperglycemia	0 (0)	0 (0)	1 (4)
arthralgia	0 (0)	0 (0)	1 (4)
myalgia	0 (0)	0 (0)	1 (4)
menorrhagia	0 (0)	0 (0)	1 (4)

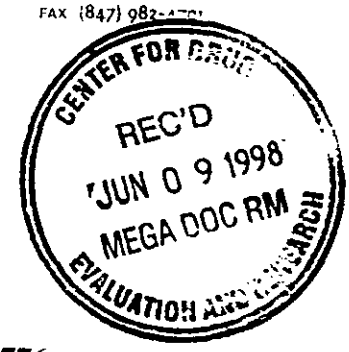
*24 hours
**eight days

SEARLE

ORIGINAL

June 8, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-[illegible]



Dr. Michael Weintraub
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Attention: Document Control Room
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Reference is made to our submission dated June 4, 1998 responding to the May 20, 1998 Action Letter and also confirming our requested meeting with you and members of the Division.

We would like to hereby amend the aforementioned submission replacing Table 3 of that document with the attached revised Table 3. A column of Table 3 describing the incidence of adverse events occurring in study #N65-93-02-015 was inadvertently omitted. We apologize for any inconvenience that this omission may have caused.

Please contact me directly with any questions concerning this submission.

Sincerely,

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

Table 3. Incidence of Adverse Events by Treatment and Study [N (%)]

Event	Oxaprozin Potassium 1800 mg Study 007 (N=19)*	Oxaprozin Acid 1800 mg Study 007 (N=7)*	Oxaprozin Acid 1800 mg Study 028 (N=25)**	Oxaprozin Acid 1800 mg Study 015 (N=23)*
nausea	5 (26)	0 (0)	6 (24)	4 (17)
dizziness	2 (11)	1 (14)	2 (8)	4 (17)
dyspepsia	2 (11)	0 (0)	0 (0)	0 (0)
pharyngitis	2 (11)	0 (0)	5 (20)	0 (0)
headache	1 (5)	2 (29)	10 (40)	0 (0)
constipation	1 (5)	0 (0)	0 (0)	0 (0)
diarrhea	1 (5)	0 (0)	3 (12)	0 (0)
paresthesia	1 (5)	0 (0)	0 (0)	2 (9)
skin cold clammy	1 (5)	0 (0)	0 (0)	0 (0)
syncope	1 (5)	0 (0)	0 (0)	0 (0)
abdominal pain	0 (0)	1 (14)	0 (0)	0 (0)
vomiting	0 (0)	0 (0)	2 (8)	1 (4)
asthenia	0 (0)	0 (0)	1 (4)	0 (0)
flatulence	0 (0)	0 (0)	1 (4)	0 (0)
hot flushes	0 (0)	0 (0)	1 (4)	0 (0)
palpitations	0 (0)	0 (0)	1 (4)	0 (0)
hyperglycemia	0 (0)	0 (0)	1 (4)	0 (0)
arthralgia	0 (0)	0 (0)	1 (4)	0 (0)
myalgia	0 (0)	0 (0)	1 (4)	0 (0)
pain	0 (0)	0 (0)	0 (0)	6 (26)
edema	0 (0)	0 (0)	0 (0)	2 (9)
somnolence	0 (0)	0 (0)	0 (0)	2 (9)

* single dose

** eight days

SEARLE

DUPLICATE NC

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

May 26, 1998

Dr. Michael Weintraub
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Attention: Document Control Room
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Reference is made to our new drug application (NDA) submitted on May 19, 1997 and the approvable letter dated May 20, 1998 for Benilas (oxaprozin potassium).

Pursuant to 21 CFR 314.110(a), we hereby inform you of our intent to file an amendment to this application.

Please contact me with any questions concerning this request.

Sincerely,

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

SEARLE

NC
DUPLICATE

May 26, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Dr. Michael Weintraub
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Attention: Document Control Room
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Pursuant to 21 CFR 314.102(d), we hereby request a teleconference with the appropriate staff members from the Anti-Inflammatory, Analgesic and Ophthalmic Drug Product Division for the purposes of clarification of the Agency's issues concerning the indication as described in the Benilas approvable letter dated May 20, 1998.

As requested by Ms. Vickey Lutwak, we also hereby notify the Agency as to our intention to utilize Benilas as the tradename for oxaprozin potassium.

Please contact me with any questions concerning this request.

Sincerely,

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

FACSIMILE TRANSMISSION RECORD

From: Vickey Lukwak

Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550

Phone 301-827-2040
Fax 301-827-2531

Date: May 22, 1998

To:

Name Daryl DeKarske
Company GD Searle
City Skokie State Il.
Phone # 847 982 8351

FAX # 847 982 8152

Number of Pages (INCLUDING COVER PAGE) (1)

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:

Daryl -

Meeting date:

June 12, 1998 @ 11:30 AM
9201 Corporate Dr.

FDA - M. Weintraub, M.J. Walling, J.E. Hyde
C. Fang, V. Lukwak

Regards

FAXED
5-22-98

V.

2 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEARLE

ORIG AMENDMENT

ORIGINAL

SEARLE
5001 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-1701

April 21, 1998

Dr. Micheal Weintraub
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Attention: Document Control Room
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Pursuant to 21 CFR 314.60, G.D. Searle & Co. hereby amends the pending oxaprozin potassium NDA submitted on May 19, 1997 to provide revised draft container labeling for the following items:

-
-
- 100 Count Bottle Label

Subsequent to the initial submission of the draft container labeling, we have had the benefit of having received comments from the reviewing chemist, Dr. Charlotte Yaciw. We have since made minor revisions to the oxaprozin potassium container labeling according to the recommendations of Dr. Yaciw, as well as incorporate the newly designated trade name; Benilas and replaced the prescription legend with "*Rx only*"

Per a request made by Ms. Vickey Lutwak for the reviewing chemist, we have enclosed three copies of each of the aforementioned container labels.

Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

enclosures

SEARLE

NC

DUPLICATE

May 26, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-1701

Dr. Michael Weintraub
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Attention: Document Control Room
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

Pursuant to 21 CFR 314.102(d), we hereby request a meeting with the appropriate staff members from the Anti-Inflammatory, Analgesic and Ophthalmic Drug Product Division to discuss the contents of the Benilas approvable letter dated May 20, 1998.

An agenda for the proposed meeting will be formally submitted to the Agency subsequent to the teleconference scheduled to occur on May 28, 1998.

Please contact me with any questions concerning this request.

