CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20753

CORRESPONDENCE

P Guinn

DEC 14 1998

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, Michigan 49001

Attention: John S. Walker
Regulatory Affairs Manager

Dear Mr. Walker:

We have received your pre-submission of Preclinical and Pharmacokinetics/Bioavailabilty information for the following:

Name of Drug Product: exemestane tablets; 25 mg

Date of Application: November 30, 1998

Date of Receipt: December 1, 1998

Our Reference Number: 20-753

We will review this early submission as resources permit. We will not, however, consider it subject to a review clock or to a filing decision by FDA. Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

If you have any questions, contact Patrick Guinn, Project Manager, at (301) 594-5657.

Sincerely,

/S/

for Dotti Pease
Chief, Project Management Staff
Division of Oncologic Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Gumm

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, Michigan 49001

FEB 2 1999

Attention: John S. Walker
Regulatory Manager, Regulatory Affairs

Dear Mr. Walker:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: exemestane, tablets

Therapeutic Classification: Standard (S)

Date of Application: December 18, 1998

Date of Receipt: December 21, 1998

Our Reference Number: 20-753

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on February 17, 1999 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 21, 1999.

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

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

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncologic Drug Products, HFD-150
Attention:
Division Document Room HFD-150
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncologic Drug Products, HFD-150
Attention:
Division Document Room HFD-150
1451 Rockville Pike
Rockville, Maryland 20852-1420

If you have any questions, contact Patrick Guinn, Project Manager, at (301) 594-5767.

Sincerely,

/S/ 2-1-99

Dotti Pease
Chief, Project Management Staff
Division of Oncologic Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

USAN

UNITED STATES ADOPTED NAMES COUNCIL

American Medical Association
515 North State Street
Chicago, Illinois 60610

Telefax: 312-464-4184
E-mail: Sophia_Fuerst@ama-assn.org

SOPHIA V. FUERST, Associate Secretary
(312) 464-5362

July 28, 1999

LL-46

Pharmacia & Upjohn, Inc.
7000 Portage Road
Kalamazoo, Michigan 49001-0199

Attn: Anthony Palmieri III, PhD
Manager, Technology Protection

Dear Dr. Palmieri:

It is my pleasure to inform you that the USAN Council adopted exemestane as the United States Adopted Name for PNU-155971; FCE24304; Aromasin™, Pharmacia & Upjohn, Inc.'s antineoplastic aromatase inhibitor used in the treatment of advanced breast cancer.

Enclosed is a copy of the Statement of Adoption on exemestane. Please review this information for accuracy, initial, and return the statement to me within 45 days of the date listed above. After 45 days the information will be submitted to Mosby for publication in the journal of *Clinical Pharmacology and Therapeutics* and to the United States Pharmacopeial Convention, Inc., for publication in the *USP Dictionary of USAN and International Nonproprietary Names*.

Sincerely yours,

Sophia V. Fuerst
Associate Secretary
USAN Council

SF

Enclosure: N99:57

Pharmacia & Upjohn

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

March 31, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

General Correspondence
120-Day Safety Update Delayed

Dear Sir/Madam:

On behalf of the Pharmacia & Upjohn Company I would like to inform you that the 4-month Safety Update for NDA 20-753 for exemestane tablets will be delayed. We anticipate submitting the Safety Update report in the week beginning with April 26, 1999. I should be grateful for confirmation from you that this is acceptable.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

ORIGINAL

Pharmacia & Upjohn

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

October 14, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
OCT 15 1999
HFD-150

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Response to FDA Request

ORIG AMENDMENT
(BZ)

Dear Sir/Madam:

Please refer to your fax, dated October 8, 1999, with an information request from the Medical and Biopharmaceutical reviewer. Enclosed please find our response.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Attachments

ORIGINAL

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA
Telephone: (616) 833-4000

Pharmacia & Upjohn

DUPLICATE
ORIG AMENDMENT
(BL)

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

October 11, 1999

CENTER FOR DRUG
RECD
OCT 12 1999
HFD-150
EVALUATION AND RESEARCH

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Sample Labeling

Dear Sir/Madam:

Please refer to your information request, dated October 6, 1999, for samples of labels.

