

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-488**

**APPROVAL LETTER**



NDA 022488  
NDA 021446/S-018

**NDA APPROVAL  
SUPPLEMENT APPROVAL**

Pfizer, Inc.  
50 Pequot Ave  
New London, CT 06320  
MS: 6025-B4162

Attention: Dr. S.I. Shah  
Associate Director, Regulatory Strategy  
Worldwide Regulatory Affairs & Quality Assurance

Dear Dr. Shah:

Please refer to your new drug application (NDA) dated and received March 4, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for LYRICA® (pregabalin) Oral Solution 20 mg/mL.

We acknowledge receipt of your submissions dated March 13, May 22 and 29, July 10, September 30, November 5 and 30, and December 23, 2009.

This new drug application, NDA 022488, provides for the use of LYRICA® (pregabalin) Oral Solution 20 mg/mL for neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN), adjunctive therapy for patients with partial onset seizures, and fibromyalgia.

We also refer to your supplemental NDA 021446/S-018, dated and received November 30, 2009, submitted under section 505(b) of the FDCA, for LYRICA® (pregabalin) Capsules. This Prior Approval supplemental NDA provides for modifications to the approved REMS for LYRICA® (pregabalin) (approved on April 23, 2009) to include reference to both formulations (i.e., capsules and oral solution).

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert and the Medication Guide). For

administrative purposes, please designate this submission, “**SPL for approved NDA 22488**” and “**SPL for approved NDA 21446/S-018.**”

### **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*.

Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 22488.**” Approval of this submission by FDA is not required before the labeling is used.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for the following indications and ages:

- (1) Neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN) in patients ages 0 to 16 years because necessary studies are impossible or highly impracticable due to the low incidence and wide geographic dispersion of pediatric patients with these specific neuropathic pain conditions.
- (2) Adjunctive therapy for patients with partial onset seizures ages 0 to 1 month because necessary studies in epilepsy patients ages 0 to 1 month are impossible or highly impracticable due to the low incidence of this condition.
- (3) Fibromyalgia in patients ages 0 to 12 years because pediatric fibromyalgia studies are impossible or highly impracticable to conduct due to the low incidence of this condition.

We are deferring submission of your pediatric studies for the following ages and indications for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

- (1) Adjunctive therapy for patients with partial onset seizures ages 1 month to 16 years.
- (2) Fibromyalgia in patients ages 13-16 years.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually in accordance with 21 CFR 314.81 and section 506B of the FDCA. These required studies are listed below.

- 1576-1. Deferred pediatric study under PREA, a randomized, double-blind, placebo-controlled study to evaluate the efficacy, pharmacokinetics, and safety of pregabalin in pediatric patients with fibromyalgia ages 13 through 16 years, inclusive.

Final Report Submission: January 31, 2012

- 1576-2. Deferred pediatric study under PREA, a randomized, double-blind, placebo-controlled study to evaluate the efficacy, pharmacokinetics, and safety of pregabalin in pediatric patients with partial onset seizures ages 1 month through 3 years, inclusive.

Final Report Submission: April 30, 2015

- 1576-3. Deferred pediatric study under PREA, a randomized, double-blind, placebo-controlled study to evaluate the efficacy, pharmacokinetics, and safety of pregabalin in pediatric patients with partial onset seizures ages 4 through 16 years, inclusive.

Final Report Submission: April 30, 2015

- 1576-4. Deferred pediatric study under PREA, a 12 month open label extension study to evaluate the safety of pregabalin in pediatric patients with partial onset seizures ages 1 month through 16 years, inclusive.

Final Report Submission: April 30, 2015

Submit final study reports to NDA 22488. Use the following designator to prominently label all submissions:

**“Required Pediatric Assessment(s)”**

## **RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS**

The REMS for LYRICA® (pregabalin) Capsules was approved on April 23, 2009. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

You submitted the previously approved REMS to NDA 022488 with proposed revisions to the Medication Guide to reflect the addition of the new formulation (oral solution, 20 mg/mL). You also proposed modifications to the timetable for submission of assessments. Although the due dates for the assessments remained the same, the timetable was revised to reflect the specific dates the assessments are due and that the assessments will be received by FDA on or before the due dates.

Your proposed REMS, appended to this letter, is approved. The same REMS was also submitted to NDA 021446 as S-018, and it is also approved. The approved REMS for both applications consists of a Medication Guide and a timetable for submission of assessments of the REMS.

The REMS assessment plan for LYRICA® (pregabalin) Oral Solution should include the same items as for LYRICA® (pregabalin) Capsules.

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify future submissions containing the REMS assessment or proposed REMS modification with the following appropriate wording in bold capital letters at the top of the first page of the submission:

**NDA 22488 / NDA 21446 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 22488 / NDA 21446**

**PROPOSED REMS MODIFICATION**

**REMS ASSESSMENT**

**NEW SUPPLEMENT FOR (NEW INDICATION FOR USE) FOR 22488 / NDA 21446**

**REMS ASSESSMENT**

**PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

### **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 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, 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>.

Please submit one market package of the drug product when it is available.

### **EXPIRATION DATING PERIOD**

An expiration dating period of 24 months is approved for LYRICA® (pregabalin) oral solution, 20 mg/mL in the 500 mL HDPE bottle packaging configuration, stored at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

A use period of 45 days is approved for open bottles of the LYRICA® (pregabalin) oral solution, 20 mg/mL in the 500 mL HDPE bottle packaging configuration, stored at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

### **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  
Suite 12B-05  
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).

If you have any questions, call Diana L. Walker, Regulatory Project Manager, at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Rigoberto Roca, M.D.  
Deputy Director  
Division of Anesthesia, Analgesia  
and Rheumatology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosures: REMS  
Package insert  
Medication Guide  
Carton and Immediate Container Labels

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-21446

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SUPPL-18

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CP  
PHARMACEUTICA  
LS CV

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LYRICA (PREGABALIN)  
CAPSULES

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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RIGOBERTO A ROCA

01/04/2010