DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021928/S-040

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT
REMS ASSESSMENT ACKNOWLEDGEMENT
RELEASE REMS REQUIREMENT

Pfizer, Inc.
235 E. 42nd Street
New York, NY 10017

Attention: Lilya I. Donohew, PhD
Senior Director, Worldwide Regulatory Affairs

Dear Dr. Donohew:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 18, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Chantix (varenicline) Tablets; 0.5 mg and 1 mg.

We also refer to our electronic communication dated December 1, 2016; and we acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated October 14, 2016. After consultation between the Office of Surveillance and Epidemiology and the Office of New Drugs, we found the REMS assessment to be complete.

This Prior Approval sNDA proposes changes to the package insert based on clinical trial data from the study titled, "A Phase 4, Randomized, Double-Blind, Active and Placebo-Controlled, Multicenter Study Evaluating the Neuropsychiatric Safety and Efficacy of 12 Weeks Varenicline Tartrate 1 mg BID and Bupropion Hydrochloride 150 mg BID for Smoking Cessation in Subjects with and Without a History of Psychiatric Disorders"; the supplement also proposes corresponding changes to the Medication Guide, and provides for proposed modification to the approved REMS for Chantix (varenicline).

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 (text for the package insert, and Medication Guide), 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 include 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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submissions dated November 16, 2015, and February 18, 2016, reporting on and containing the final report for the following postmarketing requirement listed in the March 12, 2010, post-approval postmarketing requirements letter:

1544-4 A large randomized, double-blind, active- and placebo-controlled trial to compare the risk of clinically significant neuropsychiatric events, including but not limited to suicidality, in individuals using Chantix (varenicline), bupropion, nicotine replacement therapy, or placebo as aids to smoking cessation over 12 weeks of treatment, and to determine whether individuals with prior history of psychiatric disorders are at greater risk for development of clinically significant neuropsychiatric events compared to individuals without prior history of psychiatric disorders while using Chantix (varenicline) as an aid to smoking cessation. The trial should be sufficiently powered to adequately assess clinically significant neuropsychiatric events with each treatment and in both of the two subgroups (i.e., with and without psychiatric disorders).

We have reviewed your submissions and conclude that the above requirement has been fulfilled.

We remind you that there are postmarketing requirements listed in the May 10, 2006, approval

letter, and the September 22, 2011, post-approval postmarketing requirement letter that are still open.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Chantix (varenicline) was originally approved on October 19, 2009, and the most recent modification was approved on August 12, 2016. The REMS consists of a Medication Guide, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised Medication Guide to correspond to changes to the product label.

In accordance with section 505-1 of the FDCA, we have determined that the following REMS modification is necessary to minimize burden on the healthcare delivery system of complying with the REMS:

- Removal of the Medication Guide as an element of the REMS

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Chantix (varenicline) outweigh its risks. The Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208. Like other labeling, Medication Guides are subject to the safety labeling change provisions of section 505(o)(4) of the FDCA.

Therefore, because the Medication Guide as part of the REMS is no longer necessary to ensure the benefits of the drug outweigh the risks, a REMS is no longer required for Chantix (varenicline).

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:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. 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 Ayanna Augustus, PhD, RAC, Sr. Regulatory Project Manager, at (301) 796-3980.

Sincerely,

{See appended electronic signature page}

Sharon H. Hertz, MD
Director
Division of Anesthesia, Analgesia,
and Addiction Products
Office of Drug Evaluation II
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/

SHARON H HERTZ
12/16/2016