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FDA Approves Removal Of Boxed Warning Regarding Serious Neuropsychiatric Events From CHANTIX® (varenicline) Labeling

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Labeling Revisions Also Include Updates to Corresponding Warning and Addition of Clinical Data on Superior Efficacy of CHANTIX Compared to Bupropion or Nicotine Patch1 Labeling Revisions May Further Encourage Smokers and Healthcare Providers to Discuss Smoking Cessation Treatment Options

Pfizer announced today that the U.S. Food and Drug Administration (FDA) approved updates to the CHANTIX ® (varenicline) labeling, including removal of the boxed warning regarding serious neuropsychiatric events. The removal of the boxed warning is based on the outcomes of EAGLES (**E**valuating **A**dverse Events in a **Gl**obal Smoking C**e**ssation **S**tudy), the largest smoking cessation clinical trial in patients without and with a history of psychiatric disorder, and is consistent with the recent recommendation of the FDA Psychopharmacologic Drugs and Drug Safety and Risk Management Advisory Committees. Additional labeling revisions based on EAGLES include updates to the corresponding warning regarding neuropsychiatric safety and the addition of information on the superior efficacy of CHANTIX compared to bupropion or nicotine patch.1,2

“For millions who smoke, stopping smoking is one of the most important steps they can take to improve their health, and Pfizer is committed to helping smokers in their quit journey,” said Freda Lewis-Hall, M.D., DFAPA, chief medical officer and EVP, Pfizer Inc. “We are pleased with the FDA’s decision to update the CHANTIX labeling based on EAGLES – the largest clinical trial of smoking cessation medications - and we expect this new information may further facilitate an informed discussion about quitting with CHANTIX between smokers and healthcare providers.”

“While the benefits of quitting are immediate and substantial, few smokers are able to quit on their own and need the help of counseling and smoking cessation therapy,” said Dr. A. Eden Evins, director, Massachusetts General Hospital Center for Addiction Medicine and William Cox Family Associate Professor of Psychiatry in the Field of Addiction Medicine, Harvard Medical School. “As healthcare providers work on the front lines to help people who are struggling to quit smoking, this new labeling provides clinically relevant information on the safety and efficacy of CHANTIX to help them and their patients make informed decisions about smoking cessation treatment.”

In the U.S., smoking is the leading preventable cause of death, responsible for roughly 540,000 deaths each year. 3,4 Stopping smoking has significant health benefits, including reducing the risk of tobacco-related diseases such as lung cancer, heart disease, stroke, chronic respiratory disease and other conditions.5 While smoking rates have declined overall, some segments of society have not made the same progress,6,7 including people living with mental illness, Veterans, LGBTQ and other minority communities.8-10

The updated warning in the CHANTIX labeling notes that postmarketing reports of serious or clinically significant neuropsychiatric adverse events in patients treated with CHANTIX included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide. Patients attempting to quit smoking with CHANTIX should be observed for the occurrence of such symptoms and instructed to discontinue CHANTIX and contact a healthcare provider if they experience such symptoms.1

In EAGLES, in the cohort of patients without a history of psychiatric disorder, CHANTIX was not associated with an increased incidence of clinically significant neuropsychiatric adverse events in a composite endpoint comprising anxiety, depression, feeling abnormal, hostility, agitation, aggression, delusions, hallucinations, homicidal ideation, mania, panic, and irritability.

In the cohort of patients with a history of psychiatric disorder, there were more events reported in each treatment group compared to the non-psychiatric cohort, and the incidence of events in the composite endpoint was higher for each of the active treatments compared to placebo: Risk Differences (RDs) (95%CI) vs. placebo were 2.7% (-0.05, 5.4) for CHANTIX, 2.2% (-0.5, 4.9) for bupropion, and 0.4% (-2.2, 3.0) for transdermal nicotine. The neuropsychiatric events of a serious nature were reported in 0.6% of CHANTIX-treated patients, with 0.5% involving psychiatric hospitalization. In placebo-treated patients, serious neuropsychiatric events occurred in 0.6%, with 0.2% requiring psychiatric hospitalization.

About EAGLES Clinical Trial

EAGLES is a randomized, blinded, active- and placebo-controlled clinical trial, which was conducted by Pfizer in collaboration with GlaxoSmithKline at the request of and designed in consultation with the FDA and the European Medicines Agency (EMA). The trial is the first and largest to compare the safety and efficacy of CHANTIX, bupropion and nicotine replacement patch in approximately 8,000 smokers without and with a history of psychiatric disorder. The trial was designed to compare the risk of clinically significant neuropsychiatric adverse events in patients using CHANTIX, bupropion, nicotine replacement therapy or placebo as smoking cessation aids over 12 weeks of treatment, and to determine whether smokers with a history of psychiatric disorder are at a greater risk for developing clinically significant adverse events compared to smokers without a history of psychiatric disorder.2

About CHANTIX®

CHANTIX® (also known as CHAMPIX® in the EU and other countries) was approved by the FDA in May 2006 as a prescription medication that, along with support, helps adults 18 and over stop smoking. CHANTIX is approved in more than 100 countries and has been prescribed to over 20 million patients worldwide, including more than 11 million in the U.S.11 Adults who smoke may benefit from quit-smoking support programs and/or counseling during their quit attempt.12 It’s possible that patients might slip up and smoke while taking CHANTIX. If patients slip up, they can stay on CHANTIX and keep trying to quit.1

Important CHANTIX (varenicline) Safety Information

CHANTIX is contraindicated in patients with a history of serious hypersensitivity or skin reactions to CHANTIX.