Sincerely,

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
(847) 982-8351
(847) 982-8152 fax

2 Page(s) Withheld

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

✓ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

SEARLE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

March 9, 1998

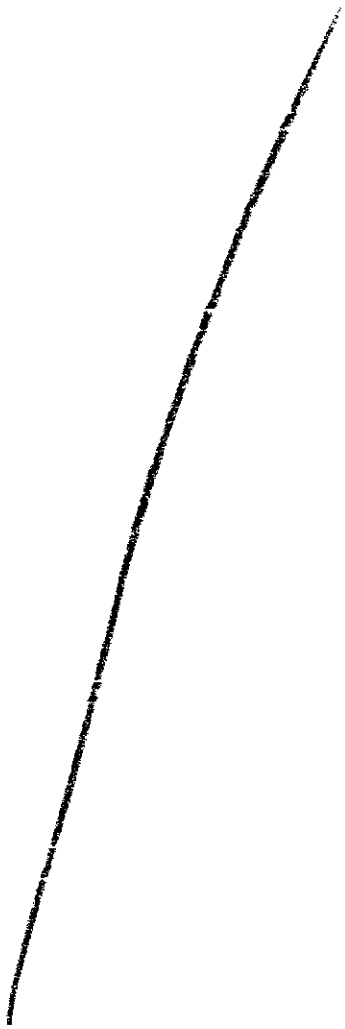
Michael Weintraub, M.D., Director
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

Re: NDA 20-776
(oxaprozin potassium)
Tradename selection

Dear Dr. Weintraub:

Ms. Lutwak, in a March 6, 1998 telephone call, relayed to Searle some concerns of the Nomenclature Committee regarding use of [redacted] as a tradename for oxaprozin potassium (NDA 20-776). Specifically she mentioned their concern with potential "look-alike" and "sound-alike" names and that it could be interpreted to mean "can endure" pain.

We have investigated the various concerns raised by the Nomenclature Committee, and offer the following information in support of [redacted] as a tradename.



In summary, for these reasons we believe that the ——— tradename is an appropriate and reasonable name for the oxaprozin potassium product and request approval of its use. I will contact you on Friday to discuss this tradename selection further.

Sincerely,

Jerome M. Prahl

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

cc: V. Lutwak
JP/022

SEARLE

February 13, 1998
(via facsimile)

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982 4701

Ms. Vickie Lutwak, Consumer Safety Officer
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Ms. Lutwak:

I would like to request that you place before the FDA Labeling and Nomenclature Committee for consideration at their February meeting, two additional alternate brand names for use in the oxaprozin potassium NDA 20-776. We request approval of:

⌜

⌟

Your assistance in this selection process is appreciated. Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Jerome M. Prahl

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

JP/013

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

January 20, 1998
(via facsimile)

Ms. Vickie Lutwak, Consumer Safety Officer
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20857

SEARLE

Re: NDA 20-776
(oxaprozin potassium)

Dear Ms. Lutwak:

I would like to request that you place before the FDA Labeling and Nomenclature Committee for consideration at their January meeting, four additional alternate brand names for use in the oxaprozin potassium NDA 20-776. We request approval of:

Your assistance in this selection process is appreciated. Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

JP/008

SEARLE

February 13, 1998
(via facsimile)

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 600//
PHONE (847) 98> /000
FAX (847) 982 4/01

Ms. Vickie Lutwak, Consumer Safety Officer
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20857

Re: NDA 20-776
(oxaprozin potassium)

Dear Ms. Lutwak:

I would like to request that you place before the FDA Labeling and Nomenclature Committee for consideration at their February meeting, two additional alternate brand names for use in the oxaprozin potassium NDA 20-776. We request approval of:

Benilas

Your assistance in this selection process is appreciated. Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Jerome M. Prahl

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

JP/013

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

December 10, 1997
(via facsimile)

Ms. Vickie Lutwak, Consumer Safety Officer
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20857

SEARLE

Re: NDA 20-776
(oxaprozin potassium)

Dear Ms. Lutwak:

I would like to request that you place before the FDA Labeling and Nomenclature Committee for consideration at their December meeting, two alternate brand names for use in the oxaprozin potassium NDA 20-776. We request approval of:

[redacted] JPrahl 12-15-97

[redacted]

The selection of a brand name by a company is a very involved process and the rejection of [redacted] has caused us to begin this process again. Although we have submitted the above two names for consideration, our selection process is continuing and we may have additional names for consideration at a later meeting of the Committee. Your assistance in this selection process is appreciated.

Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Jerome M Prahl

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

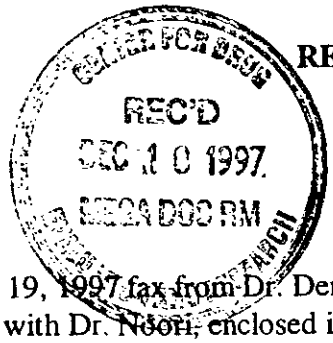
JP/092

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

December 8, 1997

ORIG AMENDMENT
BB

Michael Weintraub, M.D., Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850



RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

In response to the November 19, 1997 fax from Dr. Dennis Bashaw and the November 7, 1997 telephone conversation with Dr. Noori, enclosed is a summary of requested information for N48-96-06-005 and N48-96-06-008. This summary was previously faxed to Dr. Bashaw on December 1, 1997 to assist him in the preparation of a biopharm summary on [redacted] Also attached are analysis of variance (ANOVA) tables, requested by Dr. Bashaw, but not included in the faxed summary.

If you have any questions concerning this information, please do not hesitate to contact me.

Sincerely,

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556

RNS/pl
Enc.

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

24 November 1997

Michael Weintraub, M. D., Acting Director
Division of Anti-inflammatory, Analgesic
and Ophthalmologic Drug Products
Center for Drug Evalution and Research
9201 Corporate Boulevard
Rockville, MD 20850

SEARLE

[redacted] NDA 20-776
(oxaprozin potassium)

Dear Dr. Weintraub:

The enclosed amendments were prepared after correspondence with FDA (Charlotte Yaciw) on 13 November 1997 regarding review of the pending application for [redacted] NDA 20-776 (oxaprozin potassium)

Ms. Yaciw suggested that we reevaluate our Environmental Assessment to factor in metabolism of the product. She indicated that we might be able to file for categorical exclusion if we reduced the EIC (Expected Introduction Concentration) levels for oxaprozin drug substance to under 1 ppb.

