CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19726/S24

ADMINISTRATIVE DOCUMENTS

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Division Director's Memo

These applications will be signed off at the Division level. No memo is necessary.

JUL 2 7 1998

Team Leader Memorandum

NDA:	**19-726 #024** **20-578 #003**
Drug and Indication:	**Zoladex® (goserelin acetate implant)**
Dose:	**3.6 mg. (1 month) s.c.** **10.8 mg (3 month) s.c.**
Sponsor:	**Zeneca Pharmaceuticals, Inc.** **Wilmington, DE**
Received:	**Aug. 12,1997**
Memo Completed:	**July, 27, 1998**

Indication: For use in combination with flutamide for the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostate. Treatment with Zoladex® and flutamide should start 8 weeks prior radiation therapy and continue during radiation therapy.

Background: Zeneca received approval for Zoladex 3.6 mg (Dec. 1989) and 10.8 mg (Jan. 1996) for the palliative treatment of advanced prostate cancer. In June 1996, Schering Corporation received approval of a supplemental NDA for Eulexin (flutamide) Capsules for the use of flutamide in combination with "LHRH agonists" for treatment of stage B2-c carcinoma of the prostate in combination with radiotherapy as described above.

The study that supported Schering's supplement was conducted by the Radiation Therapy Oncology Group (RTOG). The protocol, RTOG 8610, was titled, Phase 3 study of ZOLADEX® and FLUTAMIDE (EULEXIN®) Used as Cytoreductive Agents in Locally Advanced Carcinoma of the Prostate Treated with Definitive Radiotherapy. In May 1997 Zeneca met with the Division to discuss the plans for submission of a supplemental NDA for Zoladex in combination with an antiandrogen for the indication approved for flutamide in June of 1996. The Division agreed to review the application accompanied by a literature publication of RTOG, containing more mature data than that in the Schering supplement.

Conclusion: Three major revisions of the proposed label were suggested and accepted by the sponsor. The first was that the indication would state that Zoladex® would be used in combination with flutamide not Casodex as originally proposed by the sponsor. The second was that the clinical data used would be the same as that found in the Eulexin

data not the more mature data found in the submitted literature. The third suggestion was that the adverse reactions could not be assigned to specific drugs (e.g., "flutamide toxicity").

This NDA supports the approval of Zoladex in combination with flutamide for the indication mentioned above because the identical data has been reviewed for the Eulexin® supplement and the combination has been found safe and effective.

/S/

Daniel A. Shames MD,
Team Leader (Actg.), HFD-580
CC/
NDA 19-726
NDA-20-578
M. Hirsch
M. Mann MM 7/13/98
L. Rarick
A. Dunson

DUNSON

NDA 19-726 SE1-024
NDA 20-578 SE1-003

Received: August 12, 1997
MOR complete: June 19, 1998

Medical Officer's Memorandum

Sponsor: Zeneca Pharmaceuticals, Inc.
Drug: Zoladex® (goserelin acetate implant)
Dosage: 3.6 mg Depot and 10.8 mg Depot
Route of Administration: subcutaneous injection

The following labeling comments regarding these 2 supplemental new drug applications should be conveyed to the sponsor by telefacsimile.

1. Regarding your proposed new indication:

Zoladex® was studied for use in combination with flutamide for this indication, but was not studied for this use in combination with Casodex®. Therefore, the new indication should be revised to reflect the actual drug combination studied, and the reference to Casodex® should be removed.

We will be consistent in our approach to the EULEXIN® label.

2. Regarding the Clinical Studies section of your label.

The results of RTOG 8610, as presented in the package insert for EULEXIN®, are clearly different than those in your proposed Clinical Studies section. The reasons for these differences relate to re-analysis of more mature RTOG data by Pilepich et al. This "new" data will present several clinical, analytic and regulatory issues. At this time, we recommend that you revise your proposed Clinical Studies section (specifically, the data from RTOG 8610) to mirror the data presented in the current EULEXIN® label.

