CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19726/S24

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-578/S-003

AUG 14 1997

Zeneca Pharmaceuticals
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437

Attention: W. J. Kennedy
Vice President, Drug Regulatory Affairs

Dear Dr. Kennedy:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: ZOLADEX (goserelin acetate implant) 10.8 mg Depot

NDA Number: 20-578

Supplement Number: S-003

Date of Supplement: August 11, 1997

Date of Receipt: August 12, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on October 11, 1997 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely, /S/

Lana L. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

1800 Concord Pike
PO Box 15437
Wilmington, DE 19850-5437

SENT UPS NEXT DAY AIR

JUL 24 1998

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 10.8 mg Depot
NDA 20-578, S-003
Early Stage Disease Prostate Cancer Supplement
Revised Draft Labeling

Reference is made to a supplemental New Drug Application (sNDA) submitted August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) 10.8 mg Depot in combination with an antiandrogen for the management of locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission was made for ZOLADEX 3.6 mg Depot (NDA 19-726/S-024) for the same indication.

Reference is also made to correspondence dated July 21, 1998 where Zeneca provided revised draft labeling for the Early Stage Disease Prostate Cancer Supplement.

Further reference is made to a July 24, 1998 telephone conversation between Dr. V. Jarugula and Mr. A. Dunson of FDA, and Ms. O. Begej from Zeneca where the Agency requested the following changes to the "Pharmacokinetics" section:

- In the "Absorption" subsection, the fourth sentence in the second paragraph should be changed to "Mean (Standard Deviation) pharmacokinetic data are presented in Table 1."

- Align (left justify) the results within the "Mean (SD)" and "95% CI" columns in Table 1.

The purpose of this submission is to incorporate into the labeling the above referenced changes. The revised labeling is provided in an 8½ x 11 document format, behind Tab 1, in which the revised language, in italicized text, is incorporated into the current prescribing information. The labeling is also provided on a diskette as a WORD 7.0 file entitled "ZOLNO36.DOC 10.8 RTOG." The Norton Anti Virus software was executed on the file contained on the diskette; no virus was contained within the file or is present on the diskette (Tab 2).

Sincerely,

Odarka Bezyj for KFD

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/OB/car
Attachment

Desk Copy: Alvin Dunson, HFD No. 580

ZENECA
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A Business Unit of Zeneca Inc.

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Wilmington, DE 19850-5437

COPY 2

SENT VIA RAPIFAX AND UPS NEXT DAY AIR

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

JUL 2 1 1998

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 3.6 mg Depot
NDA 19-726, S-024
Early Stage Disease Prostate Cancer Supplement
Revised Draft Labeling

Reference is made to a supplemental New Drug Application (sNDA) submitted August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) 3.6 mg Depot in combination with an antiandrogen for the management of locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission was made for ZOLADEX 10.8 mg Depot (NDA 20-578/S-003) for the same indication.

Reference is also made to a teleconference held between Zeneca and the Division of Reproductive and Urologic Drug Products on July 10, 1998 to discuss labeling submitted in the application.

Further reference is made to Clinical Pharmacology and Biopharmaceutics Review Comments received by Zeneca on July 14, 1998.

The purpose of this submission is to incorporate into the labeling changes discussed during the July 10th teleconference, as well as the Biopharmaceutics review comments received on July 14. The revised labeling is provided in an 8½ x 11 document format, behind Tab 1, in which the revised language, in italicized text, is incorporated into the current prescribing information. The labeling is also provided on a diskette as a WORD 7.0 file entitled "ZOLNO34.DOC 3.6 RTOG." The Norton Anti Virus software was executed on the file contained on the diskette; no virus was contained within the file or is present on the diskette (Tab 2).

As discussed at the July 10, 1998 teleconference, "Clinical Studies", "Adverse Reactions" and "Indications and Usage" sections have been revised to mirror the flutamide labeling for the Early Stage Disease Prostate Cancer indication. CASODEX® (bicalutamide) has been removed from the labeling in the "Indications and Usage" and "Dosage and Administration" sections.

