PRAECIS

April 16, 2004

Steve E. Phurrough, MD, MPA
Office of Clinical Standards & Quality
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Mail Stop C1-09-06
Baltimore, MD 21244-1850

Dear Dr. Phurrough:

This is a formal request for a national coverage determination ("NCD") on the use of Plenaxis™ (abarelix for injectable suspension) under the Medicare program. This request is being made pursuant to NCD development Track #1 – Requests for New National Coverage Determinations Initiated by Any Party, Including Beneficiaries, Manufacturers, Providers, or Suppliers. We believe that Plenaxis meets the qualifications for coverage in the Medicare benefit category of "drugs or biologicals," as defined under § 1861(t)(1) of the Social Security Act.

Plenaxis (abarelix for injectable suspension) is a synthetic decapeptide with potent antagonistic activity against naturally occurring gonadotropin releasing-hormones (GnRH). It is the only GnRH antagonist ever to have been approved by the Food and Drug Administration ("FDA") as a treatment for prostate cancer. Specifically, Plenaxis was first approved by FDA on November 25, 2003 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. On March 31, 2004, Plenaxis was approved for inclusion in the United States Pharmacopeia Drug Information.®

Enclosed you will find three copies of a two compact disc ("CD") set containing the supporting documentation for this NCD request. The first folder on each disc contains an index or "Read Me" file identifying the specific documents contained therein. Disc #1 includes all non-proprietary documentation and information. Disc #2 includes all confidential and proprietary data referenced in the supporting documentation. It is the understanding of PRAECIS PHARMACEUTICALS INCORPORATED that the information provided as part of this request that has been identified as "proprietary data" or "privileged information" must be kept confidential by CMS, pursuant to 42 C.F.R. § 426.110 and the accompanying commentary at 68 Fed. Reg. 63692, 63702 (Nov. 7, 2003).

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Please do not hesitate to contact me should you have any questions about this request. Thank you for your assistance with this matter.

Sincerely,

Marcia C. Morris, JD, MPA
Executive Director, Corporate and
Government Affairs

cc: Sean Tunis, MD, Director & Chief Clinical Officer
Office of Clinical Standards & Quality

# Rationale and Proposed Language for a National Coverage Determination (NCD) for Plenaxis™

## I. Rationale for a National Coverage Determination (NCD) for Plenaxis™

Plenaxis™ is a drug for advanced symptomatic prostate cancer in patients who have no alternative, approved medical therapy. It is indicated for the treatment of men with symptoms (actual or impending) that are associated with advanced prostate cancer. Patients with these symptoms are a risk of experiencing clinical flare if treated with currently available hormonal therapies. Use of other hormonal therapies is inappropriate in these patients and their labels, accordingly, contain specific warnings and/or contraindications.

Approximately 220,000 patients are diagnosed each year in the United States with prostate cancer. Nearly 70 percent are aged 65 years or older and are, thus, eligible for Medicare coverage. Praecis commissioned The Lewin Group to conduct certain limited analyses of Medicare SAF database for 1995-2000 to determine, among other data points, the percentage of prostate cancer patients treated with hormonal therapy that were symptomatic and therefore potential candidates for Plenaxis™.

Their analysis found that approximately 13.6% of prostate cancer patients indicated for hormonal therapy were coded in a manner that reflected the existence of at least one of the symptoms described in the Plenaxis™ indication. (Data collected indicated that approximately 1,200 patients in the Medicare population per year during this period were treated with bilateral orchiectomy.) Of those patients indicated for hormonal therapy, approximately 9.6% were diagnosed as having Plenaxis™ -indicated symptoms prior to initiation of therapy, and approximately 4.2% were identified as having become symptomatic within 2 to 3 weeks of initiation of hormone therapy. In the case of the latter, it is presumed that those patients were under-diagnosed and suffered a clinical flare event as a result of an LHRH agonist-induced testosterone surge.

Based on this analysis, extrapolations of published data and certain Praecis-funded research, Praecis estimates that the number of symptomatic patients diagnosed in the US each year ranges from 13,000 to 25,000. The FDA's estimate is consistent with this estimate. In its FDA Talk Paper T03-82 dated November 25, 2003 the FDA stated that "about 5-10% of men with prostate cancer have the type of advanced, symptomatic disease that would make them candidates for Plenaxis™."