We have determined that human metabolism significantly transforms the oxaprozin molecule which consequently serves as the basis for exclusion. The following "Categorical Exclusion," to the Environmental Assessment for [redacted] was prepared in accordance with the final rule describing revision of policies and procedures of the National Environmental Policy Act published in the Federal Register (v. 62, no. 145: July 29, 1997):

> "Categorical Exclusion"
> Document No.: 1995-OXZ-EA-03; dated: 24 Nov 1997
> Supercedes "Environmental Assessment," document no.: 1995-OXZ-EA-02; dated: 3 October 1997.

In addition, we amended the Stability Commitment to correct for a typographical error in the title. The following document reflecting this correction is attached as well:

> "Stability Commitment for Oxaprozin Potassium 600 mg Tablets"
> Document no.: 2117-OXZ-NC-03; dated: 24 Nov 1997
> Supercedes "Stability Commitment for Oxaprozin Potassium 600 mg Tablets," Document no.: 2117-OXZ-NC-02; dated: 12 Sep 1997

If you have questions or comments please contact me directly.

Sincerely,

Roger Nosal
Associate Director
Worldwide Regulatory Affairs Chemistry, Manufacturing and Controls

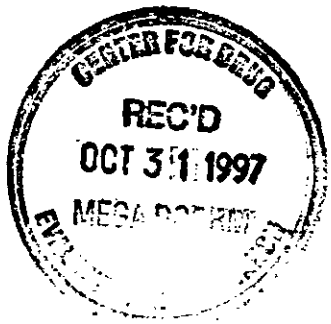
Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

RESPONSE TO FDA REQUEST FOR INFORMATION

October 30, 1997

Serial Number: 058

Michael Weintraub, M.D.,
Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Blvd.
Rockville, Maryland 20850



RE: IND 33,501
Daypro®
(oxaprozin)

Dear Dr. Weintraub:

Reference is made to a telephone call from Ms. Chin Koerner of your Division regarding Dr. R.A. Fiddes and his participation in a Daypro® clinical study. We have the following information to provide:

1. The Daypro study N65-94-02-022 was submitted to IND 33,501 on 26 Sep 1994 (SN:037).

2. This study was not part of the Daypro NDA, and was not part of the determination of safety and efficacy of Daypro.

3. Deleting patients contributed by Dr. — from the overall analyses of the study did not materially alter the conclusions. No statistically significant results changed to insignificance based on the deletion of patients from Dr. — site. Attached is a summary of any changes observed in the new analyses (Attachment 1) as well as the statistical output of these analyses (Attachment 2).

4. The deletion of Dr. — patients, because it has no impact on Daypro, similarly has no impact on our pending NDA 20-776 for———— The study contributes to the experience base of Daypro, and in the general sense, to support the new salt formulation,————

We trust this addresses the issues identified. Should you request additional information, please don't hesitate to contact me. A copy of this letter is being sent to the pending NDA 20-776 for ———

Sincerely,

/S/

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556 fax

RNS/pl
Enc.

cc: NDA 20-776 —

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

NEW CORRESP

DUPLICATE

October 30, 1997

Michael Weintraub M.D.,
Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Blvd.
Rockville, Maryland 20850

FILE

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

The purpose of this communication is to submit a copy of the enclosed letter to NDA 20-776 for completeness. This letter was submitted to Searle's IND 33,501 (SN:058) for Daypro (oxaprozin).

If you have any questions concerning this information, please do not hesitate to contact me.

Sincerely,

Richard N. Spivey

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556 fax

RNS/pl
Enc.

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

ORIG

October 28, 1997

Vicky Lutwak, CSO
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Re: **NDA 20-776**
——— (oxaprozin potassium)

Dear Ms. Lutwak:

Please refer to our submission of September 2, 1997 and to our teleconference of October 1, 1997 regarding the PK/PD modeling proposal using data from the ——— clinical study, protocol N48-95-02-007 (A Double-Blind, Placebo-Controlled, Single Dose Comparison of the Analgesic Activity of Oxaprozin Potassium 1200 mg, Oxaprozin Acid 1200 mg, Ibuprofen 400 mg and Placebo in a Postsurgical Dental Pain Model).

Enclosed is a revised proposal for these analyses which incorporates the constructive ideas and suggestions from Drs. D. Bashaw and R. Miller, as discussed during our teleconference. We would be pleased to consider any further suggestions for improvement but, meanwhile, will proceed with the analyses as proposed here.

Sincerely,

Peter F. East

Peter F. East
Associate Director,
Regulatory Affairs
Tel.: (847) 982-8606
Fax: (847) 982-8152

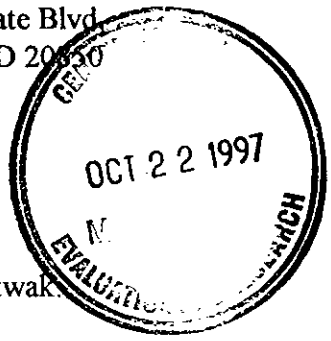
cc: R. Spivey
A. Karim
K. Kowalski

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

October 21, 1997

ORIG AMENDMENT

Vicky Lutwak, CSO
Division of Anti-Inflammatory, Analgesic,
and Ophthalmological Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850



Re: **NDA 20-776**
——— (oxaprozin potassium)

RLE

Dear Ms. Lutwak,

Enclosed, in response to your FAX request of September 7, 1997 and our teleconference of October 20, 1997, are new disks containing the raw and extrapolated efficacy data files for ——— analgesia studies N48-95-02-007, 009, 010 and 016 in the form of SAS transport files.

The files for these studies now exactly follow the format specified in your FAX for naming the efficacy variables, computational aspects and naming conventions for the files. My apologies that the versions submitted on October 7, 1997 omitted the TR variable from the derived datasets for three of the studies. Based on our discussion, we have also recalculated the Tp and Tm variables, therefore the enclosed disks include the data files for all four studies and, with the exception of study 006, completely replace those submitted previously.

In response to Dr. Stein's question on study 016, height was not recorded for this study. I hope that these data files, now in the format specified by Dr. Stein, will be helpful in his review.

Sincerely,

Peter F. East

Peter F. East
Associate Director,
Regulatory Affairs
Tel.: (847) 982-8606
Fax: (847) 982-8152

cc: R. Spivey
S. Talwalker

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

DUPLICATE

October 7, 1997

65

ORIG AMENDMENT

Vicky Lutwak, CSO
Division of Anti-Inflammatory, Analgesic,
and Opthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

EARLE

Re: **NDA 20-776**
——— (oxaprozin potassium)

Dear Ms. Lutwak:

Enclosed, in response to your FAX request of September 7, 1997, are disks containing the raw and extrapolated electronic efficacy data files for——— analgesia studies N48-95-02-007, 009, 010, 016 and for OA study N48-95-02-006 in the form of SAS transport files. We have not provided reconfigured data files for study N48-95-02-004 since this study was not pivotal and, because of its design, the efficacy variables are not amenable to the analyses of the guideline. We obtained an agreement from Dr. Stein in a pre-NDA teleconference on June 6, 1996, to exclude study 004 from any additional analyses.

