DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

JD Bernardy, J.D.
Vice President, Regulatory Affairs
Praecis Pharmaceuticals Incorporated
One Hampshire Street
Cambridge, MA 02139

RE: Plenaxis™ (abarelix for injectable suspension)
NDA [redacted]
MACMIS ID#9856

Dear Mr. Bernardy:

This letter concerns Praecis Pharmaceuticals Incorporated's (Praecis) dissemination of a journal advertisement for its investigational new drug, Plenaxis (abarelix for injectable suspension). The advertisement is titled "New Thinking in Prostate Cancer: #1 in a series. Surge and flare: is there really a difference?" The advertisement appears in the March 2001 issue, of *The Journal of Urology*. As part of its monitoring program, the Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed this advertisement and has concluded that it is false or misleading, in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Our specific objections follow.

Your advertisement is in violation of the Act because it implies that your investigational drug is superior to other available treatment options for prostate cancer. For example, your advertisement presents that "surge" is "an acute biochemical (PSA) or hormonal (T, LH, FSH) increase after LHRH agonist initiation" and that "clinical flare" is "a clinical worsening of symptoms due to LHRH agonist-inducted T surge." Your advertisement also includes the claim "Despite the drawbacks of testosterone (T) exposure on hormonally sensitive prostate cancer, the past decade of LHRH agonist use has resulted in a general acceptance of T surge when initiating therapy." The advertisement concludes "Ultimately, T surge can cause unnecessary risks to some patients. There are options to help guard against the potential effects of T surge, but the question remains: why not avoid it altogether?" This statement is followed by the claim "Amgen Praecis-changing the future of prostate cancer therapy." These statements, following the differences between surge and clinical flare, suggest that Praecis is developing a new product for prostate cancer that is not an LHRH agonist, and that this product avoids testosterone surge and its consequences. Therefore, this presentation suggests that Praecis' new product will be superior to and safer than LHRH agonists.

The regulations state that an investigational new drug may not be promoted as being safe and effective for the uses under investigation. Your advertisement is violative because it includes promotional claims of efficacy and safety for a particular drug that is under investigation for use in the specific therapeutic area.

Requested Action

Praecis should immediately discontinue these and all other promotional materials for Plenaxis that contain the same or similar claims or presentations. We request that Praecis respond, in writing, with its intent to comply with the above. DDMAC should receive your written response no later than April 9, 2001. This response should list all similarly violative materials with a description of the method for discontinuation and the discontinuation date.

If you have any questions or comments, please contact me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #9856 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Barbara S. Chong, Pharm.D., BCPS
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

/s/

Barbara Chong
3/26/01 01:33:57 PM

New **Thinking** in Prostate Cancer: #1 in a series

"Surge and flare: is there really a difference?"

Despite the drawbacks of testosterone (T) exposure on hormonally sensitive prostate cancer, the past decade of LHRH agonist use has resulted in a general acceptance of T surge when initiating therapy.[1] This may have contributed to confusion over how we can define surge and clinical flare.

In the treatment of prostate cancer, there is a difference between surge and clinical flare.

A difference, by definition

Surge

- An acute biochemical (PSA) or hormonal (T, LH, FSH) increase after LHRH agonist initiation[1-3]
- Results from upregulation of GnRH receptors[3]

Clinical flare

- A clinical worsening of symptoms due to LHRH agonist-induced T surge[1,4]

A difference, in whom it affects

Surge

- Affects recipients of LHRH agonist therapy[1]

Reported cases of clinical flare

- Occur in 4% to 33% of patients*[1] and up to 63% of advanced-stage patients (n=19)[5]

A difference, in consequences

Surge

- May cause clinical "flare"[1]

Clinical flare may include

- Acute manifestations, such as voiding symptoms[1]
- Late-stage manifestations, such as skeletal pain, spinal cord compression, uremia, paralysis, or, in isolated instances, death[1,4,6]

*This variance is due mainly to the confusion about the definition of the flare phenomenon.[1]

Ultimately, T surge can cause unnecessary risks to some patients. There are options to help guard against the potential effects of T surge,[4] but the question remains: why not avoid it altogether?

AMGEN PRAECIS

Changing the Future of Prostate Cancer Therapy

References: 1. Mahler C. Is disease flare a problem? *Cancer.* 1993;72:3799-3802. 2. Agarwal DK, Costello AJ, Peters J, Sikaris K, Crowe H. Differential response of prostate specific antigen to testosterone surge after luteinizing hormone-releasing hormone analogue in prostate cancer and benign prostatic hyperplasia. *BJU Int.* 2000;85:690-695. 3. Bhasin S, Berman N, Swerdloff RS. Follicle-stimulating hormone (FSH) escape during chronic gonadotropin-releasing hormone (GnRH) agonist and testosterone treatment. *J Androl.* 1994;15:386-391. 4. Thompson IM, Zeidman EJ, Rodriguez FR. Sudden death due to disease flare with luteinizing hormone-releasing hormone agonist therapy for carcinoma of the prostate. *J Urol.* 1990;144:1479-1480. 5. Kuhn J, Billeraud T, Navratil H, et al. Prevention of the transient adverse effects of a gonadotropin-releasing hormone analogue (buserelin) in metastatic prostatic carcinoma by administration of an antiandrogen (nilutamide). *N Engl J Med.* 1989;321:413-418. 6. Shimizu TS, Shibata Y, Jinbo H, Satoh J, Yamanaka H. Estramustine phosphate for preventing flare-up in luteinizing hormone-releasing hormone analogue depot therapy. *Eur Urol.* 1995;27:192-195.

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