Regarding the July 14, 1998 correspondence, the Clinical Pharmacology and Biopharmaceutics comments are repeated below in bold face type, followed by Zeneca's response.

FDA Comments:

With respect to the proposed labeling (see Attachment I), no major changes for the additional clinical indication sought herein were made to the Pharmacokinetic subsection of the CLINICAL PHARMACOLOGY section of the labeling, therefore, it is acceptable. However, it is recommended that i) the "Special Populations" subsection be reformatted as appropriate to include ZOLADEX's renal and hepatic information under the subheadings "Renal Insufficiency" and "Hepatic Insufficiency."

Zeneca Response:

The "Special Populations" subsection has been reformatted to include subheadings of "Renal Insufficiency" and "Hepatic Insufficiency."

As per discussions with the Agency at the July 10, 1998 teleconference, Zeneca recognizes that the Agency will progress labeling changes with Schering to include "ZOLADEX" in the flutamide prescribing information as the LHRH analogue which was used in RTOG Trial 8610. Zeneca requests assurance from the Agency that Schering will implement this change within three months or at the time of next printing of labels.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/OB/lmc
Attachment

Desk Copy: Alvin Dunson, HFD No. 580, Room No. 17B-45

ZENECA
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PO Box 15437
Wilmington, DE 19850-5437

COPY 1

SENT VIA RAPIFAX AND UPS NEXT DAY AIR

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

JUL 21 1998

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 10.8 mg Depot
NDA 20-578, S-003
Early Stage Disease Prostate Cancer Supplement
Revised Draft Labeling

Reference is made to a supplemental New Drug Application (sNDA) submitted August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) 10.8 mg Depot in combination with an antiandrogen for the management of locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission was made for ZOLADEX 3.6 mg Depot (NDA 19-726/S-024) for the same indication.

Reference is also made to a teleconference held between Zeneca and the Division of Reproductive and Urologic Drug Products on July 10, 1998 to discuss labeling submitted in the application.

Further reference is made to Clinical Pharmacology and Biopharmaceutics Review Comments received by Zeneca on July 14, 1998.

The purpose of this submission is to incorporate into the labeling changes discussed during the July 10th teleconference, as well as the Biopharmaceutics review comments received on July 14. The revised labeling is provided in an 8½ x 11 document format, behind Tab 1, in which the revised language, in italicized text, is incorporated into the current prescribing information. The labeling is also provided on a diskette as a WORD 7.0 file entitled "ZOLNO35.DOC 10.8 RTOG." The Norton Anti Virus software was executed on the file contained on the diskette; no virus was contained within the file or is present on the diskette (Tab 2).

As discussed at the July 10, 1998 teleconference, "Clinical Studies", "Adverse Reactions" and "Indications and Usage" sections have been revised to mirror the flutamide labeling for the Early Stage Disease Prostate Cancer indication. CASODEX® (bicalutamide) has been removed from the labeling in the "Indications and Usage" and "Dosage and Administration" sections.

Regarding the July 14, 1998 correspondence, the Clinical Pharmacology and Biopharmaceutics comments are repeated below in bold face type, followed by Zeneca's response.

FDA Comments:

With respect to the proposed labeling, it is recommend that the following changes be incorporated in the Pharmacokinetic section of the labeling:

Pharmacokinetics

Absorption: The pharmacokinetics of goserelin have been determined in healthy male volunteers and patients. In healthy males, radiolabeled goserelin was administered as a single 250 μg (aqueous solution) dose by the subcutaneous route. The absorption of the radiolabeled drug was rapid, and the peak blood radioactivity levels occurred between 0.5 and 1.0 hour after dosing.

The overall pharmacokinetic profile of goserelin following administration of a ZOLADEX 10.8 mg depot to patients with prostate cancer was determined. The initial release of goserelin from the depot was relatively rapid resulting in a peak concentration at 2 hours after dosing. From Day 4 until the end of the 12-week dosing interval, the sustained release of goserelin from the depot produced reasonably stable systemic exposure. Mean (SD) pharmacokinetic data are presented in Table 1. There is no clinically significant accumulation of goserelin following administration of four depots administered at 12-week intervals. Pharmacokinetic data were obtained using an method, which has been shown to be specific for goserelin in the presence of its metabolites.

