CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-807

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-807

Savient Pharmaceuticals, Inc.
One Tower Center Blvd., 14th floor
East Brunswick, NJ 08816

Attention: Murad Husain
Vice President, Regulatory Affairs

Dear Mr. Husain:

Please refer to your new drug application (NDA) dated December 23, 2004, received January 12, 2005, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Soltamox™ (tamoxifen citrate) Oral Solution 10mg/5mL.

We acknowledge receipt of your submissions dated December 29, 2004, January 7, February 3, April 30, May 5, June 7 and 15, July 21, and August 1, 12, and 25, 2005.

This new drug application provides for the use of Soltamox™ (tamoxifen citrate) Oral Solution for the following indications:

- **Metastatic Breast Cancer:** Tamoxifen citrate is effective in the treatment of metastatic breast cancer in women and men. In premenopausal women with metastatic breast cancer, tamoxifen citrate is an alternative to oophorectomy or ovarian irradiation. Available evidence indicates that patients whose tumors are estrogen receptor positive are more likely to benefit from tamoxifen citrate therapy.

- **Adjuvant Treatment of Breast Cancer:** Tamoxifen citrate is indicated for the treatment of node-positive breast cancer in postmenopausal women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation. In some tamoxifen citrate adjuvant studies, most of the benefit to date has been in the subgroup with four or more positive axillary nodes.

  Tamoxifen citrate is indicated for the treatment of axillary node-negative breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation.

  The estrogen and progesterone receptor values may help to predict whether adjuvant tamoxifen citrate therapy is likely to be beneficial.

  Tamoxifen citrate reduces the occurrence of contralateral breast cancer in patients receiving adjuvant tamoxifen citrate therapy for breast cancer.

- **Ductal Carcinoma in Situ (DCIS):** In women with DCIS, following breast surgery and radiation, tamoxifen citrate is indicated to reduce the risk of invasive breast cancer (see **BOXED WARNING** at the beginning of the label). The decision regarding therapy with tamoxifen for the reduction in breast cancer incidence should be based upon an individual assessment of the benefits and risks of tamoxifen therapy.

  Current data from clinical trials support five years of adjuvant tamoxifen citrate therapy for patients with breast cancer.

- **Reduction in Breast Cancer Incidence in High Risk Women:** Tamoxifen citrate is indicated to reduce the incidence of breast cancer in women at high risk for breast cancer. This effect was shown in a study of 5 years planned duration with a median follow-up of 4.2 years. Twenty-five percent of the participants received drug for 5 years. The longer term effects are not known. In this study, there was no impact of tamoxifen on overall or breast cancer-related mortality (see **BOXED WARNING** at the beginning of the label).

  Tamoxifen citrate is indicated only for high-risk women. "High risk" is defined as women at least 35 years of age with a 5-year predicted risk of breast cancer $\geq$ 1.67%, as calculated by the Gail Model.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, Medication Guide, immediate container and carton labels) and must also include the Gail Model Risk Assessment Tools (CD-ROM and calculator) as submitted on July 21, 2005. Marketing the product(s) 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 21-807**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Christy Cottrell, Consumer Safety Officer, at (301) 796-1347.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.
Acting Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure