DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 022496

**NDA APPROVAL**

Pacira Pharmaceuticals, Inc.
10450 Science Center Dr.
San Diego, CA 92121

Attention: Dwain Allen
Director, Regulatory Affairs

Dear Mr. Allen:

Please refer to your New Drug Application (NDA) dated and received September 28, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for EXPAREL (bupivacaine liposome injectable suspension).

We acknowledge receipt of your amendments dated October 21, November 8, 12, 18, and 23, December 9 and 22, 2010, and January 28, February 1, 4, 9 (2), and 24, March 2, and 17, April 5, 7, 14, 18 and 27, May 5, 13, 20 and 25, June 14, July 1, 14, 15, 22, 25, 26, and 27 (2), August 26, September 2, 6, 12, 13, 20, 22, 26 (2) and 29, and October 17, 20, and 24, 2011.

This new drug application provides for the use of EXPAREL (bupivacaine liposome injectable suspension) for single-dose infiltration into the surgical site to produce postsurgical analgesia.

We have completed our review of this application, as amended. It is 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, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## 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 (June 2008)." 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 022496**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) 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 deferring submission of your pediatric studies for ages 0 to less than 17 years for this application because this product is ready for approval for use in adults and pediatric studies have not been completed.

Your deferred pediatric studies required under 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 according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1834-1 Multicenter, randomized, double-blind, parallel-group, bupivacaine- and placebo-controlled study to evaluate the safety, efficacy and pharmacokinetic profile of a single intraoperative administration of Exparel for postoperative analgesia in adolescent subjects 12 to less than 17 years old undergoing multiple surgical procedures.

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| Final Protocol Submission: | October 2012 |
| Study/Trial Completion: | November 2013 |
| Final Report Submission: | February 2014 |

1834-2 A multicenter, randomized, double-blind, parallel-group, Bupivacaine- and placebo-controlled study to evaluate the safety, efficacy and pharmacokinetic

profile of a single intraoperative administration of Exparel for postoperative analgesia in children 6 to 11 years old undergoing multiple surgical procedures.

Final Protocol Submission: April 2014
Study/Trial Completion: May 2015
Final Report Submission: August 2015

1834-3 A multicenter, randomized, double-blind, parallel-group, bupivacaine- and placebo-controlled study to evaluate the safety, efficacy and pharmacokinetic profile of a single intraoperative administration of Exparel for postoperative analgesia in young children 2 to 5 years old undergoing multiple surgical procedures.

Final Protocol Submission: October 2015
Study/Trial Completion: November 2016
Final Report Submission: February 2017

1834-4 A multicenter, randomized, double-blind, parallel-group, bupivacaine- and placebo-controlled study to evaluate the safety, efficacy and pharmacokinetic profile of a single intraoperative administration of Exparel for postoperative analgesia in young children 0 to 1 years old undergoing multiple surgical procedures.

Final Protocol Submission: August 2017
Study/Trial Completion: February 2019
Final Report Submission: May 2019

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

## 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.

**EXPIRATION DATING PERIOD**

A 24-month expiration dating period is granted for the drug product, when stored at 2° C to 8°C (36°F to 46°F).

**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 Sharon Turner-Rinehardt, Senior Regulatory Health Project Manager, at (301) 796-2254.

Sincerely,

*{See appended electronic signature page}*

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Carton and Container Labeling

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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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BOB A RAPPAPORT
10/28/2011