DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-320

Praecis Pharmaceuticals, Incorporated
Attention: J.D. Bernardy, J.D.
Vice President, Regulatory Affairs & Quality Assurance
830 Winter Street
Waltham, MA 02451-1420

Dear Mr. Bernardy:

Please refer to your new drug application (NDA) dated December 11, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Plenaxis™ (abarelix for injectable suspension, 100mg).

We acknowledge receipt of your submissions dated January 5; March 13, 14, 15, 26, 27, 29, and 30; April 6, 9, 10, 13, 17, 19, 26, and 27(2); May 4, 7, 10, 22, 24, 25(2), and 29; June 14 and 15; and July 26, 2001; February 25, March 19 and 20; April 25(2); May 8 and 16(2); June 3, 5, 17, 19, 25, 27, and 30; July 9, 11, 14, 16, 17, 18, 29, and 31; August 8; September 10, 12, 17, 24, and 29; October 3, 14, 20, 24, and 30(2); and November 3, 4, 7, 11, 13, 16, 17, 18(2), 19, 21(2), and 24, 2003.

The February 25, 2003 submission constituted a complete response to our Not Approvable letter of June 11, 2001. The original submission was not approved because of the risk of serious allergic reactions, including anaphylaxis with hypotension and syncope, and because the risk of loss of efficacy over time. For your then proposed target population of men with local, regional, or advanced carcinoma of the prostate where androgen suppression is appropriate, the Agency determined that risks of Plenaxis™ exceeded its benefits.

This resubmission of the application provides for the use of Plenaxis™ (abarelix for injectable suspension, 100mg) for the palliative treatment of men with advanced symptomatic prostate cancer, in whom LHRH agonist therapy is not appropriate and who refuse surgical castration, and have one or more of the following: (1) risk of neurological compromise due to metastases, (2) ureteral or bladder outlet obstruction due to local encroachment or metastatic disease, or (3) severe bone pain from skeletal metastases persisting on narcotic analgesia.

The resubmitted application, considered for approval under 21 CFR Part 314, Subpart H at your request, narrows the originally proposed indication to use of the drug in a population for whom the benefits of the drug may outweigh the risks, but in whom the drug can be safely used only if distribution and/or use is restricted. The application provides for a risk management program that will help ensure the safe use of Plenaxis™ in the approved indicated population.

We completed our review of this application, as amended, and have concluded that adequate information has been presented to approve this application for Plenaxis™ (abarelix for injectable suspension, 100mg) under 21 CFR Part 314 Subpart H for the proposed indication in your resubmission. You have indicated your agreement with approval with restrictions to ensure safe use. Accordingly, this application is approved under 21 CFR Part 314, Subpart H. Approval is effective on the date of this letter. Marketing of this drug product and related activities are to be accordance with applicable provisions of the Act and FDA regulations, including the specific restrictions on distribution and use described below.

Plenaxis™ Risk Management Program

We remind you that your Plenaxis™ Risk Management Program is an important part of postmarketing risk management for Plenaxis™, and must include each of the following components in order to ensure distribution only to physicians with the training and experience necessary to assure safe use of the drug, and to ensure use of Plenaxis™ only in patients for whom the drug is indicated, as set forth in the INDICATIONS AND USAGE section of the FDA-approved labeling:

1. Enrollment of qualified physicians in a physician prescribing program that ensures that Plenaxis™ is distributed only to these enrolled physicians and that the use of Plenaxis™ is in the approved indicated population.
2. Implementation of a program to educate physicians, hospital pharmacists, patients, and distributors about the risks and benefits of Plenaxis™ and responsibilities of being part of the prescribing program.
3. Implementation of a reporting and collection system for serious adverse events associated with the use of Plenaxis™ that complies with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).
4. Implementation of a plan to evaluate the effectiveness of the Plenaxis™ Risk Management Program.

The Plenaxis™ Risk Management Program, as described in the attached documents, adequately addresses each of these requirements. Any change to the program must be discussed with the FDA prior to its institution and is subject to FDA approval. We expect your continued cooperation to resolve any problems regarding the Plenaxis™ Risk Management Program that may be identified following approval of your application.

Within the first year of the initiation of the Risk Management Program, and annually thereafter, you must provide the FDA with a report under 21 CFR 314.80(b)(2) that describes how each element of the program has been implemented, provides implementation data, and evaluates the success of the program using, among other available data, the studies, audits, and evaluations described in the Plenaxis™ Risk Management Program and postmarketing commitments #1, 2, 3, and 4 below.