Enclosed please find samples of the labels for the packaging containers;

1) Complimentary package containing one blister card with 15 tablets
2) Package containing two blister cards (30 tablets)
3) Child-resistant container called "Slider-Pack" containing two blister cards (30 tablets)
4) Bottle containing 30 tablets

Enclosed is also a sample of the copy of the blister card (15 tablets).

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Attachments

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

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October 7, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

DUPLICATE
NEW CORRESP
NC

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence

Dear Sir/Madam:

Pharmacia & Upjohn request that correspondence regarding the exemestane package insert, prior to action being taken, will be done by e-mail. We understand that the e-mail link is not secured.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
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Regulatory Manager
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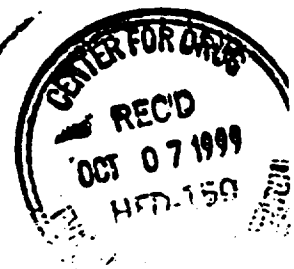
Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

October 6, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

DUPLICATE
NEW CORRESP
N C



Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence

Dear Sir/Madam:

Please refer to your fax to Pharmacia & Upjohn, dated October 1, 1999.

The patient data listings can be found in volume 2.19 and 2.20 of the NDA. They begin on page 8/11/73 and the information on the laboratory data endocrinology tests begins on page 8/12/137.

Please let me know if further clarification is needed.

This information has also been sent by fax to Ms. Ann Staten on October 1, 1999.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH

DUPLICATE

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
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Facsimile No. (616) 833-8237

September 20, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT
(BM)

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
SEP 21 1999
HFD-150

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to your fax, dated September 10, 1999. Enclosed please find four tables which show the number of reassignments by center as for the following prognostic factors:

-any prognostic factors (i.e. the sum of the three prognostic factors shown below, if a patient falls in more than one category, it is counted only once)

- prognostic factor 1: response to prior TAM

- prognostic factor 2: prior chemotherapy

- prognostic factor 3: site of metastasis

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:mlw
Enclosures

DUPLICATE

Pharmacia & Upjohn

7000 Portage Road
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Regulatory Manager
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Facsimile No. (616) 833-8237

ORIGINAL
ORIG AMENDMENT
(32)

September 15, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to your fax, dated September 3, 1999 regarding additional dates request/minimization procedure information.

Enclosed please find our response with attached diskette.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:mlw

Enclosures

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
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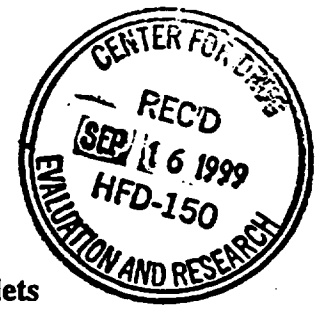
Facsimile No. (616) 833-8237

DUPLICATE
ORIG AMENDMENT
BM

September 15, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857



Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to your fax, dated September 7, 1999 to Pharmacia & Upjohn regarding a request for medical information.

Enclosed please find our response.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:crdt

Enclosures

Pharmacia & Upjohn

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September 15, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

DUPLICATE
ORIG AMENDMENT
BS

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to your fax, dated September 6, 1999 with an information request from Dr. Clare Gnecco. Enclosed please find our response.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:crdt

Enclosures

Pharmacia & Upjohn

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September 14, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

DUPLICATE
ORIG AMENDMENT
(BM)

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Responses to FDA Request

Dear Sir/Madam:

Please refer to your fax, dated September 1, 1999 concerning an information request from the Medical reviewer.

Enclosed is a copy of table 20.2 of the study report on study 94 OEXE 018.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:mlw
Enclosures

Pharmacia&Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

September 14, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 14 1999
HFD-150

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Response to FDA Request

DUPLICATE
ORIG AMENDMENT
(35)

Dear Sir/Madam:

Please refer to your fax, dated September 10, 1999 regarding a request for SAS datasets with each patient's treatment duration and evaluability status in study 94 OEXE 018 with exemestane tablets.

Enclosed please find a diskette with the requested information.