Postmarketing reports of serious or clinically significant neuropsychiatric adverse events have been reported in patients treated with CHANTIX. These included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide. Observe patients attempting to quit smoking

with CHANTIX for the occurrence of such symptoms and instruct them to discontinue CHANTIX and contact a healthcare provider if they experience such adverse events.

During clinical trials and the postmarketing experience, there have been reports of seizures in patients treated with CHANTIX, with or without a history of seizures. CHANTIX should be used cautiously in patients with a history of seizures or other factors that can lower the seizure threshold. Instruct patients to discontinue CHANTIX, and contact a healthcare provider immediately if they experience a seizure while on treatment.

There have been postmarketing reports of patients experiencing increased intoxicating effects of alcohol while taking CHANTIX, including unusual and sometimes aggressive behavior directed to oneself or to others and often accompanied by amnesia. Advise patients to reduce the amount of alcohol they consume while taking CHANTIX until they know whether CHANTIX affects their tolerance for alcohol.

Cases of somnambulism have been reported in patients taking CHANTIX. Some cases described harmful behavior to self, others, or property. Instruct patients to discontinue CHANTIX and notify their healthcare provider if they experience somnambulism.

Patients should be informed that there have been reports of serious skin reactions, such as Stevens Johnson Syndrome and Erythema Multiforme and of angioedema, with swelling of the face, mouth, and neck that can lead to life-threatening respiratory compromise.

Patients should be instructed to discontinue CHANTIX and immediately seek medical care if they experience these symptoms or at the first sign of rash with mucosal lesions or any other signs of hypersensitivity.

In a meta-analysis of clinical trials including a trial in patients with stable cardiovascular disease, while serious cardiovascular events were infrequent overall, certain serious cardiovascular events were reported more frequently in patients treated with CHANTIX than placebo. These events occurred primarily in patients with known cardiovascular disease. Instruct patients to notify their health care providers of new or worsening cardiovascular symptoms and to seek immediate medical attention if they experience signs and symptoms of myocardial infarction or stroke.

The most common adverse reactions include nausea (30%), abnormal dreams, constipation, flatulence, and vomiting. Patients should be informed that they may experience vivid, unusual, or strange dreams during treatment with CHANTIX. Patients should be advised to use caution driving or operating machinery or engaging in other potentially hazardous activities until they know how CHANTIX may affect them.

Safety and efficacy of CHANTIX in combination with other smoking cessation drug therapies have not been studied. Dosage adjustment with CHANTIX is recommended in patients with severe renal impairment or in patients undergoing hemodialysis.

Smoking cessation, with or without treatment with CHANTIX, may alter the pharmacokinetics or pharmacodynamics of some drugs, such as theophylline, warfarin, and insulin. Dosage adjustment for these drugs may be necessary.

Click here for full Prescribing Information and Medication Guide.

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manufacture of healthcare products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. For more information, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube, and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of December 16, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about CHANTIX/CHAMPIX (varenicline), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial impact of the results of the EAGLES trial and the updates to the U.S. label for CHANTIX, including removal of the boxed warning regarding serious neuropsychiatric events; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of CHAMPIX (including uncertainties regarding the impact of the EAGLES trial on the product labeling for CHAMPIX in other jurisdictions); the risk that clinical trial data are subject to differing interpretations, including by regulatory authorities; the uncertainties inherent in research and development; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References:

1. Pfizer Laboratories Div Pfizer Inc. CHANTIX® (varenicline) Prescribing Information.

2. Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet*. 2016 Apr 19: e1-e14.[Epub ahead of print].

3. Centers for Disease Control and Prevention. Smoking & Tobacco Use: Fast Facts. http://www.cdc.gov/tobacco/data_statistics/fact_sheets/fast_facts/. Accessed August 19, 2016.

4. Carter BD et al. Smoking and Mortality — Beyond Established Causes. *N Engl J Med. 372*;7:631-640.

5. Centers for Disease Control and Prevention (CDC). The Surgeon General's 1990 Report on the Health Benefits of Smoking Cessation Executive Summary – Preface. MMWR. 1990, 39(RR-12), 8-15.

6. Ng MA et al. Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012. *JAMA*. 2014; 311(2):183-192.

7. Cook BL, Wayne GF, Kafali EN, et al. Trends in Smoking Among Adults With Mental Illness and Association Between Mental Health Treatment and Smoking Cessation. *JAMA* 2014;311:172-82.

8. SAMHSA 2014. Results from the 2014 National Survey on Drug Use and Health: Mental Health Detailed Tables. http://www.samhsa.gov/data/sites/default/files/NSDUH-MHDetTabs2014/NSDUH-MHDetTabs2014.htm#tab1-10b. Accessed July 2016.

9. Centers for Disease Control and Prevention. Tips from Former Smokers: Burden of Tobacco in the U.S. http://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html#eleven. Accessed August 19, 2016.

10. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. (2015). Current Cigarette Smoking Among Adults — United States, 2005–2014. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6444a2.htm?s_cid=mm6444a2_w. Accessed June 25, 2016.

11. Data on File. Pfizer Laboratories.

12. Centers for Disease Control and Prevention (CDC). Smoking & Tobacco Use: Quitting Smoking. http://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/quitting/. Accessed August 29, 2016.

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