



NDA 19-385/S-028, S-030

Eli Lilly and Company  
Attention: Gregory T. Brophy, Ph.D.  
Director, U.S. Regulatory Affairs  
Lilly Corporate Center  
Indianapolis, Indiana 46285

Dear Dr. Brophy:

Please refer to your supplemental new drug applications dated June 15, 2000, and November 30, 2000, received June 20, 2000, and December 1, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Permax (pergolide mesylate) Tablets, 0.05, 0.25 and 1.0 mg.

The "Changes Being Effected" supplemental new drug application S-028 provides revised final printed labeling (FPL) in response to an Agency letter dated October 6, 1999. Specifically, the revisions include: 1) the addition of "L" to "L-methionine" in the DESCRIPTION section, 2) a change in terminology from "mammalian cell point mutation assay" to the current terminology "mammalian cell gene mutation assay" in the PRECAUTIONS section, 3) the deletion of the RxPak terms in the HOW SUPPLIED section, and 4) a change in the corporate signature of Athena Neurosciences at the end of the HOW SUPPLIED section of labeling.

The "Changes Being Effected" supplemental new drug application S-030 provides revised FPL that includes two new sentences in the *Information for Patients* subsection of the PRECAUTIONS section in response to an Agency letter dated April 6, 2000. These sentences read:

"Because pergolide mesylate may cause somnolence, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that pergolide mesylate therapy does not affect them adversely. Due to the possible additive sedative effects, caution should also be used when patients are taking other CNS depressants in combination with pergolide mesylate."

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert PV2279UCP, submitted on November 30, 2000). Accordingly, these supplemental applications are approved effective on the date of this letter.

However, at the next printing of the labeling, we request the implementation of the following labeling changes:

DESCRIPTION Section

The sentence, "The formula weight of the base is 314.15; 1 mg of base corresponds to 3.18: ml." should be replaced with the following:

"The empirical formula is  $C_{19}H_{26}N_2SCCH_4O_3S$ , representing a molecular weight of 410.60."

HOW SUPPLIED Section

1. The tablet description should be revised to include the tablet shape, such as:  
"Tablets (modified rectangle shaped, scored)"
2. The storage temperature statement should be revised to conform to the draft Guidance Document on stability. The storage temperature should read as follows:

**Store at 25° (77°F); excursions permitted to 15-30°C (59-86°F)**  
[See USP Controlled Room Temperature]

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21CFR 314.80 and 314.81.

If you have any questions, call Merrill Mille, Sr. Regulatory Management Officer, at (301) 594-5528.

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

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Russell Katz  
nulldate