The two datasets contain the following variables:

DUR_TREA.SD2

PNO Protocol number
PATNO Patient number
WEEK_TXT Duration of treatment (weeks)
REAS Reason for treatment withdrawal

EVAL.SD2

PNO Protocol number
PATNO Patient number
EVAL Evaluable for efficacy
REASON Primary reason for non-evaluability
DESCRIP Description

The dataset DUR_TREA contains 769 records, one record for each patient.

The dataset EVAL contains instead 783 records, as a small number of patients has more than one reason for non-evaluability.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:crdt

Enclosures

DUPLICATE

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
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September 13, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

DUPLICATE
ORIG AMENDMENT
B2

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Responses to FDA Request

Dear Sir/Madam:

Please find below the responses to FDA Clinical Pharmacology and Biopharmaceutics Reviewer dated August 20, 1999 concerning NDA 20-753 (exemestane tablets).

1) Status of the studies enrollment

1.1 Study 95-OEXE-015

In the study report No. 9850242, dated October 1998, plasma and safety data were provided on six healthy volunteers (HV), eight subjects with moderate hepatic impairment (MHI) and three subjects with severe hepatic impairment (SHI). Urinary data were, however, provided only on a subset of subjects, i.e.two HV, three MHI and one SHI, as these were the only data available at the time of preparation of the study report. The study protocol described the accrual of nine subjects/group. To date, the accrual and the treatment have been completed for further three HV and four SHI, with two outstanding SHI remaining to be enrolled.

1.2 Study 95-OEXE-016

In the study report No. 9850135, dated February 1998, pharmacokinetic and safety data were provided concerning three HV, three subjects with moderate renal impairment (MRI) and four subjects with severe renal impairment (SRI). The study protocol described the accrual of six subjects/group. The accrual and the treatment of the subjects have now been completed as per protocol, with further three HV, three MRI and two SRI.

2) Update of the database of the study 95-OEXE015 and interim study report preparation

Urinary analyses are currently , 5 subjects with MHI and 2 subjects with SHI, for which no data were available at the time of preparation of study report no.9850242. Complete results on these subjects together with an interim report which will include the full set of plasma and urinary data on the six healthy volunteers (HV), nine subjects with moderate hepatic impairment (MHI) and three subjects with severe hepatic impairment (SHI) that had been enrolled at that time are planned to be available by the end of September 1999.

3) Time line of final reports of studies 95-OEXE-015 and 95-OEXE016

Plasma and urinary analyses are currently on the additional subjects who were recruited since the issuing of the preliminary reports. Based on the current program, the availability of the final report of study 95-OEXE-016 is foreseen by December 1999; that of study 95-OEXE- 015 is also foreseen by December 99, provided that the accrual of the two remaining subjects is successful over the coming weeks.

The report of study 95-OEXE-016 included in the NDA, although entitled as preliminary report, is an interim report in all respects as it includes the final data on the effect of renal impairment on the pharmacokinetics and safety of exemestane for those subjects entered into the study at the time of preparation of the report. The same will apply to the interim report of study 95-OEXE-015, which will be available by the end of September 99. In both studies, the systemic exposure of exemestane (i.e., the area under the plasma concentration-time curve) was on average 2-3 times higher in those subjects suffering from renal or hepatic insufficiency, compared with that observed in healthy volunteers. The planned number of subjects in each study was calculated assuming much smaller differences between treatment groups (30 and 50% for 95-OEXE-015 and 95-OEXE-016, respectively) than those actually observed. Thus, the number of subjects analyzed in the submitted reports has already provided sufficient statistical power to detect significant differences. As a consequence, the results presented in these two reports are considered robust enough to allow reliable conclusions on the effect of the impairment of the hepatic and renal functions on the drug pharmacokinetics.

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

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Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
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DUPLICATE

ORIG AMENDMENT

(BM)

September 10, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 13 1999
HFD-150

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Responses to FDA Request

Dear Sir/Madam:

I refer to your phone call of August 30, 1999.