The enclosed files for the remaining studies follow the format specified in your FAX for naming the efficacy variables, computational aspects and naming conventions for the files. We note that there is only one deviation from the guidance document affecting analgesia study N48-95-02-007. Three patients (059, 148, 175) receiving oxaprozin potassium have "actual" 24-hour assessments recorded even though they took rescue medication after their 12-hour assessment. Using the WOCF approach, the 24-hour assessment for patient 059 would be "severe"; instead it appears as "moderate" as recorded on the CRF. For the other two patients, the "moderate" assessments would be unchanged.

For the efficacy variables in OA study N48-95-02-006, the LOCF convention was used. For patients who ended study participation early, values recorded at the "early termination" (ET) visit (Week 24 CRF) were used to replace missing assessments at scheduled times subsequent to the last visit. For example, a patient who terminated early (after week 6) and had missing assessments at weeks 2, 4, 12 and 24 would be assigned LOCF values as follows:

	Baseline	Week 2	Week 4	Week 6	Week 12	Week 24	ET (from Wk. 24 CRF)
Actual	1	-	-	2	-	-	4
LOCF	1	1	1	2	4	4	

I hope that these data files, in the format specified by Dr. Stein, will be helpful in his review.

Sincerely,

Peter F. East

Peter F. East
Associate Director,
Regulatory Affairs
Tel.: (847) 982-8606
Fax: (847) 982-8152

cc: R. Spivey
S. Talwalker

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

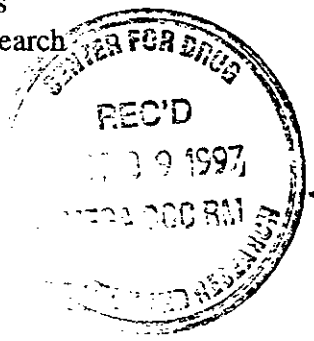
ORIGINAL

7 October 1997

BC

ORIG AMENDMENT

Michael Weintraub, M. D., Acting Director
Division of Anti-inflammatory, Analgesic
and Ophthalmologic Drug Products
Center for Drug Evalution and Research
9201 Corporate Boulevard
Rockville, MD 20850



NDA 20-776
(oxaprozin potassium)

IRLE

Dear Dr. Weintraub:

The enclosed submission has been prepared in reference to FDA correspondence dated 29 August 1997 regarding the pending application for NDA 20-776 (oxaprozin potassium). The attached information was assembled in response to FDA comments from review of the Chemistry, Manufacturing and Control sections of the application.

Searle has provided complete responses to all but two comments. The response to Comment #7 requesting identification of proposed tablet markings is contingent on a decision by the FDA Nomenclature Committee as to whether approval of the brand name will be granted. The exact imprint of the tablet is pending resolution of the final product tradename with the agency.

Searle agrees to amend the storage statement on the package insert and container labels as recommended by FDA, (Comment #14) however the revisions will be submitted during review of the labeling.

In addition, an amended version of the Environmental Assessment for has been prepared in accordance with the final rule describing revision of policies and procedures of the National Environmental Policy Act published in the Federal Register (v. 62, no. 145: July 29, 1997).

If you have questions or comments please contact me directly.

Sincerely,

Roger Nosal

Roger Nosal
Associate Director
Worldwide Regulatory Affairs Chemistry, Manufacturing and Controls

Searle
4901 Searle Parkway
Skokie Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

September 30, 1997

Michael Weintraub, M.D., Director
Office of Drug Evaluation V
Division of Anti-Inflammatory, Analgesic & Ophthalmologic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

Re: NDA 20-776
(oxaprozin potassium)
Tradename selection

Dear Dr. Weintraub:

Ms. Lutwak, in a September 25, 1997 telephone call, relayed to Searle some concerns of the Nomenclature Committee regarding use of ~~~~ as a tradename for oxaprozin potassium (NDA 20-776). Specifically she mentioned their concern with the "pain" sound in the name and also with potential "look-alike" and "sound-alike" names.

We have investigated the various concerns raised by the Nomenclature Committee, and while they may have merit in some instances, we have concluded that they are not applicable in this case. We continue to feel that ~~~~ is an acceptable tradename and has little likelihood of conveying misleading information or being confused with another prescription drug product and offer the following information in support of that position.

2 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

In summary, for these reasons we believe that the ——— tradename is an appropriate and reasonable name for the oxaprozin potassium product and request approval of its use.

Please direct any further comments or questions concerning this subject to my attention.

Sincerely,

Jerome M. Prahl

Jerome M. Prahl
Associate Director
Regulatory Affairs
(847) 982-4573
(847) 982-8152 fax

enclosure
cc: V. Lutwak

JP/059

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

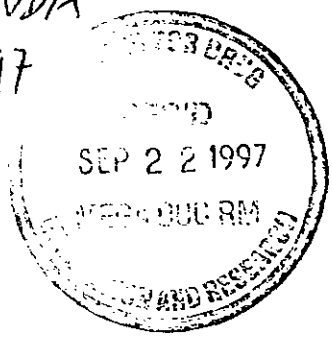
Noted

September 19, 1997

SU
ORIG AMENDMENT

This application is reviewed with the NDA
C-Fang 10/19/97

Michael Weintraub, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic &
Ophthalmic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850



RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

Pursuant to 21 CFR 314.50 we have enclosed a 4-month safety update in support of our pending NDA 20-776 for ———.

Please direct any comments or questions concerning this submission to my attention.

Sincerely,

Richard N Spivey

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556 Fax

RNS/pl
Enc.