Comment

- TABLE 1 SHOULD BE INSERTED HERE. ALSO IN TABLE 1, STANDARD ERROR VALUES SHOULD BE REPLACED WITH STANDARD DEVIATION (SD) VALUES.

Serum goserelin concentrations in prostate cancer patients administered three 3.6 mg depots followed by one 10.8 mg depot are displayed in Figure 1. The profiles for both formulations are primarily dependent upon the rate of drug release from the depots. For the 3.6 mg depot, mean concentrations gradually rise to reach a peak of about 3 ng/mL at around 15 days after administration and then decline to approximately 0.5 ng/mL by the end of the treatment period. For the 10.8 mg depot, mean concentrations increase to reach

a peak of about 8 ng/mL within the first 24 hours and then decline rapidly up to Day 4. Thereafter, mean concentrations remain relatively stable in the range of about 0.3 to 1 ng/mL up to the end of the treatment periods.

Comment

- FIGURE 1 SHOULD BE INSERTED HERE.

Administration of four ZOLADEX 10.8 mg depots to patients with prostate cancer resulted in testosterone levels that were suppressed to and maintained within the range normally observed in surgically castrated men (0-1.73 nmol/L or 0-50 ng/dL), over the dosing interval in approximately 91% (145/160) of patients studied. In 6 of 15 patients that escaped from castrate range, serum levels of testosterone were maintained below 2.0 nmol/L (58 ng/dL) and in only one of the 15 patients did the depot completely fail to maintain serum testosterone levels within the castrate range over a 336-day period (4 depot injections). In the 8 additional patients, a transient escape was followed 14 days later by a level within the castrate range.

Distribution: The apparent volume of distribution determined after subcutaneous administration of 250 μg aqueous solution of radiolabeled goserelin was 44.1 ± 13.6 liters for healthy males. The plasma protein-binding of goserelin was found to be about 27%.

Metabolism: Metabolism of goserelin, by hydrolysis of the C-terminal amino acids, is the major clearance mechanism. The major circulating component in serum appeared to be the 1-7 fragment, and the major component presented in the urine of one healthy male volunteer was the 5-10 fragment. The metabolism of goserelin in humans yields a similar but narrow profile of metabolites found in other species. All metabolites found in humans have also been found in toxicological species.

Excretion: Clearance of goserelin following subcutaneous administration of radiolabeled solution of goserelin was very rapid and occurred via a combination of hepatic and urinary excretion. More than 90% of a subcutaneous radiolabeled solution formulation dose of goserelin was excreted in urine. Approximately 20% of the dose recovered in urine was accounted for by unchanged goserelin.

Special Populations:

The information included in this section is appropriate and no changes are recommended.

Zeneca Response:

The above referenced recommendations have been incorporated into the labeling, including replacing standard error with standard deviation values, with one exception. The Distribution section does not include "radiolabeled" goserelin, as this data was derived from a dose which was not radiolabeled.

As per discussions with the Agency at the July 10, 1998 teleconference, Zeneca recognizes that the Agency will progress labeling changes with Schering to include "ZOLADEX" in the flutamide prescribing information as the LHRH analogue which was used in RTOG Trial 8610. Zeneca requests assurance from the Agency that Schering will implement this change within three months or at the time of next printing of labels.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/OB/lmc
Attachment

Desk Copy: Alvin Dunson, HFD No. 580

P:\DENOBLE\FDA\ZOLADEX\20578DRAFTLAB.DOC

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

DUPLICATE

1800 Concord Pike
PO Box 15437
Wilmington, DE 19850-5437

NDA SUPP AMEND
SEQ/000 3
APR 9 1998

SENT VIA UNITED PARCEL SERVICE

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 10.8 mg Depot
NDA 20-578, S-003
Early Stage Disease Prostate Cancer Supplement
Four-Month Safety Update

Reference is made to Zeneca's supplement submitted August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) 10.8 mg Depot in combination with an antiandrogen for the management of locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission was made for ZOLADEX 3.6 mg Depot (NDA 19-726/S-024) for the same indication.

