DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-411/S-008

Eli Lilly and Company
Attention: David O. Clarke, Ph.D., D.A.B.T., R.A.C.
Manager, Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Clarke:

Please refer to your supplemental new drug application dated July 28, 2004, received July 29, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Strattera (atomoxetine hydrochloride) Capsules.

We acknowledge receipt of your additional submissions dated January 25, 2005, February 21, 2005, February 22, 2005, April 22, 2005, and May 20, 2005.

This supplemental new drug application provides for additional labeling information regarding Strattera's effects on growth.

We have completed our review of this application, as amended. This application 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 submitted labeling (package insert submitted via electronic mail on May 25, 2005 [provided below] and patient package insert submitted July 28, 2004).

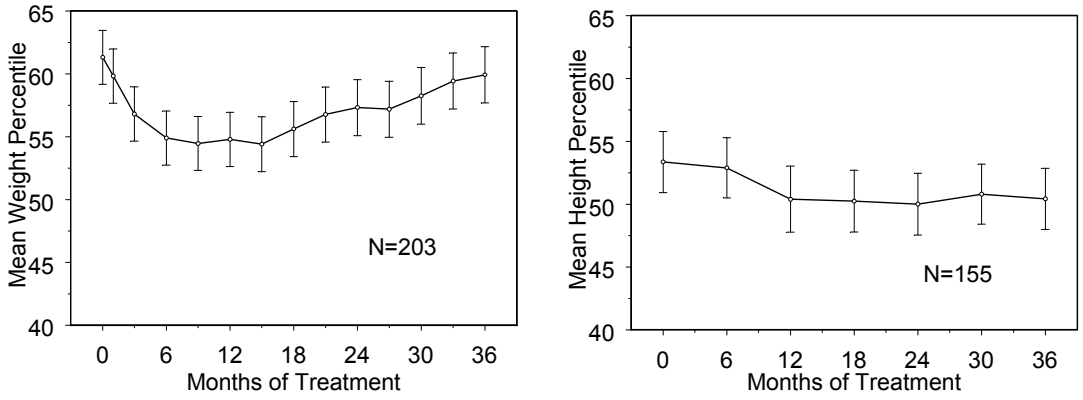
The new **Effects on Growth** sub-section in the **PRECAUTIONS** section replaces the **Growth** sub-section currently in the **WARNINGS** section of labeling.

PRECAUTIONS
General
[Please place the new **Effects on Growth** sub-section immediately after the **Effects on Urine Outflow from the Bladder** sub-section.]

> **Effects on Growth**
> Data on the long-term effects of Strattera on growth come from open-label studies, and weight and height changes are compared to normative population data. In general, the weight and height gain of pediatric patients treated with Strattera lags behind that predicted by normative population data for about the first 9-12 months of treatment. Subsequently, weight gain rebounds and at about 3 years of treatment, patients treated with Strattera have gained 17.9 kg on average, 0.5 kg more than predicted by their baseline data. After about 12 months, gain in

height stabilizes, and at 3 years, patients treated with Strattera have gained 19.4 cm on average, 0.4 cm less than predicted by their baseline data (See Figure 1 below).

Figure 1: Mean Weight and Height Percentiles Over Time for Patients With Three Years of STRATTERA Treatment



This growth pattern was generally similar regardless of pubertal status at the time of treatment initiation. Patients who were pre-pubertal at the start of treatment (girls ≤8 years old, boys ≤9 years old) gained an average of 2.1 kg and 1.2 cm less than predicted after three years. Patients who were pubertal (girls >8 to ≤13 years old, boys >9 to ≤14 years old) or late pubertal (girls >13 years old, boys >14 years old) had average weight and height gains that were close to or exceeded those predicted after three years of treatment.

Growth followed a similar pattern in both extensive and poor metabolizers (EMs, PMs). PMs treated for at least two years gained an average of 2.4 kg and 1.1 cm less than predicted, while EMs gained an average of 0.2 kg and 0.4 cm less than predicted.

In short-term controlled studies (up to 9 weeks), Strattera-treated patients lost an average of 0.4 kg and gained an average of 0.9 cm, compared to a gain of 1.5 kg and 1.1 cm in the placebo-treated patients. In a fixed dose controlled trial, 1.3%, 7.1%, 19.3%, and 29.1% of patients lost at least 3.5% of their body weight in the placebo, 0.5, 1.2, and 1.8 mg/kg/day dose groups.

Growth should be monitored during treatment with Strattera.

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 supplement NDA 21-411/S-008**." Approval of this submission by FDA is not required before the labeling is used.

Post Marketing Commitment (November 26, 2002) Fulfilled
In addition, we note that this supplemental application reports on your post marketing study commitment listed in the Division's November 26, 2002 approval letter for NDA 21-411. Your commitment is listed below:

- Conduct post marketing studies to assess long-term efficacy and effects on growth.

We have reviewed your submission and conclude that the above commitment was fulfilled.

Pediatric Research Equity Act (PREA)
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 note that you have fulfilled the pediatric study requirement for this application.

Promotional Materials
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/ the Division of Neuropharmacological Drug Products and two copies of both the promotional materials and the package insert directly to:

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

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

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Richardae Taylor, Pharm.D., Regulatory Project Manager, at (301) 594-5793.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Russell Katz
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