As requested, please find copies of the CRFs on every other patient (Patient ID's 096 001, 003, 005, 007, 009, 011, 013, 015, 017, 019, 021, 023, 025, 027, 029, 031, 033, 035, 037, 039, 041, 043, 045, 047, 049, 051, 053, in total 27 patients) and lists of all adverse events at center 096 (Prof. Bajetta, Italy) of study 94 OEXE 018 with exemestane tablets.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Enclosures

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

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Facsimile No. (616) 833-8237

DUPLICATE

ORIG AMENDMENT
(BM)

September 7, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence
Responses to FDA Request

Dear Sir/Madam:

Please refer to your fax to Pharmacia & Upjohn, dated August 23, 1999, regarding an information request from the Medical Reviewer.

Enclosed please find CRFs for Patient ID's: 084 001 00, 086 002 00, 132 001 00 and 603 010 00 in study 94 OEXE 018.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Enclosures

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
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August 30, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION
RECD
AUG 31 1999
HFD-150

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

General Correspondence
Response to FDA Questions

DUPLICATE

NEW CORRESP
NC

Dear Sir/Madam:

Please refer to your fax to P&U, dated August 26, 1999.

We have checked the original CRF on patient #06900300 and have not found any indication of elevated bilirubin at baseline.

The bilirubin was 8.0 umol/L at registration on 6/13/97 and 3.42 umol/L at baseline (on 6/27/97).

The units reported in the listing of the normal lab value ranges are umol/L for the period considered, and the max normal lab value was 17.2 umol/L.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf/Enclosures

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
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DUPLICATE

ORIG AMENDMENT
(BS)

August 30, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Amendment No. 012

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

Dear Sir/Madam:

Please refer to the request for statistical information faxed to P&U on August 20, 1999.

Enclosed diskette has additional data from study 94 OEXE 018. It contains information already present in the SAS data set ANALYSIS.SD2 plus the following additional items:

DT_START	Treatment start date
DT_TP	Tumor progression/censoring date
DT_TF	Treatment failure/censoring date
DT_R	CR/PR date
DT_SURV	Death/censoring date

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf

Enclosures

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
20-753

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pharmacia & Upjohn Company	August 30, 1999
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
(616) 833-0774	(616) 833-8237

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*

7000 Portage Road
Kalamazoo, Michigan 49001

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State,ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Exemestane	AROMASIN®

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
	PNU-155971

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Tablets	25 mg	Oral

(PROPOSED) INDICATION(S) FOR USE: Advanced breast cancer.

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION
Amendment No. 012

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telepone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Drug Substance: Antibioticos SpA, Rodano, Italy
Drug Product: Pharmacia & Upjohn, Rodano, Italy

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

ND

EF

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

July 12, 1999

NDA ORIG AMENDMENT (BC)

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
JUL 13 1999
HFD-150

ORIGINAL

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

Amendment No. 009

Dear Sir/Madam:

As indicated in a letter from Pharmacia & Upjohn, dated June 17, 1998, we herewith submit an updated section H: Stability data on drug product, which replaces pages 159-218 of Volume 2.5 of the NDA 20-753.

In this new document, data up to 12 months (both at 25°C and 30°C in either blister and HDPE bottles are given for batches 7001, 8001 and 8002. Furthermore, in the supportive stability section, data at 36 months (both at 25°C and 30°C) are given for batch C12F20.

A new statistical evaluation has been carried out which takes into account the new data.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia Blomqvist

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf

Enclosure

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

NEW CORRESP
NC

July 9, 1999

DUPLICATE

Division of Oncology Drug Products HFD150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

General Correspondence

Dear Sir/Madam:

This letter is to inform you that exemestane obtained orphan drug designation in 1991.

Please find enclosed the official notification of orphan drug designation for exemestane (6-methylenandrosta-1,4-diene-3,17-dione), dated September 19, 1991.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia Blomqvist

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf
Enclosures

Patrick Gunn

Pharmacia&Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

July 30, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Amendment No. 010

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

Dear Sir/Madam:

Please find below the responses to FDA questions dated July 8, 1999 concerning NDA 20-753 (exemestane tablets).

Question 1: , are preliminary reports. Are the studies still ongoing? If the studies are completed, the final reports should be submitted for review.