3. Regarding the Adverse Reactions section of your label.

It is not acceptable to assign specific adverse reactions to individual drugs used in combination. Therefore, the reference to should be removed.

In addition, your label should present the most frequently reported adverse experiences reported during the clinical trial for treated patients (hormonal therapy + radiation) and control patients (radiation alone). We recommend that the presentation of this data mirror the current EULEXIN® label.

/S/
Mark S. Hirsch, MD
Medical Officer
DRUDP

concur – MSH MD

cc Orig NDA 19-726/Orig NDA 20-578
HFD-580 Division File
HFD-580/LRarick/MMann/DShames/ADunson

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Safety Update Review

Included in Medical Officer review dated 7/15/98.

Zeneca Pharmaceuticals
A Business Unit of Zeneca Inc.
1800 Concord Pike
Wilmington, DE 19850-5437

ZOLADEX® (goserelin acetate implant) 3-Month Depot 10.8 mg
NDA 20-578

ITEM 13: Pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act, the information following below is made of record.

PATENT INFORMATION ON ANY PATENT WHICH CLAIMS THE DRUG OR A METHOD OF USING THE DRUG

Certification

Pursuant to 21 CFR Section 314.53(d)(ii), Zeneca Limited, through its agent Zeneca Pharmaceuticals, A Business Unit of Zeneca Inc., certifies that US Patent No. 4,100,274; US Patent No. 4,767,628; and US Patent No. 5,366,734, information relative to each of which has been submitted previously, claim the formulation, composition and/or method of use of ZOLADEX® (goserelin acetate implant) 3-Month Depot 10.8 mg which is the subject of this supplemental new drug application.

/S/

RUTH H. NEWTSON
CHIEF IP COUNSEL
PHARMACEUTICALS

acr

August 7, 1997

TO WHOM IT MAY CONCERN:

Re: RTOG 86-10

In response to the requirements of the Generic Drug Enforcement Act of 1992, I hereby certify on behalf of the American College of Radiology (for the Radiation Therapy Oncology Group), that we did not and will not use in connection with this application, the services of any person in any capacity debarred under section 306 (a) or (b).

Thomas M. Caldwell

Thomas M. Caldwell
Senior Director, Philadelphia Office

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

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

NDAs: 19-726/S-024 and 20-578/S-003 Circle one: SE1

HFD 580 Trade and generic names/dosage form: Zoladex (goserelin acetate) Action: AP AE NA

Applicant Zeneca Pharmaceuticals, Inc. Therapeutic Class 3S

Indication(s) previously approved: Prostate Cancer, Endometriosis, Endometrial Thinning, Breast Cancer.
Pediatric information in labeling of approved indication(s) is NOT APPLICABLE.

Proposed indication in this application is to add the following paragraph to the previously approved label "ZOLADEX is indicated for use in combination with flutamide for the management of locally confined-State T2b-T4 (Stage B2-C) carcinoma of the prostate. Treatment with ZOLADEX and flutamide should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy."

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.
IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? ___Yes (Continue with questions) X No (Sign and return the form)

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

__Neonates (Birth-1month) __Infants (1month-2yrs) __Children (2-12yrs) __Adolecents(12-16yrs)

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

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

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

- ___ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
- ___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.
- ___ c. The applicant has committed to doing such studies as will be required.
  - ___ (1) Studies are ongoing,
  - ___ (2) Protocols were submitted and approved.
  - ___ (3) Protocols were submitted and are under review.
  - ___ (4) If no protocol has been submitted, attach memo describing status of discussions.
- ___ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

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

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

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? ___ Yes X No
ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from the Medical Reviewer.

/S/ / Project Manager
Signature of Preparer and Title

7/24/98
Date

cc: Orig NDA19-726
HFD-580/Div File
NDA/Action Package
HFD-006/ KRoberts

(revised 10/20/97)

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

EXCLUSIVITY SUMMARY FOR NDA # 19-726 SUPPL # 024 JUL 27 1998

Trade Name: Zoladex Generic Name: goserelin acetate

Applicant Name: Zeneca Pharmaceuticals Inc. HFD # 580

Approval Date If Known:_____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it an original NDA?
YES/___/ NO /_X_/

b) Is it an effectiveness supplement?
YES /_X_/ NO /__/
If yes, what type? (SE1, SE2, etc.) SE1

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

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

_____

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

_____

Form OGD-011347 Revised 8/27/97
cc: Original NDA Division File HFD-93 Mary Ann Holovac

d) Did the applicant request exclusivity?

