CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

021928Orig1s032

Trade Name:	CHANTIX
Generic or Proper Name:	varenicline tartrate
Sponsor:	Pfizer, Inc.
Approval Date:	09/19/2014
Indication:	CHANTIX is a nicotinic receptor partial agonist indicated for use as an aid to smoking cessation treatment.

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NDA 021928/S-032

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021928/S-032, S-036, S-038

SUPPLEMENT APPROVAL

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 Applications (sNDAs) dated and received October 24, 2013(S-032), April 8, 2014 (S-036), and September 3, 2014 (S-038), 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 acknowledge receipt of your amendments dated November 8, and December 20, 2013, April 30, and September 18, 2014 (S-032), April 29, May 2, 5, and 8, August 1, and September 18, 2014 (S-036), and September 3, and 18, 2014 (S-038), and your proposed risk evaluation and mitigation strategy (REMS) modification dated November 8, 2013 (S-032) and September 3, 2014 (S-038).

We also refer to our letter dated August 6, 2014, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Chantix. This information pertains to the risk of seizures and the potentiation of the intoxicating effects of alcohol.

Finally we refer you to our September 4, 2013, and August 6, 2014, letters notifying you, under section 505-1(g)(4)(B) of the FDCA, that your REMS must be modified based on findings from your 18-month REMS assessment and the new safety information described above.

Supplement S-032 proposes revisions to the **DRUG INTERACTIONS** section of the Package Insert regarding a potential interaction between alcohol and varenicline and includes a proposed modification to the approved risk evaluation and mitigation strategy (REMS), including revisions to the Medication Guide and revisions to the Chantix REMS goal.

Supplement S-036 proposes changes to the Package Insert based on meta-analyses of varenicline clinical trials and published observational studies pertaining to serious neuropsychiatric events.

Supplement S-038 proposes revisions to the labeling for Chantix. The agreed upon changes to the language included in our August 6, 2014, letter are included in the appended labeling text.

S-038 also includes additional proposed modifications to the approved risk evaluation and mitigation strategy (REMS), comprising further revisions to the Medication Guide as well as revisions to the Chantix REMS goal.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended, and they are 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 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).

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

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

The REMS for Chantix (varenicline) was originally approved on October 19, 2009, and the most recent modification was approved on July 22, 2011. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of revisions to the Medication Guide to describe the risk of seizures and the potentiation of the intoxicating effects of alcohol, and revise the "What is the most important

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