Data to support this indication were based on the published results of a single clinical trial, Trial 8610, sponsored by the National Cancer Institute and conducted by the Radiation Therapy Oncology Group (RTOG). RTOG Trial 8610 (Pilepich et al 1995) evaluated the effects of complete androgen blockade by use of a luteinizing hormone releasing hormone analog (ZOLADEX) and an antiandrogen (flutamide) in combination before and during radiotherapy, compared with the effects of radiotherapy alone, on the treatment of patients with Stage T2b to T4 (B2-C) tumors of the prostate.

The purpose of this communication is to satisfy the reporting requirements for updated safety information in accordance with 21 CFR 314.50(d)(5)(vi)(b). The clinical study used to support this supplement was complete at the time of its submission. There are no new safety data to report.

Zeneca continues to routinely provide safety information as part of the IND Annual Progress Reports and NDA Periodic Adverse Drug Experiences Reports. Literature searches are provided as part of the NDA Annual Reports, as well. These updates have shown that there are no new safety issues to cause the labeling to be revised.

Should you have any questions or require additional information, please do not hesitate to contact me.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/OB/car

COPY 1 ORIGINAL

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Wilmington, DE 19850-5437

NDA SUPP AMEND
SE1-034

AUG 28 1997

SENT VIA AIRBORNE EXPRESS

Mr. Alvis Dunson
Consumer Safety Officer
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
AV 9/4/97
CSO INITIALS DATE

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
AUG 29 1997
HFD-580

Dear Mr. Dunson:

Re: ZOLADEX® (goserelin acetate implant) 10.8 mg Depot
NDA 20-578, Supplement S-003
Early Stage Disease Prostate Cancer Supplement

Reference is made to a supplemental application submitted to the Agency on August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) in combination with an antiandrogen and radiotherapy for the management of locally confined Stage T2b - T4 (Stage B2 - C) carcinoma of the prostate. Reference is also made to a telephone discussion between Dr. Nigel T. Ratcliffe of Zeneca Pharmaceuticals and yourself on August 14, 1997 regarding an environmental assessment statement for this application. In response, please find enclosed a statement from Zeneca Pharmaceuticals requesting categorical exclusion for an environmental assessment in accordance with 21 CFR 25.31 and the Final Rule on the National Environmental Policy Act; Revision of Policies and Procedures published in the July 29, 1997 Federal Register Notice.

Should you have any questions or require any further information, please do not hesitate to contact me.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/lmc

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DUPLICATE

ZENECA
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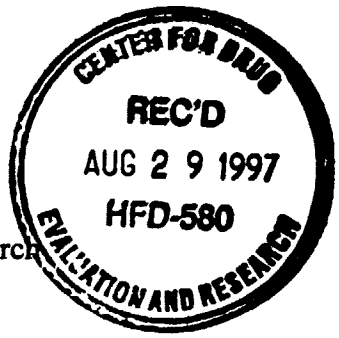
Wilmington, DE 19850-5437

COPY 2

NDA SUPP AMEND
SE1-054
BC

SENT VIA AIRBORNE EXPRESS

AUG 2 8 1997



Mr. Alvis Dunson
Consumer Safety Officer
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-20
5600 Fishers Lane
Rockville, MD 20857

Dear Mr. Dunson:

Re: ZOLADEX® (goserelin acetate implant) 3.6 mg Depot
NDA 19-726, Supplement S-024
Early Stage Disease Prostate Cancer Supplement

Reference is made to a supplemental application submitted to the Agency on August 11, 1997 for the use of ZOLADEX® (goserelin acetate implant) in combination with an antiandrogen and radiotherapy for the management of locally confined Stage T2b - T4 (Stage B2 - C) carcinoma of the prostate. Reference is also made to a telephone discussion between Dr. Nigel T. Ratcliffe of Zeneca Pharmaceuticals and yourself on August 14, 1997 regarding an environmental assessment statement for this application. In response, please find enclosed a statement from Zeneca Pharmaceuticals requesting categorical exclusion for an environmental assessment in accordance with 21 CFR 25.31 and the Final Rule on the National Environmental Policy Act; Revision of Policies and Procedures published in the July 29, 1997 Federal Register Notice.