Answer 1: Studies are still ongoing and there are no final or new preliminary reports available.

Question 2: In the report for study , the normalization of CLCR value to 1.73 m^2 is not necessary based on "Guidance for Industry Pharmacokinetics in Patients with Impaired Renal Function – Study Design, Data Analysis, and Impact on Dosing and Labeling." If the group of moderate renal impairment subjects has been enrolled, as the protocol planned, the data should be submitted.

Answer 2: The normalization of CLCR value to 1.73 m^2 was carried out as this was set forth in the protocol. In the preliminary report, due to the limited number of entered subjects, it was considered appropriate to perform together the analyses of the moderate renal impairment subjects (which had borderline values) with the severe renal impaired subjects. The stratification at this stage would have resulted in too limited a number of moderate and severely impaired subjects, which would have been insufficient to draw any clear conclusion. The required number of moderate renal impairment subjects (6) has now entered the study, however, the relevant analyses have not been completed yet and there are therefore no new data to submit.

Question 3: Table 15 is missing in study report for 95-OEXE-016. Please provide the missing data.

Answer 3: Table 15 of study report 95-OEXE-016 is provided as Attachment 1.

Question 4: No assay description and validation for exemestane could be found in the study reports. Please provide detailed description and validation for the assays in the studies.

Answer 4: The assay description and validation for exemestane was not included in the submitted study reports as these were preliminary ones. A full description of the method and its validation were, however, included in the NDA in Volume 1.53, page 6 21 188.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Enclosures

cc: Patrick Guinn (FDA)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: GMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
20-753

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pharmacia & Upjohn Company	July 30, 1999
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
(616) 833-0774	(616) 833-8237

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State,ZIP Code, telephone & FAX number)* IF APPLICABLE
7000 Portage Road Kalamazoo, Michigan 49001	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Exemestane	AROMASIN®

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
	PNU-155971

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Tablets	25 mg	Oral

(PROPOSED) INDICATION(S) FOR USE: Advanced breast cancer.

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION
Amendment No. 010

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telepone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Drug Substance: Antibioticos SpA, Rodano, Italy
Drug Product: Pharmacia & Upjohn, Rodano, Italy

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

IND

EF

This application contains the following items: *(Check all that apply)*	
	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER *(Specify)*

CERTIFICATION

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Cecilia S. Blomqvist, Reg Affairs Manager	July 30, 1999

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
7000 Portage Road, Kalamazoo, Michigan 49001	(616) 833-0774

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Projec. (0910-0338)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

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

Please DO NOT RETURN this form to this address.

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

June 14, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

DUPLICATE
ORIG AMEN...
(BL)

RECD
JUN 16 1999
HFD-150
EVALUATION AND RESEARCH

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

Amendment No. 008

Dear Sir/Madam:

Please refer to the Fax sent from Patrick F. Guinn to Pharmacia & Upjohn on February 11, 1999.

Enclosed please find the following draft labels:

- Labeling for bottle containing 30 tablets
- Copy on blister card (15 tablets)
- Labeling for package containing one blister card (15 tablets)
- Labeling for package containing two blister cards (30 tablets)

We would appreciate your review and comments on the labels before September 1, 1999, if possible.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf
Enclosure

Pharmacia&Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

ORIGINAL
NEW CORRESP
(NC)

June 4, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG
REC'D
JUN 7 1999
HFD-150
EVALUATION AND RESEARCH

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

Amendment No. 007

Dear Sir/Madam:

We have discovered some typographical errors in Items 4 and 6 of the NDA 20-753. Enclosed you will find the corrected pages. For your convenience I have also included one version of the pages with the changes highlighted.

Corrected pages:

Item 4: Vol. 1/Page 26

Item 6: Vol. 1/ Pages 130, 132, 133, 134,141-147, 153, 154, 159, 163, 164

Please replace the above mentioned pages.