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

September 15, 1997

Michael Weintraub, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

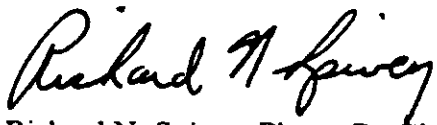
In response to a request from Dr. Stein following our telephone conversation with him on September 12; 1997, we are providing an analysis of the

During this telephone conversation Searle was again queried about "summaries of controlled trials, foreign post-marketing reports, and a summary of literature for Daypro (oxaprozin)" in support of the NDA. We have already responded to this request by providing summaries of Daypro clinical data and Daypro post-marketing adverse event reports, which have previously been submitted to the Daypro NDA. We have also indicated that literature reviews, etc. are already contained in the NDA Annual Reports for Daypro and do not even understand why these are pertinent to the NDA review. It was also pointed out that Daypro is currently marketed in very few countries, with Searle holding rights only in the United States. We believe that there is substantial Daypro information already submitted and in many cases re-submitted to FDA in support of This information is referred to in a supporting role to the clinical information generated from clinical trials, and we cannot understand the focus being put on Daypro literature.

We trust that we have adequately fulfilled your requests for supportive information.

Please do not hesitate to contact me should you have further questions.

Sincerely,



Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182
(847) 982-4556 Fax

RNS/pl
Enc.

FACSIMILE TRANSMISSION
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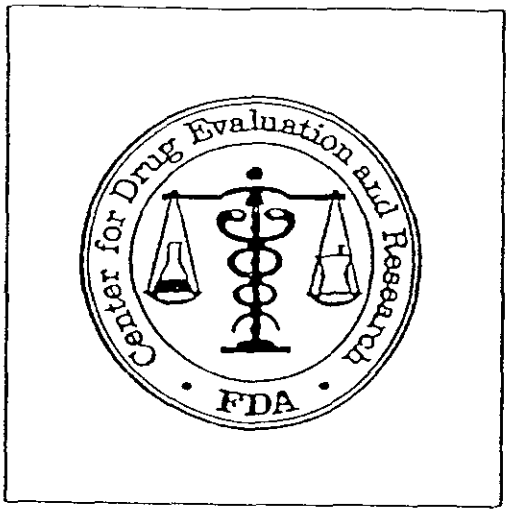

From Vickey Lukosak

Division of Anti-Inflammatory, Analgesic,
and Ophthalmic Drug Products, HFD-550

Phone 301-827-2040
Fax 301-827-2531

Date: Sept. 10, 1997
Sept. 11, 1997

To:
Name Winifred Bagley
Company G.D. Searle & Co
City Skokie State IL
Phone # 847-982-8182

FAX # 847-982-~~4701~~ 8090
Number of Pages (INCLUDING COVER PAGE) 3

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:

Winifred E

Thanks so much!

What we need is #5 on the last page -

Vickey

FAXED
9/10/97 VL

2 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

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RECORD

From Vickey Lukoak

Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550

Phone 301-827-2040
Fax 301-827-2531

Date Sept. 16 17 1997

To:

Name Rich Spivey
Company G. D. Searle & Co
City Skokie State IL
Phone # (847) ~~932-4701~~ 982-8182

FAX # (847) 982-4701

Number of Pages (INCLUDING COVER PAGE) 3

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:

Rich - . Call to confirm 301-827-2522

BEST Times For telecon with D. Strein & V. Lukoak

	OUR Time	YOUR Time
Wed.	2:00 PM - 3.00 P.M	1:00 - 2:00 PM P.M.
Thurs -	no good time	———
Fri	" "	NO GOOD TIME
Mon	9:00 or 9:30 - 10:30 am	8:00 or 8:30 - 9:30 am
or	10:00 - 11:00 AM	9:00 - 10:00 AM

The next best days are Thurs. 25 or Fri. 26, 1997.

SEARLE

REGULATORY AFFAIRS

FACSIMILE TRANSMISSION

Searle
4901 Searle Parkway
Skokie, Illinois 60077
U.S.A.

TELEX: 282475
FAX NUMBER: (847) 982-8090 or (847) 982-8152

	Name:	Location:
TO:	V. LUTWAK	
CC:		
FROM:	R. NOSAL	

NO. OF PAGES: 7
(Including Cover Page)

MESSAGE: NDA 20-776 - 11/24/97

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

24 November 1997

Michael Weintraub, M. D., Acting Director
Division of Anti-inflammatory, Analgesic
and Ophthalmologic Drug Products
Center for Drug Evalution and Research
9201 Corporate Boulevard
Rockville, MD 20850

[redacted] NDA 20-776
(oxaprozin potassium)

SEARLE

Dear Dr. Weintraub:

The enclosed amendments were prepared after correspondence with FDA (Charlotte Yaciw) on 13 November 1997 regarding review of the pending application for [redacted] NDA 20-776 (oxaprozin potassium)

Ms. Yaciw suggested that we reevaluate our Environmental Assessment to factor in metabolism of the product She indicated that we might be able to file for categorical exclusion if we reduced the EIC (Expected Introduction Concentration) levels for oxaprozin drug substance to under 1 ppb.

We have determined that human metabolism significantly transforms the oxaprozin molecule which consequently serves as the basis for exclusion. The following "Categorical Exclusion," to the Environmental Assessment for [redacted] was prepared in accordance with the final rule describing revision of policies and procedures of the National Environmental Policy Act published in the Federal Register (v. 62, no. 145: July 29, 1997):

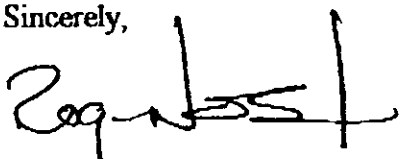
> "Categorical Exclusion"
> Document No.: 1995-OXZ-EA-03; dated 24 Nov 1997
> Supercedes "Environmental Assessment," document no.: 1995-OXZ-EA-02; dated. 3 October 1997.

In addition, we amended the Stability Commitment to correct for a typographical error in the title. The following document reflecting this correction is attached as well:

> "Stability Commitment for Oxaprozin Potassium 600 mg Tablets"
> Document no.: 2117-OXZ-NC-03; dated: 24 Nov 1997
> Supercedes "Stability Commitment for Oxaprozin Potassium 600 mg Tablets," Document no.: 2117-OXZ-NC-02; dated: 12 Sep 1997

If you have questions or comments please contact me directly.

