DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-128

NDA APPROVAL

Pfizer Inc.
Attention: Leilani V. Kapilli, MA
Director, Worldwide Regulatory Affairs and Quality Assurance
50 Pequot Avenue
New London, CT 06320

Dear Ms. Kapilli:

Please refer to your new drug application (NDA) dated December 19, 2006, received December 20, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SELZENTRY™ (maraviroc) 150 mg , and 300 mg tablets.

We acknowledge receipt of your submissions dated December 22, 2006, January 16, 2007, January 17, 2007, January 29, 2007(2), February 5, 2007 (2), February 12, 2007 February 13, 2007, February 15, 2007, February 16, 2007, February 19, 2007, February 20, 2007, February 21, 2007 (2), February 22, 2007, February 23, 2007, February 27, 2007, February 28, 2007, March 1, 2007, March 2, 2007, March 7, 2007, March 12, 2007, March 13, 2007 (2), March 20, 2007(4), March 22, 2007 (3), March 23, 2007 (3), April 2, 2007, April 4, 2007, April 5, 2007, April 6, 2007, April 9, 2007 (2), April 12, 2007, April 19, 2007, April 27, 2007, May 4, 2007(4), May 10, 2007 (2), May 11, 2007 (2), May 16, 2007, May 17, 2007 (2), May 21, 2007, May 22, 2007, May 24, 2007 (3), May 29, 2007, June 1, 2007, June 4, 2007 (2), June 5, 2007, June 12, 2007, June 14, 2007 (2), June 19, 2007, June 21, 2007, June 22, 2007, July 6, 2007, July 10, 2007 and July 25, 2007.

The July 25, 2007 submission constituted a complete response to our June 20, 2007 action letter.

This new drug application provides for the use of SELZENTRY™ (maraviroc) 150 mg and 300 mg tablets for the treatment of patients infected with CCR5-tropic HIV-1.

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.510), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

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/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and Medication Guide). 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 22-128."

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 22-128."** 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.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your postmarketing study commitment specified in your submission dated June 5, 2007. This commitment, along with any completion dates agreed upon, is listed below.

1. Submit Week 48 reports and datasets for Studies A4001027 and A4001028.

   Week 48 report submission: August 2007

Please submit final study reports to NDA 22-128 as a supplemental application. For administrative purposes, all submissions relating to this postmarketing study commitment must be clearly designated **"Subpart H Postmarketing Study Commitment."**

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.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

2. Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from 2 to 18 years of age. This study will determine the maraviroc exposure (pharmacokinetics profile) followed by 48 weeks of dosing, with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from 2 to 18 years of age to support maraviroc dose selection, safety and efficacy.

   Protocol Submission Date: December 2007
   Final Study Report Submission Date: December 2011

3. Deferred pediatric study under PREA for the treatment of HIV in pediatric subjects from birth to ≤ 2 years of age. This study will determine the maraviroc exposure (pharmacokinetic profile) followed by 48 weeks of dosing with efficacy based on viral load reduction through 48 weeks of dosing, and safety monitored over 96 weeks for pediatric subjects from birth to 2 years of age to support maraviroc dose selection, safety and efficacy.

   Protocol Submission Date: December 2007
   Final Study Report Submission Date: December 2015

Submit final study reports to this NDA. For administrative purposes, all submissions related to these pediatric postmarketing study commitments must be clearly designated **"Required Pediatric Study commitments."**

We remind you of your postmarketing study commitments in your submission dated June 5, 2007 and in teleconferences held June 12, 2007 and August 3, 2007. These commitments are listed below.

Clinical

4. Submit Week 96 reports and datasets for Studies A4001027 and A4001028.

   Report submission: July 2008

5. Conduct a five-year follow-up for subjects in Studies A4001027 and A4001028 for mortality, liver failure, malignancy, myocardial ischemia or infarction and rhabdomyolysis, as well as for infections reported as serious adverse events or qualify as a CDC Category C event.

   Final 5 year study report submission: August 2011

6. Conduct and submit a final report for a non-randomized, controlled, observational study to provide additional safety data regarding the incidence of mortality, liver failure, malignancy, myocardial ischemia or infarction, and rhabdomyolysis, as

well as for infections that qualify as a CDC Category C event. Follow-up of subjects will be at least every 6 months for a total of 5 years.

Protocol Submission: December 2007
Final Report Submission: June 2016

7. Conduct and submit a study in patients with HIV-1 who are co-infected with hepatitis C and/or B, including some subjects with a Child-Pugh score of C.

Protocol Submission: April 2008
Interim Report Submission: December 2011
Final Report Submission: December 2013

8. Submit Week 48 and Week 96 reports for Study A4001026. Subjects in this study will also be followed for a total of 5 years for mortality, liver failure, malignancy, myocardial ischemia or infarction, rhabdomyolysis, as well as for infections reported as serious adverse events or qualify as a CDC Category C events.

Week 48 interim report submission: October 2007
Week 96 study report submission: November 2008
Final 5 year study report submission: October 2011

Microbiology

9. Perform cell culture combination activity of maraviroc with darunavir and tipranavir, and submit complete study report of these assessments.

Final Report Submission: May 2008

Clinical Pharmacology

10. Conduct a study to evaluate the effect of renal impairment on the pharmacokinetics of maraviroc.

a) at a dose of 150 mg when combined with a boosted protease inhibitor (e.g., saquinavir/ritonavir) in subjects with mild and moderate renal impairment and subjects with End-Stage Renal Disease (ESRD) that require dialysis.
b) at a dose of 300 mg alone in subjects with severe renal impairment and subjects with end stage renal disease who require dialysis.

Protocol Submission: December 30, 2007
Final Report Submission: December 30, 2008

11. Conduct a study to evaluate the potential for maraviroc metabolite(s) to inhibit CYP2D6 enzymes at a maraviroc dose of 600 mg.

Protocol Submission: December 30, 2007
Final Report Submission: June 30, 2008

12. Conduct a study to evaluate the potential of maraviroc to inhibit P-gp.

    Protocol Submission: December 30, 2007
    Final Report Submission: June 30, 2008

13. Conduct a study to investigate the potential for maraviroc to induce CP1A2.

    Protocol Submission: December 30, 2007
    Final Report Submission: June 30, 2008

14. Conduct and submit a clinical study to evaluate the potential for pharmacodynamic interaction between maraviroc and inhibitors of phosphodiesterase type 5 (PDE5).

    Protocol Submission: December 2007
    Final Report Submission: June 2008

We acknowledge your commitment to participate in the Antiretroviral Pregnancy Registry.

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 should be prominently labeled **"Postmarketing Study Commitment Protocol", Postmarketing Study Commitment Final Report" or "Postmarketing Study Commitment Correspondence."**

As required by 21 CFR 314.550, submit all promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of all promotional materials 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

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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Kenny Shade, Regulatory Project Manager, at (301) 796-0807.

Sincerely,

{See appended electronic signature page}

Edward Cox, M.D., M.P.H.
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

Enclosure:

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

/s/

Debra Birnkrant
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