VARENICLINE (CHANTIX) AND BUPROPION (ZYBAN) SAFETY UPDATE

This New Drug FAX Sheet issue provides information from the FDA regarding new boxed warnings and patient medication guides for the smoking cessation aids, varenicline and bupropion. The verbatim communication from the FDA is provided below. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.

FDA has required the manufacturers of the smoking cessation aids varenicline (Chantix) and bupropion (Zyban and generics) to add new Boxed Warnings and develop patient Medication Guides highlighting the risk of serious neuropsychiatric symptoms in patients using these products. These symptoms include changes in behavior, hostility, agitation, depressed mood, suicidal thoughts and behavior, and attempted suicide. The same changes to the prescribing information and Medication Guide for patients will also be required for bupropion products (Wellbutrin and generics) that are indicated for the treatment of depression and seasonal affective disorder.

The added warnings are based on the continued review of postmarketing adverse event reports for varenicline and bupropion received by the FDA. These reports included those with a temporal relationship between the use of varenicline or bupropion and suicidal events and the occurrence of suicidal ideation and suicidal behavior in patients with no history of psychiatric disease. Some of these cases may have been confounded by symptoms typically seen in people who have stopped smoking and are experiencing withdrawal from nicotine.

Healthcare professionals should advise patients to stop taking varenicline or bupropion and contact a healthcare provider immediately if they experience agitation, depressed mood, and any changes in behavior that are not typical of nicotine withdrawal, or if they experience suicidal thoughts or behavior. If varenicline or bupropion is stopped due to neuropsychiatric symptoms, patients should be monitored until the symptoms resolve.

Family members and caregivers should also be alerted to the potential for changes in mood or behavior and contact the health care provider if they observe these changes in the person taking varenicline or bupropion. Varenicline and bupropion are effective smoking cessation aids. The possible risks of serious adverse events occurring while using varenicline or bupropion should always be weighed against the significant health benefits of quitting smoking. The health benefits of quitting smoking include a reduction in the chance of developing lung disease, heart disease, or cancer.

This information reflects FDA’s current analysis of data available to FDA concerning these drugs. FDA is not advising practitioners to discontinue prescribing these products. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of these drugs, please contact the FDA MedWatch program using the information at the bottom of the page.

FDA last informed healthcare professionals and patients of the addition of suicidal ideation, attempted and completed suicide, changes in behavior, agitation, and depressed mood in the WARNINGS and PRECAUTIONS sections of the varenicline prescribing information and patient Medication Guide on May 16, 2008. Varenicline (marketed as Chantix) Information FDA is now requiring the addition of this information to the BOXED WARNING and to the Medication Guides for patients who are prescribed varenicline and bupropion under the authorities provided in the Food and Drug Administration Amendments Act (FDAAA).

Recommendations and Considerations for Healthcare Professionals

- It is important to discuss the possibility of serious neuropsychiatric symptoms in the context of the benefits of quitting smoking with patients before prescribing these medications. Varenicline and bupropion are both effective smoking cessation aids and the health benefits of smoking cessation are immediate and substantial.
• **Healthcare professional should monitor all patients taking varenicline and bupropion for serious neuropsychiatric symptoms.** These symptoms include changes in behavior, hostility, agitation, depressed mood, suicidal ideation, suicidal behavior and attempted suicide. These symptoms have occurred in patients without pre-existing psychiatric illness and have worsened in some patients with pre-existing psychiatric illness. In most cases, neuropsychiatric symptoms developed during treatment with varenicline or bupropion but in others, symptoms developed after stopping drug treatment.

• **Patients should be informed that it is not unusual to have symptoms such as irritability, feeling anxious, depressed mood and trouble sleeping when they are withdrawing from nicotine, independent of whether they are taking varenicline or bupropion.**

• **Patients with serious psychiatric illness such as schizophrenia, bipolar disorder, and major depressive disorder, may experience worsening of their pre-existing psychiatric illness while taking varenicline or bupropion.**

• **Patients who discontinue treatment because of neuropsychiatric events should continue to be monitored until symptoms resolve.** Although symptoms resolved after treatment was stopped in many cases, there were also some cases where the symptoms persisted.

**Information for healthcare professionals to discuss with patients, family members, and caregivers:**

• **Quitting smoking can decrease the chances of lung and heart disease and getting cancer.** These important health benefits should be weighed against the small, but real, risk of serious adverse events with use of varenicline or bupropion.

• **Worsening or recurrence of psychiatric illness.** Patients should be told that some patients taking varenicline or bupropion have experienced worsening of their psychiatric illness, even when the illness was under control and some patients have experienced a recurrence of a previous psychiatric illness when taking these drugs for smoking cessation.

• **Unusual changes in mood and behavior.** Patients should be instructed to contact their healthcare provider immediately if they observe or develop thoughts about suicide or attempting suicide, feel agitated, aggressive or violent and other unusual changes in mood or behavior.

• **Some symptoms are to be expected when quitting smoking.** Patients should be told that it is not unusual to have symptoms such as irritability, feeling anxious, depressed mood and trouble sleeping when they are withdrawing from nicotine, independent of whether they are taking varenicline or bupropion and that vivid, unusual, or strange dreams may occur while taking Chantix and are not a cause for alarm.

• **Discuss other methods of quitting smoking if it is decided that varenicline or bupropion are not the best treatment option**

**Background Information and Data**

FDA first informed the public about the possibility of serious neuropsychiatric symptoms with varenicline in the November 20, 2007 FDA Early Communication About an Ongoing Safety Review. A complete history of related communications on varenicline and bupropion can be found at: Varenicline (marketed as Chantix) Information. Since that time, information about serious neuropsychiatric symptoms in patients taking varenicline has been added to the POST-MARKETING EXPERIENCE section of the prescribing information.

As FDA received additional information the suggestion of a possible association between both varenicline and bupropion (which was evaluated as a comparator to varenicline) and serious neuropsychiatric symptoms, in both patients with and those without previous history of psychiatric illness, became more evident as its review progressed. As a result, FDA has required the manufacturers of the smoking cessation products varenicline, and bupropion to add information regarding neuropsychiatric symptoms to the Boxed Warning, and Warnings sections of the varenicline and bupropion prescribing information and update the Medication Guides for patients so that healthcare professionals and patients can be more alert to these issues.

A summary of the data from FDA’s review of varenicline and bupropion were published in FDA Drug Safety Newsletter, Volume 2, Number 1, 2009. This analysis was for all reports received by FDA from the time of marketing approval to November 2007. Access to the article is provided in the link below. FDA has continued to receive reports of neuropsychiatric events in association with use of varenicline and bupropion since the data cut off date for the analysis presented in the Drug Safety Newsletter analysis.

**FDA Drug Safety Newsletter Volume 2, Number 1, 2009 - PDF.**

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Varenicline (Chantix) and Bupropion (Zyban) Safety Update. *New Drug Fax Sheet. 2009 July 1;14(23):1-2.*