

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-864

APPROVAL LETTER



NDA 21-864

Wyeth Pharmaceuticals
Attention: Robert DiGregorio, D.O., F.A.C.O.O.G
Director, Global Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. DiGregorio:

Please refer to your new drug application (NDA) dated May 27, 2005, received May 27, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lybrel™ (levonorgestrel and ethinyl estradiol).

We acknowledge receipt of your submissions dated August 21, October 2, November 1, December 22, 2006, and February 2, March 15 and 21, April 18 and 27, May 4, 11(2), 16, 2007. The August 21, 2006, submission constituted a complete response to our June 27, 2006, action letter and the December 22, 2006, submission constituted a major amendment to this complete response.

This new drug application provides for the use of Lybrel (levonorgestrel and ethinyl estradiol) tablets for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

We completed our review of this application, as amended. It 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 enclosed labeling and the revised immediate container and carton labels submitted on March 15, 2007. 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 21-864.**" Approval of this submission by FDA is not required before the labeling is used.

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.

We remind you of your postmarketing study commitment in your submission dated May 11, 2007. This commitment is listed below.

To conduct and submit a final study report for a postmarketing study of thromboembolic events among women prescribed Lybrel compared to women prescribed cyclic oral contraceptives containing 20mcg ethinyl estradiol. The postmarketing study will be a prospective claims database study and will enroll enough participants to achieve 80% power to detect a relative risk of 2.0.

Protocol Submission: by July 21, 2007
Study Start: within 4 months of product launch
Final Report Submission: within 5 years of study start date

Submit clinical protocols to your IND for this product. Submit the final report 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 this 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 the number of patients entered into the study. All submissions, including supplements, relating to this postmarketing study commitment must be prominently labeled "Postmarketing Study Commitment Protocol," "Postmarketing Study Commitment Final Report," or "Postmarketing Study Commitment Correspondence."

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 the Division of Reproductive and Urologic Products and two copies of both the promotional materials and the approved labeling directly 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

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 John Kim, R.Ph., J.D., Regulatory Health Project Manager, at (301) 796-0932.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Deputy Director
Office of Drug Evaluation III
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/

Daniel A. Shames
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