Sincerely,



Roger Nosal
Associate Director
Worldwide Regulatory Affairs Chemistry, Manufacturing and Controls

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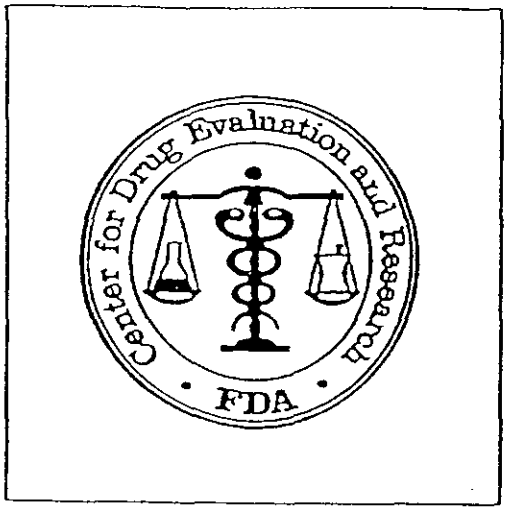


From: Vickey Lutcsak

Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550

Phone 301-827-2040
Fax 301-827-2531

Date: Sept 4, 1997

To:

Name Rich Spidey
Company G.D. Searle & Co
City Skokie State IL
Phone # (847) 982-8182

FAX # (847) 982-4701

Number of Pages (INCLUDING COVER PAGE) 2

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:

FAXED
9-5-97 AF

September 4, 1997
NDA 20-776

Rich,

Enclosed is the boilerplate for the categorical exclusion. If you want to request an exclusion, Please withdraw the original environmental assessment from the NDA and submit the following request for exclusion. This will help the chemist breathe easier because this needs to be done for her to complete her review.

Thanks,
VL
Vickey Lutwak

An environmental assessment section is still required, however, the Federal Register notice published on July 29, 1997, revising 21 CFR 25, may allow a categorical exclusion for your application . The new regulations are in effect as of August 28, 1997.
Acceptable wording for a categorical exclusion is

> "The requested action, approval of NDA xx-xxx, qualifies for a categorical exclusion from the requirement to prepare an environmental assessment under 21 CFR 25.31(b). To the applicants knowledge, no extraordinary circumstances exist that would warrant the preparation of an environmental assessment."

If a categorical exclusion is not claimed, an environmental assessment report must be submitted with the NDA, preferably as a separate volume. See the Guidance for Industry for information on preparing the document.

This is taken out of context, but the statement is provided.

Thanks -
Vickey

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

BB

ORIG AMENDMENT

DUPLICATE

September 2, 1997

Michael Weintraub, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic &
Ophthalmic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

SEARLE

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

Reference is made to a request from Dr. Dennis Bashaw to perform pharmacokinetic/ pharmacodynamic modeling on data from ——— with study N48-95-02-007. This draft proposal is being submitted for review and comment as agreed during our teleconference.

Should you have any questions please do not hesitate to contact me at (847) 982-8182 or (847) 982-4556 (Fax).

Sincerely,

Richard N. Spivey

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs

RNS/pl
Enc.

Desk Copies: Dr. Dennis Bashaw
Ms. Vicki Lutwak (cover letter)

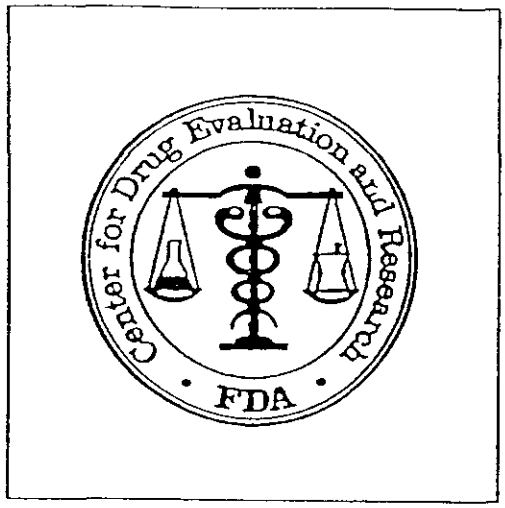
3 Page(s) Withheld

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

___✓___ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

FACSIMILE TRANSMISSION RECORD



From: Vickey Lukosek JEH

Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550

Phone 301-827-2040
Fax 301-827-2531

Date: 8/29/97

To:

Name Rich Spivey
Company G.D. Searle
City Skokie State Il.
Phone # 847- 982-8181

FAX # 847 982 4701

Number of Pages (INCLUDING COVER PAGE) 4

Please telephone (301) 827-2040 IMMEDIATELY if re-transmission is necessary.

Additional message:

REVIEWER'S COMMENTS TO BE RELAYED TO SPONSORS

~~IND~~: NDA - 20-776

DRUG: _____

SPONSOR: G.D. Searle

SUBMISSION DATE: 5/19/79 & amendment 6/25/97

Please find attached comments from our reviewer pertaining to the submission as listed above. Any response to these comments should be sent in triplicate, as an ammendment to the IND referenced, to:

Center for Drug Evaluation and Research
Division of Anti-Inflammatory, Analgesic,
and Ophthalmic Drug Products, HFD-550
9201 Corporate Blvd
Rockville, MD 20850

If you have any questions please call Vickey Lutwak, Project Manager, (301) 827-2090.

Rich,

Some comments from the chemist -

Vickey

NDA 20-776 Comments and Deficiencies from Review #1

1. Methodology and specification(s) should be developed to show that the drug substance is —, potassium oxaprozin.

2. Please provide information on the container/closure system to be used for shipping and storage of the oxaprozin potassium drug substance.

3. Th — rocedure for stability testing should be identified either as the regulatory test or the procedure provided. The term "USP" is meaningless in this context.

4. A retest date should be established for the drug substance. See the ICH Q1A guideline.

5. The manufacturing description and flow chart indicate that — — Please reconcile this discrepancy.

6. Please provide the control procedures used during the tablet manufacturing process.

7. The tablets should be marked with an unique identifier. The proposed text should be included in the product description.

8. In the procedure for drug product assay, (page 248 of volume 4) is the statement "Calculate the percentage of impurities/degradation products (other than — — Since no standard materials for these compounds are used, how are these peaks identified?

9. Please provide additional stability data to support your requested — xpiration dating period.

10. The stability commitments currently state that "one lot" per year will be placed on stability. This should be revised to "at least one lot".

11. In the stability protocol for expiration extension, the second paragraph should refer to approved protocols, i.e., "... although they may follow a different approved protocol design."

12. In the Description section of the package insert please replace "structured formula" with "structural formula".

13. The How Supplied section of the package insert lists "bottles of 100" but the NDA document only contains information on — 500 tablet bottles. If bottles of 100 tablets are to be marketed, the container information and stability data must be submitted.

14. A storage condition of , nor is '
The correct statement is "Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]". The package insert and the container labels should be revised to incorporate this statement.

15. The stability data indicate that the tablets are —
— are not necessary.

Drafted August 21, 1997

COVER SHEET

SEARLE FAX

To: Vicki Lutlak
Fax #: 301 827-2531
Subject: IND
Date: August 18, 1997
Pages: 2, including this cover sheet.