Should you have any questions or require any further information, please do not hesitate to contact me.

Sincerely,

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/jr
Enclosure

ZOLADEX SUPPLEMENT TO NEW DRUG APPLICATION - ENVIRONMENTAL ASSESSMENT

Zeneca Pharmaceuticals requests categorical exclusion for an environmental assessment for the supplement to the new drug application for Zoladex in accordance with 21 CFR 25.31 (a) & (b).

This is the fifth indication/efficacy claim for Zoladex. Zoladex is currently approved in the US for the treatment of advanced prostrate cancer (NDA 19-726, approved December 29th 1989) and the treatment of endometriosis (NDA 19-726/S-005, approved February 2nd 1993) and the treatment of advanced breast cancer in pre and post menopausal women (NDA 20-515, approved December 18th 1995) and as an agent for endometrial thinning prior to endometrial ablation (NDA 19-726/S-018, approved 27th June 1997).

The additional claim is for the indication for use in combination with flutamide or Casodex (bicalutamide) for the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostrate. Treatment with Zoladex and the anti androgen should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy.

A complete disclosure of the manufacturing process and the controls to protect the environment have been reported in applicants previous submissions to the FDA. These remain unchanged.

Approval of this application will not result in the introduction of additional material into the environment and the total amount of Zoladex introduced into the environment as the result of this submission and all previous approvals will not result in a concentration of the material entering the aquatic environment to exceed 1ppb.

In addition the applicant has no knowledge that any exceptional circumstances exist that would require any additional controls to be imposed on the use of Zoladex in order to protect the environment.

The undersigned official certifies that the information presented is true and complete to the best of the knowledge of the firm of agency responsible for the preparation of the environmental assessment.

22/8/97

Martin Rackham MSc BSc MIoH
Environmental Affairs Manager
International Safety Health and Environment Department
Zeneca Pharmaceuticals

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A Business Unit of Zeneca Inc.

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Wilmington, DE 19850-5437

SENT VIA AIRBORNE EXPRESS

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

AUG 11 1997

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 3.6 mg Depot
NDA 19-726
Supplement - Early Stage Disease Prostate Cancer Supplement

Zeneca Pharmaceuticals, Macclesfield, Cheshire, England, owner of the patent, safety and efficacy information for ZOLADEX® (goserelin acetate implant) hereby submits a supplemental application. The application conforms to the content and format requirements established under 21 CFR 314.50. The application presents data to establish the safe and effective use of ZOLADEX in combination with an antiandrogen for the management of locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when combined with radiotherapy. This supplemental New Drug Application (sNDA) consists of a total of 10 volumes and includes a blue (archival) copy and review copy for each applicable technical section of the sNDA. Each technical review section includes a copy of the application summary.

ZOLADEX is a synthetic agonist analogue of the naturally occurring gonadotrophin-releasing hormone (GnRH). By acting on the pituitary receptors of the hypothalamic-pituitary-gonadal axis, ZOLADEX causes an initial stimulatory effect followed by down-regulation of the receptors and a reduction in the secretion of gonadotrophins. ZOLADEX in combination with an antiandrogen offers complete androgen blockade. The LHRH-A lowers the level of serum testosterone from the testes. The antiandrogen blocks the androgen receptors, thus decreasing the effects of both the residual testicular testosterone present after LHRH-A therapy and the testosterone produced by the adrenal gland. This pharmacological effect of ZOLADEX and an antiandrogen as an adjuvant therapy before and during radiation therapy, with reduction in tumor volume before starting radiation, can lead to increased control of the primary tumor.

This application provides evidence of the efficacy and safety for the use of ZOLADEX in combination with an antiandrogen for the management locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission is being made to NDA 20-578 for ZOLADEX 10.8 mg Depot based on discussions with the Agency outlined below.

