



NDA 200603/S-001

**SUPPLEMENT APPROVAL**

Sunovion Pharmaceuticals, Inc.  
Attention: Bridget Walton, MS, RAC  
Director, Regulatory Affairs  
One Bridge Plaza  
Suite 510  
Fort Lee, NJ 07024

Dear Ms. Walton:

Please refer to your supplemental new drug application dated November 9, 2010, received November 9, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Latuda (lurasidone) tablets (NDA 200603).

We acknowledge receipt of your submission dated November 9, 2010.

This “Changes Being Effected” supplemental new drug application provides for changes to the Hyperprolactinemia section (5.6). Proposed changes to the labeling are as follows:

## 5.6 Hyperprolactinemia

As with other drugs that antagonize dopamine D<sub>2</sub> receptors, LATUDA elevates prolactin levels.

Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotrophin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male patients [see *Adverse Reactions (6)*].

In short-term placebo-controlled studies, the median change from baseline to endpoint in prolactin levels for LATUDA-treated patients was (b) (4) 1.1 ng/mL and was – (b) (4) 0.6 ng/mL in the placebo-treated patients. The increase in prolactin was greater in female patients; the median change from baseline to endpoint for females was 1.5 ng/mL (b) (4) and was 1.1 ng (b) (4) mL in males. The increase in prolactin concentrations was dose-dependent (Table 5).

**Table 1: Median Change in Prolactin (ng/mL) from Baseline**

	Placebo	LATUDA 20 mg/day	LATUDA 40 mg/day	LATUDA 80 mg/day	LATUDA 120 mg/day
All Patients	-0.6 (n=430)	-1.1 (n=70)	0.3 (n=351)	1.1 (n=259)	3.3 (n=284)
Females	-1.5 (n=102)	-0.7 (n=19)	-0.9 (n=99)	2.0 (n=78)	6.7 (n=70)
Males	-0.5 (n=328)	-1.2 (n=51)	0.5 (n=252)	0.9 (n=181)	3.1 (n=214)

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text.

### **CONTENT OF LABELING**

Within 14 days from the date of this letter, please amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format that includes the changes approved in this supplemental application.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **LETTERS TO HEALTH CARE PROFESSIONALS**

If you issue a letter communicating important safety related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch  
Food and Drug Administration  
5600 Fishers Lane, Room 12B05  
Rockville, MD 20857

## **REPORTING REQUIREMENTS**

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, please email Ann Sohn, Regulatory Project Manager, at [ann.sohn@fda.hhs.gov](mailto:ann.sohn@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Thomas Laughren, M.D.  
Director  
Division of Psychiatry Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure  
Content of Labeling

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

/s/  
-----

THOMAS P LAUGHREN  
12/10/2010