There is a significant unmet need among this small subset of patients with advanced symptomatic prostate cancer who are not appropriate for LHRH agonist therapy and who refuse surgical castration. Plenaxis™ is the only FDA approved medical alternative for these patients. As described in the "Overview of Plenaxis™" paper on CD #1, *Plenaxis™ NCD Request: Non-proprietary Information*, improved health outcomes in Medicare-age patients have been demonstrated in numerous clinical trials. It is,

therefore, "reasonable and necessary" for the treatment of a very serious illness, and should be covered by the Medicare program.

By granting coverage through an NCD, CMS will speed the uptake of this very important therapy to patients who may otherwise be deprived of its use if the more time- and resource-consuming process of seeking coverage from each of the individual Medicare carriers and fiscal intermediaries. The process of achieving local coverage determinations across the US is not only inherently longer, but also poses a substantial risk of inconsistent determinations based on confusion with LHRH agonists, which have been the subject of materially differing coverage determinations made piecemeal over the course of years.

In addition, the NCD process should result in the issuance of codes in a far more expeditious manner. It is Praecis' experience, having launched Plenaxis™ starting in February 2004, that providers are restricting their investment in all hormonal therapies based on the uncertainty of reimbursement levels under the Medicare Prescription Drug, Improvement, and Modernization Act ("MMA") enacted in December 2003. That concern is escalated for a new hormonal therapy for which there is no statement of coverage or guarantee of reimbursement.

Providers have positioned themselves to prescribe Plenaxis™ by filing the requisite Physician Attestation pursuant to the PLUS (risk management) program, and establishing new accounts if they have none with any of the four distributors who will be allowed to distribute Plenaxis™ in the US pursuant to the PLUS program. However, many of these providers are waiting for a clear and formal coverage determination and designation of the correct code for reporting Plenaxis™ before delivering the drug to their patients.

Coverage by an NCD will also help to alleviate concerns that the risk management program agreed upon by Praecis with the FDA will be disregarded by providers and that uncontrolled off label use of Plenaxis™ will result. By clarifying coverage and non-coverage as suggested in this request, off label use not conforming to the risk management plan can be checked. Without an NCD, uneven, inconsistent and inappropriate coverage is almost certain to occur.

**II. Proposal Language for a National Coverage Determination (NCD) for Plenaxis™**

We propose the following language for a national coverage determination (NCD) for Plenaxis™:

> "Abarelix is a synthetic decapeptide with potent antagonistic activity against naturally occurring gonadotropin releasing-hormone (GnRH). Abarelix inhibits gonadotropin and related androgen production by directly and competitively blocking GnRH receptors in the pituitary. Abarelix exerts its pharmacological action by directly suppressing luteinizing hormone (LH) and follicle stimulating hormone (FSH) secretion and thereby reducing the secretion of testosterone by the testes. Due to the direct inhibition of the secretion of LH by abarelix, there is

no initial increase in serum testosterone concentrations as there is with luteinizing hormone-releasing hormone (LHRH) agonists. Abarelix is administered intramuscularly to the buttock.

Abarelix was first approved by the Food and Drug Administration (FDA) on November 25, 2003 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. Abarelix subsequently was approved for inclusion in the United States Pharmacopoeia on March 31, 2004, thereby meeting Medicare's definition of a drug as defined under §1861(t)(1) of the Social Security Act.

Effective October 1, 2004, Abarelix is covered only when it is used:

- For an FDA approved indication specified on the labeling;
- For an indication that is included (or approved for inclusion) in the United States Pharmacopeia Drug Information (USPDI) or the American Hospital Formulary Service–Drug Information (AHFS-DI);
- For an indication approved by a Medicare contractor in accordance with instructions on "Unlabeled Use for Anti-Cancer Drugs" in Section 50.4.5 of Chapter 15 of the Medicare Benefit Policy Manual (CMS Publication 100-2);
- In a clinical trial that is intended to establish the safety and effectiveness of abarelix for a potential new FDA approved indication; or,
- In a pragmatic clinical trial or practical clinical trial (PCT) that compares abarelix to clinically relevant alternative interventions such as LHRH agonists, includes a diverse population of study participants, recruits participants from a variety of practice settings, and collects data on a broad range of health outcomes.

All uses of abarelix other than those specified above are non-covered."

The first three indications are consistent with Medicare's current instructions for its contractors regarding coverage of drugs. A notable difference is that no other off-label uses are permitted with the exception of the final two indications which are intended to make the drug available to Medicare beneficiaries who participate in selected clinical trials. Coverage of Plenaxis™ during these trials will allow important new data to be collected in a controlled fashion that is not possible under the current process which permits haphazard coverage of off-label uses. Examples of the clinical trails that are underway or in the planning stages are described on CD #2, *Plenaxis™ NCD Request: Proprietary Information*