COMMENTS:

Vicki;

We thought it might be helpful to outline the questions that we have for Dr. Stein during our teleconference tomorrow morning (Tuesday, Aug. 19) at 10:00 am EDT. You'll find them attached.

Regards,

Peter F. East

Searle, Regulatory Affairs
4901 Searle Parkway
Skokie, IL 60077

FAX: 847 982-8152
TEL: 847 982-8606

1 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

August 13, 1997

Michael Weintraub, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic &
Ophthalmic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Weintraub:

Reference is made to a telephone call from Ms. Vicky Lutwak of your Division requesting that we provide safety information from marketing experience and other sources for Daypro. This information is in support of our pending NDA 20-776 for ——— (oxaprozin potassium) tablets.

While we had responded that the Daypro NDA and IND contained this information already, e.g., in Periodic Reports and Annual Reports, we are submitting a summary of this information in an attachment to this letter. We believe this information fully addresses the medical officer request and look forward to a continued, rapid review of our data in support of the NDA.

Should you have any questions please do not hesitate to contact me at (847) 982-8182 or (847) 982-4556 (Fax).

Sincerely,

Richard N. Spivey, Pharm.D., Ph.D.
Vice President,
Worldwide Regulatory Affairs

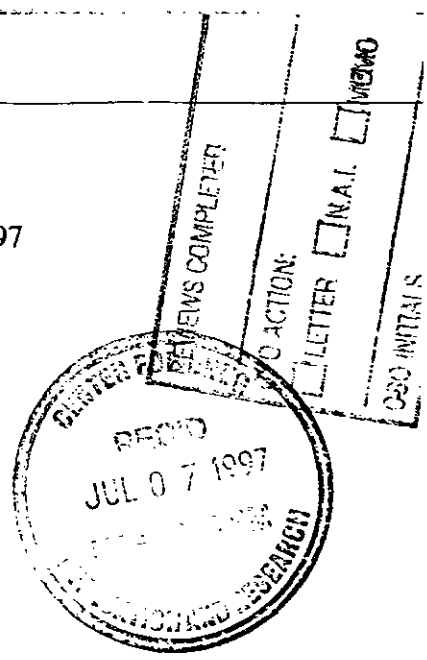
RNS/pl
Enc.

DUPLICATE

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

RX
Received from Vicky
7/7/97

July 3, 1997



Wiley A. Chambers, M.D., Acting Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-776

BM
NDA ORIG AMENDMENT **(oxaprozin potassium)**

Dear Dr. Chambers:

Reference is made to a teleconference held on June 27, 1997 between Searle and members of your Division, including yourself. The purpose of this teleconference was to seek clarification of issues raised during a telephone call initiated by FDA on June 23. Below is a brief summary of the issues discussed during our clarifying teleconference call on June 27.

Please refer to the attached for a more detailed discussion and responses to the issues raised. We look forward to the filing of the NDA and to a continuing dialogue during the review of the Xopane NDA.

Sincerely,

Richard N. Spivey

Richard N. Spivey, Pharm.D, Ph.D.
Vice President,
Worldwide Regulatory Affairs
(847) 982-8182

RNS/br
Enclosures

[redacted] 13264O [redacted]

ORIGINAL

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

RAS Received from Hon 7/16/97

June 27, 1997

Ms. Vicky Lutwak
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

NEW CORRESPONDENCE

ARLE

Dear Vicky,

Based on our conversations over the last few days this is our understanding of what Dr. Stein (FDA Statistician) has requested. We are to provide graphical plots of:

/

Items 1-3 are to be done by individual groups for age, race and sex (i.e. age: <25, 25-44, 45-64, >64 years; race: Caucasian, Black, Asian, Hispanic, Other; sex: male, female) for dental pain studies -007, -009, -010, -016. Could Dr. Stein please clarify whether he needs these graphs by individual groups for the data pooled from studies -007, -009, -010, -016 or each individual study. Please note most patients in each study are young <30 years and Caucasian therefore graphs for pooled data from these 4 studies seems more appropriate than individual graphs. We understand that these graphs are not needed prior to the filing date of July 19 but are needed for review.

Please could you confirm that this understanding is correct and notify me of any changes needed.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

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

BC

NDA SUPPL AMEND

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

DUPLICATE

25 June 1997

Wiley A. Chambers, M. D., Acting Director
Division of Anti-inflammatory, Analgesic and Ophthalmic Drug Products
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850
Attn: Ms. Chin Koerner
Ms. Vicki Lutwak

RE: NDA 20-776 ——
(oxaprozin potassium)
Amendment

Dear Dr. Chambers,

At FDA request, Searle amends NDA 20-776 to provide for an additional copy of a document submitted in Section 6; Human Pharmacokinetics and Bioavailability, volume 1.7, pages 048 - 052 of the original registration to be included in Section 3: Chemistry Manufacturing and Controls, volume 1.3 as well. The enclosed document identifies all clinical trial formulations and is entitled:

"Summary of Oxaprozin Potassium Clinical Trial Formulations,"
Document No.: 1702-OXZ-SU-01
Document Date: 2 Nov 1996

In conjunction with the document entitled "Tabular Summary of Oxaprozin Potassium Drug Substance and Drug Product Lots, Stability Studies and Clinical Studies," (document no.: 2020-OXZ-SU-01, dated: 30 Sep 1996, located in Section 3, volume 1.3, page 194), this amendment provides a comprehensive summary of information for all lots used in clinical evaluations of —— within Section 3 of the registration.

Sincerely yours,

Roger Nosal
Associate Director
Regulatory CMC

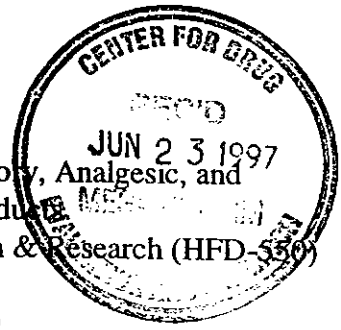
cc: W. Begley

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

NEW CORRES

June 20, 1997

ORIGINAL



Wiley A. Chambers, M.D.
Acting Director
Division of Anti-inflammatory, Analgesic, and
Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Blvd.
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Chambers:

In response to a telephone request from Ms. Chin Koerner on June 13, 1997, enclosed please find a copy of the ——— CANDA to be used as the archival copy for the NDA. This submission consists of eight CD-ROMs. Also included in this volume is the overall Index to the NDA.

If you have any questions concerning this information, please do not hesitate to contact me directly.