On May 5, 1997, Zeneca met with the Division of Reproductive and Urologic Drug Products to discuss the submission strategy for the use of ZOLADEX in combination with an antiandrogen and radiotherapy for the management of locally confined Stage T2b through T4 (Stage B2-C) prostate cancer. During that meeting, the following decisions were reached:

- the Agency accepted the use of the published results of RTOG Trial 8610 as support for this indication for ZOLADEX (Pilepich et al 1995) 3.6 mg Depot and 10.8 mg Depot;
- the Division agreed to obtain direct access to the RTOG 8610 trial data;
- safety data in the form of an update would be provided with the submission; and
- the Agency agreed to review data to support the use of other antiandrogens for this indication.

The US agent for this application representing Zeneca Pharmaceuticals (UK) will be Zeneca Pharmaceuticals (US), A Business Unit of Zeneca Inc., Wilmington, Delaware 19850-5437. The appropriate letter of authorization is enclosed.

Zeneca considers all information contained in this supplemental NDA, except for the published articles, to be trade secrets and therefore, confidential, and hereby requests that the FDA treat this information accordingly. Confidentiality of this information is claimed under Provisions 21 USC Section 331 (j) and/or 18 USC, Section 1905.

Should you have any questions regarding this application, please do not hesitate to contact me at (302) 886-4079.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
Assistant Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-4079
(302) 886-2822 (fax)

KFD/OB/jr
Enclosure

Desk Copy: Mr. Alvis Dunson, HFD No. 580 (Cover Letter Only)

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

ORIGINAL

1800 Concord Pike
PO Box 15437
Wilmington, DE 19850-5437

COPY 1

SENT VIA AIRBORNE EXPRESS

NDA NO. 20-578 REF. NO. 003
NDA SUPPL FOR SE1

AUG 11 1997

Lisa D. Rarick, M.D.
Division Director
Division of Reproductive
and Urologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 580, Room No. 17B-45
5600 Fishers Lane
Rockville, MD 20857

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

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
AUG 12 1997
HFD-580

Dear Dr. Rarick:

Re: ZOLADEX® (goserelin acetate implant) 10.8 mg Depot
NDA 20-578
Supplement - Early Stage Disease Prostate Cancer Supplement

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This application provides evidence of the efficacy and safety for the use of ZOLADEX in combination with an antiandrogen for the management locally confined Stage T2b through T4 (Stage B2-C) carcinoma of the prostate when used with radiotherapy. A duplicate submission is being made to NDA 19-726 for ZOLADEX 3.6 mg Depot based on discussions with the Agency outlined below.

On May 5, 1997, Zeneca met with the Division of Reproductive and Urologic Drug Products to discuss the submission strategy for the use of ZOLADEX in combination with an antiandrogen and radiotherapy for the management of locally confined Stage T2b through T4 (Stage B2-C) prostate cancer. During that meeting, the following decisions were reached:

- the Agency accepted the use of the published results of RTOG Trial 8610 as support for this indication for ZOLADEX (Pilepich et al 1995) 3.6 mg Depot and 10.8 mg Depot;
- the Division agreed to obtain direct access to the RTOG 8610 trial data;
- safety data in the form of an update would be provided with the submission; and
- the Agency agreed to review data to support the use of other antiandrogens for this indication.

The US agent for this application representing Zeneca Pharmaceuticals (UK) will be Zeneca Pharmaceuticals (US), A Business Unit of Zeneca Inc., Wilmington, Delaware 19850-5437. The appropriate letter of authorization is enclosed.

Zeneca considers all information contained in this supplemental NDA, except for the published articles, to be trade secrets and therefore, confidential, and hereby requests that the FDA treat this information accordingly. Confidentiality of this information is claimed under Provisions 21 USC Section 331 (j) and/or 18 USC, Section 1905.

Should you have any questions regarding this application, please do not hesitate to contact me at (302) 886-4079.

Sincerely,

Kimi F. DeNoble

Kimi F. DeNoble
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KFD/OB/jr
Enclosure

Desk Copy: Mr. Alvis Dunson, HFD No. 580 (Cover Letter Only)