DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202570/S-6

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING REQUIREMENT
FULFILLMENT OF POSTMARKETING REQUIREMENTS/COMMITMENT

PF PRISM C.V.
Attention: Mindy S. Meader
Associate Director, Worldwide Regulatory Strategy
Pfizer Inc.
10646 Science Center Drive
San Diego, CA 92121

Dear Ms. Meader:

Please refer to your Supplemental New Drug Application (sNDA) received February 28, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xalkori (crizotinib) capsules, 200mg, 250 mg.

We acknowledge receipt of your amendments submitted on March 14, March 27, April 8, April 10, April 18, April 23, May 15, May 28, June 5, June 10, June 21, June 24, August 2, August 21, September 11, September 30, October 8, October 9, October 10, October 24, October 28, November 6, November 13, November 14 and November 20, 2013.

This Prior Approval Supplemental New Drug Application provides for inclusion in product labeling of the efficacy, clinical pharmacology, and adverse reaction data from Study A8081007 and the clinical pharmacology study results on the effect of gastric pH elevating agents on crizotinib pharmacokinetics.

APPROVAL & LABELING

We have completed our review of this supplemental 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 (package insert and patient information) with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling. 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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

SUBPART H FULFILLED

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills the below postmarketing requirement (PMR) made under 21 CFR 314.510.

1789-1 Clinical trial report and datasets from A8081007: Phase 3, Randomized, Open-label Study of the Efficacy and Safety of PF-02341066 vs. Standard of Care (Pemetrexed or Docetaxel) in Patients with Advanced Non-Small Cell Lung Cancer Harboring a Translocation or Inversion Event Involving the Anaplastic Lymphoma Kinase Gene Locus.

RELEASE FROM POSTMARKETING REQUIREMENT

Since we have determined that the data provided in this supplement verify that clinical benefit is conferred by XALKORI (crizotinib) capsules, you are released from PMR 1789-2, also required under 21 CFR 314.510.

1789-2 Clinical trial report and datasets from A8081014: Phase 3, Randomized, Open-label Study of the Efficacy and Safety of Crizotinib vs. Pemetrexed/Cisplatin or Pemetrexed/Carboplatin in Previously Untreated Patients with Non-Squamous Carcinoma of the Lung Harboring a Translocation or Inversion Event Involving the Anaplastic Lymphoma Kinase Gene Locus.

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.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

This supplement contains your PMR final trial report for the following PMR listed in the August 26, 2011 approval letter.

1789-10 Conduct a trial in humans to determine how to dose crizotinib with regard to gastric pH elevating agents (*i.e.,* a proton-pump inhibitor, an H2-receptor antagonist, and an antacid).

We have reviewed your final trial report and conclude that the above requirement is fulfilled.

FULFILLMENT OF POSTMARKETING COMMITMENT

This supplement contains your postmarketing commitment (PMC) final trial report for the following PMC listed in the August 26, 2011 approval letter.

1789-12 To conduct exposure-response analysis for progression-free survival, response rate, overall survival and safety endpoints utilizing data from confirmatory trial A8081007 and to submit the analysis plan for review.

We have reviewed your final trial report and conclude that the above commitment is fulfilled.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the August 26, 2011 approval letter that are still open.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

2100-1 To submit the final trial report for Study A8081007 that includes the final analysis of overall survival as specified in the version of Study A8081007 submitted on February 5, 2013, in order to characterize the effects of Xalkori (crizotinib) treatment on overall survival.

The timetable you submitted on November 14, 2013, states that you will conduct this trial according to the following schedule:

Trial Completion (Final OS Analysis) Date: June 2015
Final Report Submission: September 2016

2100-2 Clinical trial report and datasets from A8081014: Phase 3, Randomized, Open-label Study of the Efficacy and Safety of Crizotinib vs. Pemetrexed/Cisplatin or Pemetrexed/Carboplatin in Previously Untreated Patients with Non-Squamous Carcinoma of the Lung Harboring a Translocation or Inversion Event Involving the Anaplastic Lymphoma Kinase Gene Locus.

The timetable you submitted on November 13, 2013, states that you will conduct this trial according to the original schedule outlined in our August 26, 2011 approval letter:

Trial Completion Date: December 2015
Final Report Submission: June 2016

Submit clinical protocols to your IND 73544 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing 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/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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 Mona Patel, Pharm.D., Regulatory Project Manager, at (301) 796-4236.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

PATRICIA KEEGAN
11/20/2013