Sincerely,

Pamela Larsen for

Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090

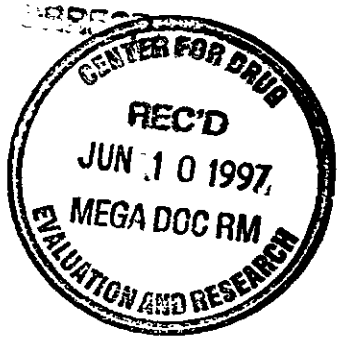
Enc.

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
Fax 847 982 4701

The Sponsor is required to submit safety updates No waiver will be granted. C. Tanz 6/24/97.

ORIGINAL

June 9, 1997



Wiley A. Chambers, M.D.
Acting Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Chambers,

Regarding the above NDA which was submitted on May 19, 1997 we would like to request a waiver from CFR section 314.50 (5) (vi) b which states: The applicant shall submit these reports (safety updates) 4 months after the initial submission. We currently have 3 on-going studies:

- N48-96-02-014 OA double blind study of ——— (oxaprozin potassium) versus Lodine and placebo for 6 weeks treatment
- N48-97-02-015 OA double blind study of ——— versus Lodine and placebo for 6 weeks treatment
- N48-97-02-017 open label study in OA for 6 months treatment with ———

In the above studies approximately 290 patients of which 150 will be treated with oxaprozin potassium, will have completed treatment in time to be included in a 120 day safety update. We do not believe that preparing a safety update on the additional 290 patients in light of the 2293 patients submitted in the NDA (987 treated with oxaprozin potassium) would provide additional useful data at this time. We will of course provide a safety update upon FDA request as necessary.

We trust that this proposal is acceptable, if not please advise immediately.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Searle
4901 Searle Parkway
Skokie, Illinois 60077
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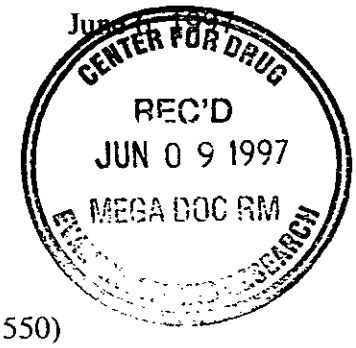
GENERAL CORRESPONDENCE
FDA REQUEST FOR INFORMATION

ORIGINAL

BC

June 11, 1997



SUPPL

Wiley A. Chambers, M.D.
Acting Director
Division of Anti-inflammatory, Analgesic, and
Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Chambers:

The purpose of this communication is to supply chemistry, manufacturing and control information requested by the reviewer to facilitate review of Section 3 of the NDA #20-776.

Please note that this data does not reside in the CANDA submitted with the NDA. This information was previously submitted to the Daypro (oxaprozin) NDA 18-841. A Cross-Reference Table of Contents is included at the beginning of the volume.

If you have any questions regarding this submission, do not hesitate to contact me.

Sincerely,

P.A. Larsen for:
Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090

/pl
enc.

Searle
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 847 982 7000
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May 19, 1997

Wiley A. Chambers, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

SEARLE

RE: NDA 20-776

(oxaprozin potassium)

Dear Dr. Chambers:

Pursuant to 21 CFR 314.50, we are submitting a New Drug Application for ——— (oxaprozin potassium) caplets.

The proposed indications for ——— are:

In the Pre-IND meeting on 16 December 1994 (1) and an End-of-Phase II meeting on 27 November 1995 (2) it was confirmed that:

- No preclinical studies were required for oxaprozin potassium
-

This submission contains the results of five pivotal studies in a post-operative dental pain model and one 6 month study in the treatment of osteoarthritis of the knee. The rheumatoid arthritis indication is requested by cross-reference to the Daypro® NDA 18-841 as was agreed with FDA in a meeting on November 27, 1995 (2)

A waiver of the requirements for submission of paper copies of case report forms (Section 12) and case report tabulations (Section 11) was granted on July 12,1996 (Attachment 1).

On 16 May 1996 a CANDA demonstration was held with representatives from the Division (3). Various requests were made by each reviewer and are accommodated in the electronic delivery of information pertinent to this NDA. The electronic portion of this NDA consists of 8 CDS and are included herein. A description of the contents is included in attachment 2.

Under separate cover a check for $102,500 has been sent to the US Food and Drug Administration to cover 50% of the User Fee.

Any questions that may arise during the review of this submission should be directed to:

Winifred M. Begley

Winifred M. Begley
Director
Regulatory Affairs
Tel (847)-982-8155
Fax (847)-982-8090

(1) IND 47,340 SN 000, dated February 15, 1995 (Section 15, Vol 72, page 8)
(2) IND 47,340 SN 017, dated February 8, 1996 (Section 15, Vol 72, page 26)
(3) IND 47,340 SN 031, dated May 31, 1996. (Section 15, Vol 72, page 69)

Searle
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April 10, 1997

Chin Koerner, Consumer Safety Officer
Division of Anti-inflammatory, Analgesic
and Ophthalmologic Drug Products
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: Naming Committee
Request for Review

SEARLE

Dear Ms. Koerner:

I would like to request that you place before the FDA Naming Committee for consideration at their next meeting, the following brand name for use in the oxaprozin potassium NDA 20-776. We request approval of the following name:

[redacted]

If you have any questions, please do not hesitate to contact me.

Sincerely,

Winifred M Begley

Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090

WB/pl

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-841

OCT 29 1992

Searle
4901 Searle Parkway
Skokie, Illinois 60077

Attention: Donald R. Peckels
Associate Director
Regulatory Affairs

Dear Mr. Peckels:

Please refer to your August 10, 1982 new drug application submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Daypro (oxaprozin) 600mg caplet for the management of the signs and symptoms of osteoarthritis and rheumatoid arthritis.

We also acknowledge receipt of many amendments dated 1986 through 1992.

We have completed the review of this application including the draft labeling which was communicated to you and accepted in your letter of October 22, 1992. There were two additional communications with minor editorial changes on October 23 and 28, 1992. We have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed draft labeling. Accordingly, the application is approved on the date of this letter with these labeling revisions.

These revisions are terms of the NDA approval. Marketing the product before making, exactly as agreed to, the revisions in the product's labeling may render the product misbranded and an unapproved new drug.

Please submit twelve copies of the final printed version of the FPL when it is available. This submission should be designated for administrative purposes as "FPL for approved NDA 18-841". Approval of this labeling is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available prior to our receipt of the final printed labeling, revision of that labeling may be required.