YES /___/ NO /X/

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

_____

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

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

YES /X/ NO /___/

YES /X/ NO /___/

If yes, NDA #19-726. Drug Name Zoladex (goserelin acetate).

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

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

YES /___/ NO /___/

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

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

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

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

2. Combination product.

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

YES /___/ NO /___/

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

NDA# _____ _____

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

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

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

YES /___/ NO /___/

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

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

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

YES /___/ NO /___/

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

_____

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

YES /___/ NO /___/

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

YES /___/ NO /___/

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

YES /___/ NO /___/

If yes, explain:

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

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

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

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

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

_____ _____

_____ _____

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

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

_____ _____

_____ _____

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

_____ _____

_____ _____

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

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

Investigation #1

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

Investigation #2

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

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

Investigation #1

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

_____ _____

_____ _____

Investigation #2

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

_____ _____

_____ _____

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

YES /___/ NO /___/

If yes, explain: _____

_____

Signature: /S/
Date: 7/24/98
Title: Project Manager

Signature of Office/Division Director
Signature: M Mathur for L Rarick
Date: 7/27/98

cc: Original NDA Division File HFD-93 Mary Ann Holovac
Previous Page

EXCLUSIVITY SUMMARY FOR NDA # 20-578 SUPPL # 003 JUL 27 1998

Trade Name: Zoladex Generic Name: goserelin acetate

Applicant Name: Zeneca Pharmaceuticals Inc. HFD # 580

Approval Date If Known:

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it an original NDA?
YES/___/ NO /_X_/

b) Is it an effectiveness supplement?
YES /_X__/ NO /__/
If yes, what type? (SE1, SE2, etc.) SE1__

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

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

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

---

d) Did the applicant request exclusivity?

YES /___/ NO /X/

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

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

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

YES /X/ NO /___/

YES /X/ NO /___/

If yes, NDA #20-578. Drug Name Zoladex (goserelin acetate).

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

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

YES /___/ NO /___/

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

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

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

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

2. Combination product.

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

YES /___/ NO /___/

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

NDA# _____ _____

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

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

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

YES /___/ NO /___/

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

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

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

YES /___/ NO /___/

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

_____

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

YES /___/ NO /___/

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

YES /___/ NO /___/

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

YES /___/ NO /___/

If yes, explain:

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

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

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

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

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

_____ _____

_____ _____

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

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

_____ _____

_____ _____

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

_____ _____

_____ _____

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

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

Investigation #1

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

Investigation #2

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

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

Investigation #1

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

_____ _____

_____ _____

Investigation #2

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

_____ _____

_____ _____

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

YES /___/ NO /___/

If yes, explain: _____

_____

Signature: /S/
Date: 7/24/98
Title: Project Manager

Signature of Office/Division Director
Signature: for L Rarick
Date: 7/24/98

cc: Original NDA Division File HFD-93 Mary Ann Holovac
Previous Page

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Advisory Committee Meeting Minutes

These applications were not the subject of an Advisory Committee Meeting.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Federal Register Notices

These applications were not the subject of any Federal Register Notices.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Advertising Material

No advertising material has been submitted.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Statistical Review

No statistical review is required.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Pharmacology Review

No pharmacology review is required.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

Chemistry Review

No chemistry review is required.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

EER

There were no manufacturing changes - no EER is required.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
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Microbiology Review

No microbiology review is required.

NDA 19-726/S-024, Zoladex (goserelin acetate implant), 3.6 mg
NDA 20-578/S-003, Zoladex (goserelin acetate implant), 10.8 mg

DSI Audit of Clinical Studies

No clinical sites were audited for these supplements.