I apologize for any inconvenience this may cause you.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia Blomqvist

Cecilia S. Blomqvist
Regulatory Affairs Manager
CSB:mlw
Enclosure

Pharmacia & Upjohn

7000 Portage Road
Kalamazoo, MI 49001-0199
Telephone: (616) 833-4000

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

ORIGINAL
NEW CORRESP
(NC)

May 24, 1999

CENTER FOR
RECD
MAY 25 1999
HFD-150
EVALUATION AND

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets
(Exemestane Tablets)

General Correspondence

Dear Sir/Madam:

Please refer to the information request sent from FDA to Pharmacia & Upjohn on April 29,1999 and to the teleconference between Pharmacia & Upjohn and the Agency on May 7, 1999.

Enclosed is a CD with the requested information in SAS format together with a document that describes the data sets.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia Blomqvist

Cecilia S. Blomqvist
Regulatory Affairs Manager
CSB:lmf
Enclosure

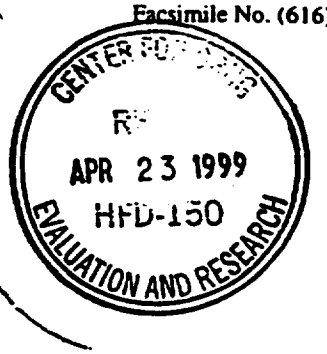
Pharmacia & Upjohn

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

ORIGINAL

ORIG AMENDMENT
(BS)



April 22, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Amendment No. 004

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

Dear Sir/Madam:

Please refer to the Fax from Patrick Guinn to Cecilia Blomqvist Pharmacia & Upjohn, dated March 19, 1999.

Enclosed please find one CD, dated April 16, 1999, containing SAS datasets of clinical data along with a binder of supportive documentation of the datasets.

The file contains, for each patient, the best tumor response considered in all our analyses and the calculation of the following time-dependent variables, expressed in weeks:

- time to objective response (CR, PR)
- duration of objective response (CR, PR)
- duration of overall success (CR, PR, NC $\geq$ 24 weeks) - time to progression
- time to treatment failure
- time to death (survival)

The corresponding censoring variables are provided. For study 018, the randomized treatment and the prognostic factors used in the adjusted analyses are provided as well.

Enclosed please also find two CDs, dated April 16, 1999, with the clinical data in Access format. These CDs are intended to replace the previous CDs, dated December 11, 1998 and sent to FDA with the original NDA submission on December 18, 1998 and on March 26, 1999 as an additional desk copy. These new CDs are provided since during a revision of the database, we discovered the following mistakes/omissions in the below specified tables:

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

ACCESS TABLES	REASON FOR REPLACEMENT
INCLUSION_EXCL	This table contains the response Yes/No to the inclusion/ exclusion criteria. An erroneous correspondence between the field INCLUS that contains the number of the criteria and the field DESC that contains the description of the criteria. For example, in the old version, criteria 1 could have a description that referred to criteria 2.
LABRANGE	This table contains all the laboratory data coming from all the sections of the CRF. In the previous version, the hematology and the chemistry laboratory data, which were requested at registration to confirm the inclusion criteria, were not included. This applies to studies 017, 018 and 022. Now these data are provided.
SYS_THER_ON	This table contains the possible anti-tumoral treatments collected in the form "Death on therapy" or "Follow-up". These data are available for studies 017/018/022 only. In the old version, no information was provided for the "Death on therapy".

All the other tables are unchanged.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf
Attachment

Pharmacia & Upjohn

ORIGINAL

NEW CORRES
(NC)

Office of:
Cecilia S. Blomqvist
Regulatory Manager
U.S. Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

February 25, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to the fax from Patrick Guinn to Cecilia S Blomqvist, P&U, dated February 24, 1999.

Below please find the address and the contact person where the Plasma Sample Assays were analyzed:

Italo Poggesi
Pharmacokinetics
Drug Metabolism Research
Pharmacia & Upjohn
Via Pasteur, 10
20014 Nerviano
Milan
Italy

Tel Int+2-48383172
Fax Int+2-48383012
email: Italo.Poggesi@eu.pnu.com

Pharmacia & Upjohn

DUPLICATE

NEW CORRESP
(NC)

Office of:
Cecilia S. Blomqvist
Regulatory Manager
U.S. Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

February 25, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

General Correspondence
Response to FDA Request

Dear Sir/Madam:

Please refer to the fax from Patrick Guinn to John S. Walker, P&U, dated February 11, 1999.

