

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-088

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-088

Wyeth Pharmaceuticals
Attention: Patricia Johnson
Director, Regulatory Affairs
35 CambridgePark Drive
Cambridge, MA 02140

Dear Ms. Johnson:

Please refer to your new drug application (NDA) dated October 5, 2006, received October 5, 2006, submitted under 505(b) of the Federal Food, Drug, and Cosmetic Act for TORISEL™ (temsirolimus) injection.

We acknowledge receipt of your submissions dated October 18, 2006; November 16, 21, and 22, 2006; December 5, and 13, 2006; January 19, and 26, 2007; February 20, 22, and 23, 2007; March 7, and 9, 2007; April 5, 12, 17, and 30, 2007, and May 4, 2007.

This new drug application provides for the use of TORISEL™ (temsirolimus) injection, for the treatment of advanced renal cell carcinoma.

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.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/oc/datacouncil/spl.html>, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved NDA 22-088."

The final printed labeling (FPL) for immediate container and carton labels must be identical to the enclosed labeling. 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 22-088**". Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated May 24, 2007.

These commitments are listed below.

1. Submit the completed report and data sets for the thorough QT prolongation evaluation for study entitled "A single-dose, single-blind, placebo and moxifloxacin controlled 2- period, randomized, crossover, 3rd-period sequential study of the effects of tamsirolimus on cardiac repolarization in healthy subjects".

Protocol Submission: March 2006

Study Start: March 2006

Final Report Submission: September 2007

2. Submit the completed report and datasets for the hepatic impairment study (NCI study 6813 (3066K1-152-US))

Protocol Submission: November 2005

Study Start: January 2006

Final Report Submission: September 2008

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.**"

We have the following comments and risk management statements regarding CMC.

1. As stated in the April 5, 2007 meeting, your proposed Chemistry, Manufacturing and Controls (CMC) Regulatory Agreement, submitted as part of the CMC Pilot program, was not reviewed and is not part of this approval action. Existing regulations and guidances should be followed, as appropriate, for all postapproval CMC changes. We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).
2. We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified during this process.

We remind you of our agreements that were made in the April 5, 2007 teleconference and in your submission dated April 12, 2007. These agreements are listed below:

1. You have agreed to investigate the use of a flag label, or a suitable alternative, in order to incorporate additional information in the container labels for both the diluent and active vials.
2. You have agreed to submit the developed strategy for the above agreement in a

Prior Approval supplement.

3. You have agreed to further discussions with the Agency regarding packaging technology options available, to ensure the physical connection of the two copackaged vials.

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 two copies of both the promotional materials and the package insert 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).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Carl Huntley, Regulatory Project Manager, at (301) 796-1372.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Office of Oncology Drug Products
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Enclosure