We remind you of your specific reporting obligations regarding adverse events of patients who have received Plenaxis™. As set forth in the attached document, in addition to the usual postmarketing reporting of adverse drug experiences (21 CFR 314.80(c)), you will initiate a 15-day report for each of the following:

1. All spontaneous reports of anaphylaxis, anaphylactic reaction, anaphylactoid reaction, anaphylactic shock, angioedema of the throat, angioedema of the tongue, laryngeal obstruction,

laryngeal angioedema, upper respiratory tract obstruction, systemic allergic reaction, immediate hypersensitivity reaction, acute bronchospasm, or wheezing.
2. All spontaneous reports of syncope, near-syncope, loss of consciousness, shock, or hypotension.
3. All spontaneous reports involving treatment with epinephrine, parenteral antihistamine, inhaled bronchodilators, parenteral corticosteroids, intubation, tracheostomy, or cricothyroidotomy.
4. All spontaneous reports of hospitalizations or emergency room visits for urticaria or angioedema.
5. All spontaneous reports of death, regardless of causality.

Postmarketing Commitments

You have committed to conduct the postmarketing studies, specified in your submission dated November 21, 2003 that are listed below:

1. Conduct studies of a random sample of all enrolled prescribers as part of your risk management evaluation program to survey physician knowledge and understanding of risks and benefits of Plenaxis™ and responsibilities under the prescribing program. Praecis Pharmaceuticals Incorporated and FDA will review the study findings and agree to educational and/or other activities that may be needed to address observations.

Protocol Submission:	by February 27, 2004
Study Start:	by September 30, 2004
Final Report Submission:	by September 30, 2008

2. Conduct a study ancillary to the 2000 patient "Plenaxis™ Experience Study" (see commitment #5) as part of the risk management evaluation program to evaluate use of Plenaxis™ by physicians in the approved, indicated population. Provide an assessment of the frequency of signed Patient Information signature pages filed in the patient's medical record, frequency of serum testosterone testing, and other physician responsibilities accepted as part of the Plenaxis™ Prescribing Program. Praecis Pharmaceuticals Incorporated and FDA will review study findings and agree to educational and/or other activities that may be needed to address observations.

Protocol Submission:	by January 30, 2004
Study Start:	by June 30, 2004
Final Report Submission:	by September 30, 2008

3. Conduct a study involving use of Plenaxis™ through a case claims survey performed by a managed care organization. The survey will provide an assessment of whether Plenaxis™ is being used in the indicated population (e.g., review of formulary restrictions and patient information concerning age, sex, and diagnosis). Praecis Pharmaceuticals Incorporated and FDA will review study findings and agree to educational and/or other activities that may be needed to address observations.

Protocol Submission:	by February 27, 2004
Study Start:	by September 30, 2004
Final Report Submission:	by September 30, 2008

4. Conduct a study as part of the risk management evaluation program to evaluate adherence to attested responsibilities of the prescribing program for hospital pharmacies. Praecis

Pharmaceuticals Incorporated and FDA will review study findings and agree to educational and/or other activities that may be needed to address observations.

Protocol Submission:	by February 27, 2004
Study Start:	by September 30, 2004
Final Report Submission:	by September 30, 2008

5. Conduct a study of 2,000 patients to estimate the incidence of immediate-onset systemic allergic reactions (anaphylaxis, hypotension and/or syncope) in the indicated population receiving Plenaxis™ and to determine whether the hazard rate changes over time.

Protocol Submission:	by January 30, 2004
Study Start:	by June 30, 2004
Final Report Submission:	by September 30, 2008

6. Conduct a clinical study to characterize Plenaxis™-induced immediate-onset system allergic reactions by evaluating skin test reactivity to Plenaxis™ and determining anti-abarelix IgG and IgE antibody levels for patients experiencing immediate-onset systemic allergic reactions.

Protocol Submission:	by January 30, 2004
Study Start:	by June 30, 2004
Final Report Submission:	by September 30, 2008

7. Conduct a clinical study to assess the effectiveness of pre-treatment with oral antihistamine with or without oral steroids for patients who experience Plenaxis™-induced urticaria and/or pruritis within 2 hours of drug administration and continue Plenaxis™ therapy.

Protocol Submission:	by January 30, 2004
Study Start:	by June 30, 2004
Final Report Submission:	by September 30, 2008

Submit your clinical study protocols to your IND for this product. We encourage you to submit your study protocols to the Division of Reproductive and Urologic Drug Products for review and comment prior to the initiation of your postmarketing studies. Submit nonclinical protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

The final printed labeling (FPL) must be identical to the enclosed agreed upon labeling text submitted on November 24, 2003, for the Product Information insert, the Patient Information form, and the Physician Attestation form; and identical to the immediate container and carton labels submitted on November 24, 2003. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15

of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-320**." Approval of this submission by FDA is not required before the labeling is used.

Under 21 CFR 314.550, after the initial 120 day period following approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Reproductive and Urologic Drug Products and two copies of both the promotional materials and labeling directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Florence Houn, MD MPH
Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures

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

/s/

Florence Houn

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