

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-724**

**APPROVAL LETTER**



NDA 21-724

C.P. Pharmaceuticals International C.V.  
c/o Pfizer Inc.  
Attention: Jonathon M. Parker, R.Ph. M.S.  
Global Regulatory Leader, Regulatory Strategy  
Worldwide Regulatory Affairs  
2800 Plymouth Road  
Ann Arbor, Michigan 48105

Dear Mr. Parker:

Please refer to your new drug application (NDA) dated October 30, 2003, received October 31, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lyrica™ (pregabalin) 25, 50, 75, and 100, 150, 200, 225, and 300-mg capsules.

We acknowledge receipt of your additional submissions dated August 23, 2004, August 25, 2004, September 7, 2004, December 30, 2004 (2), February 22, 2005, March 11, 2005, March 18, 2005, March 31, 2005, April 11, 2005, April 19, 2005, May 5, 2005, and June 9, 2005.

Your April 11, 2005, submission constituted a complete response to our August 31, 2004 action letter.

This new drug application provides for the use of Lyrica™ (pregabalin) 25, 50, 75, and 100, 150, 200, 225, and 300-mg capsules as adjunctive therapy for adult patients with partial onset seizures.

We have completed our review of this application, as amended, 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 enclosed, agreed-upon labeling text. Accordingly, this application is approved, effective on the date of this letter.

### **Labeling**

The final printed labeling (FPL) must be identical to the enclosed approved labeling text (text for the package insert, text for the patient package insert). Marketing the product 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 21-724.” Approval of this submission by FDA is not required before the labeling is used.

### **Scheduling**

As you know, the final scheduling of this product under the Controlled Substances Act is currently proceeding, but not yet complete as of the date of this letter. We note your commitment of December 30, 2004 (reaffirmed on June 9, 2005) not to market this drug until the scheduling is finalized. We further note that, when finalized, appropriate revisions will be made to the package insert, the patient-package insert, and the product labeling through supplementation of your NDA. These revisions would include the statements detailing the scheduling of Lyrica in the labeling, as required under 21 CFR 201.57(h)(1).

### **Postmarketing Study Commitments**

We remind you of your additional postmarketing study commitments described in your submission dated June 9, 2005. These commitments are listed below.

1. Complete an adequate and well-controlled clinical study or studies to better assess the ophthalmologic effects of pregabalin.\*

Protocol Submission: by 08/05  
Study Start: by 07/06  
Final Report Submission: by 01/09

[\* This commitment has already been accepted for NDA 21-446 on December 30, 2004.]

2. Conduct an adequate and well-controlled clinical study of male reproductive function to confirm lack of effects on sperm motility and provide additional data on sperm concentration, FSH, and testosterone.

Protocol Submission: by 04/06  
Study Start: by 03/07  
Final Report Submission: by 08/10

3. Conduct a study or studies to further characterize and, if possible, to determine the mechanism(s) underlying the ocular lesions (retinal atrophy and corneal inflammation/mineralization) observed in the lifetime carcinogenicity studies in Wistar rats.

Protocol Submission: by 07/06  
Study Start: by 06/07  
Final Report Submission: by 08/09

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including

supplements, relating to these postmarketing study commitments must be prominently labeled “**Postmarketing Study Commitment Protocol**”, “**Postmarketing Study Commitment Final Report**”, or “**Postmarketing Study Commitment Correspondence.**”

### **Pediatrics**

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 ages birth up to 1 month and deferring pediatric studies for ages 1 month [44 weeks gestational age] to 16 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

4. Deferred pediatric study under PREA for the treatment of partial onset seizures in pediatric patients ages 1 month [44 weeks gestational age] to 16 years.

Final Report Submission: May 31, 2010

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated “**Required Pediatric Study Commitments**”.

### **Chemistry, Manufacturing, and Controls**

As described in your August 25, 2004 submission, we note your agreement to test the first 3 commercial lots of pregabalin for (b) (4) ) once the (b) (4) process has been implemented in Ringaskiddy. If the observed levels are (b) (4), the data will be reported in a prior-approval supplement, and a specification of NMT (b) (4) for this impurity will be established.

### **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 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

**Dear Healthcare Professional Letters**

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 the original NDA 21-446 for this drug product, not to this NDA, and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
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). All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 21-446 for this drug product, not to this NDA. In the future, do not make submissions to this NDA except for the final printed labeling requested above.

If you have questions, call Jacqueline H. Ware, Pharm.D., Senior Regulatory Project Manager, at 301-594-2850.

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

Enclosure

-----  
**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  
6/10/05 04:03:28 PM