Please find attached the following information:

1. CD-ROM with the following files as requested under No.3 in the above mentioned fax:

   9850243b.pdf: The complete scanned Study Report 9850243 with table and figures, corresponding to Volumes 2.79 and 2.80 of the NDA

   9850243a.pdf: The complete scanned Study Protocol 94 OEXE 018 corresponding to appendix 1 in Volume 2.81 of the NDA

   RPT018.doc: Body text of Study Report 9850243

   EXE018PR.doc: Body text of Study Protocol 94 OEXE 018 (Amendments 1&2 included)

   018PRA#3.doc: Amendment 3 to Study Protocol 94 OEXE 018

2. Diskette with raw Biopharmaceutic/Pharmacokinetic Data as requested under No.6 in the above mentioned fax

With reference to request No. 5 of the above mentioned fax, please note that no PK information is available from the phase III trial (94-OEXE-018).

The remaining requested information will be submitted as soon as we have it available.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:lmf
Attachments

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
20-753

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pharmacia & Upjohn Company	February 25, 1999
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
(616) 833-0774	(616) 833-8237

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*

7000 Portage Road
Kalamazoo, Michigan 49001

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State,ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Exemestane	AROMASIN®

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*

CODE NAME *(If any)*: PNU-155971

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Tablets	25 mg	Oral

(PROPOSED) INDICATION(S) FOR USE: Advanced breast cancer.

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☒ OTHER

REASON FOR SUBMISSION
General Correspondence

PROPOSED MARKETING STATUS (check one) ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 — THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telepone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Drug Substance: Antibioticos SpA, Rodano, Italy
Product: Pharmacia & Upjohn, Rodano, Italy

Drug

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

ND

EF

Pharmacia & Upjohn

DUPLICATE

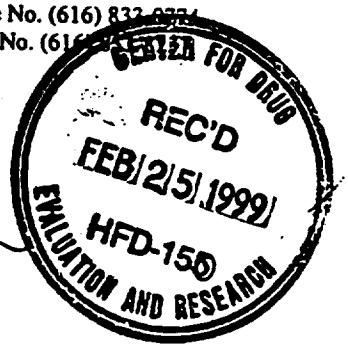
NEW CORRES.
(NC)

Office of:
Cecilia S. Blomqvist
Regulatory Manager
Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8897

February 23, 1999

Noted 3/3/99



Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Amendment No. 002

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

Dear Sir/Madam:

Please find enclosed revised Items 13 & 14 (Volume 2.1, Attachment 7), dated 22 February, 1999, of the above mentioned NDA. In the original Items 13 & 14 tablets were erroneously mentioned instead of the correct "exemestane" tablets. A page showing the correction is also enclosed.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia Blomqvist

Cecilia S. Blomqvist
Regulatory Affairs Manager

CSB:SEH
Attachment

Pharmacia & Upjohn

Office of:
Cecilia S. Blomqvist
Regulatory Manager
U.S. Regulatory Affairs

Telephone No. (616) 833-0774
Facsimile No. (616) 833-8237

February 16, 1999

Division of Oncology Drug Products HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Forwarded To DSI 2/19/99

Re: NDA 20-753
AROMASIN® Tablets (Exemestane Tablets)

DESK COPIES

Dear Sir/Madam:

Please refer to the fax from Patrick Guinn to John S. Walker, P&U, dated February 11, 1999.

Please find attached additional copies of volumes 1.46, 1.47, 1.48 and 2.9 as requested under Nos. 1. and 2. in the above-mentioned fax. Please also refer to Amendment No. 1 that has been sent to the FDA today which contains an amendment to Study Report 9850239 which is included in Volumes 1.46, 1.47 and 1.48.

The remaining requested information will be submitted as soon as we have it available.

If you have questions related to this submission, please contact me at (616) 833-0774 or address correspondence to mailstop 0635-298-113.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Cecilia S. Blomqvsit
Regulatory Affairs Manager

CSB:SEH
Attachment

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000