



# The Pharmacist Activist

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Editorial

## The FDA Should Provide Pharmacists with the Authority to Dispense Chantix Without a Prescription

**T**he consequences of smoking cigarettes represent the most important public health challenge in the United States. Pharmacists are in a position to do much more to help individuals stop smoking, and one strategy is to provide pharmacists with the authority to dispense varenicline (Chantix) without a prescription. I have provided below my letter to Dr. Robert Califf, the FDA Commissioner,

in which I urge that this action be taken. If the FDA is not interested or is not able to take this action on a timely basis, pharmacists should seek this authority in individual states. Our profession should actively seek support for this strategy and, pharmacists who wish to use any of the following comments in such efforts should feel free to do so, verbatim or paraphrased.

### A Letter to the FDA Commissioner

May 4, 2016

Dr. Robert M. Califf, Commissioner  
U. S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

Dear Dr. Califf:

I am writing to urge the Food and Drug Administration to provide pharmacists with the authority to dispense varenicline (Chantix) without a prescription to individuals who wish to stop smoking.

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Smoking cigarettes is responsible for more deaths in the United States than any other single cause. More than 440,000 deaths each year result from cancers, heart and respiratory problems, and other diseases in which smoking is an important causative or complicating factor. There have been positive initiatives to encourage individuals to not start smoking, and to help current smokers stop smoking. However, much more must be done.

The nicotine replacement therapy (NRT) gum, lozenge, and patch formulations are available without a prescription and have been of value in helping many individuals stop smoking. However, many other individuals who have used these products have not been successful in stopping smoking. Varenicline is regarded by many as the most effective product in helping individuals stop smoking. In addition, its use is not associated with a continued dependence/addiction to nicotine that may occur with NRT formulations, resulting in their continued use over many months and years.

At the present time, a prescription is needed to obtain varenicline. For a variety of reasons, many individuals who smoke will not make an appointment to see a physician and, as a consequence, do not have access to this medication. Pharmacists have the expertise and judgment to recommend varenicline for individuals for whom use is appropriate, and to provide information and counseling that will result in optimum use.

I recognize that there have been concerns regarding the possible occurrence of neuropsychiatric adverse events with the use of varenicline, and that there is a boxed warning in its labeling that addresses this. However, recent studies and observations, such as the following examples, indicate that there is not a greater risk of such events with this medication.

The results of a study conducted by Robert M. Anthenelli, et al. were published online in *The Lancet* on April 22, 2016 – “Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomized, placebo-controlled clinical trial.” The authors’ interpretation of the study results reads: “The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo. Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.”

The *Medical Letter on Drugs and Therapeutics* provides a report, “Drugs for Tobacco Dependence,” in Issue 1489 published on February 29, 2016. The commentary regarding varenicline includes the following statements with the pertinent references: “...a retrospective cohort study in almost 165,000 patients found no increased risk of any cardiovascular or neuropsychiatric event with varenicline compared to NRT or bupropion. Varenicline has increased smoking cessation rates in patients with psychiatric illnesses, with no significant psychiatric adverse effects. Recent analyses of clinical trials have found no increase in suicidal behavior in patients treated with varenicline compared to those treated with NRT, bupropion, or placebo.”

Some have observed that a medication with a boxed warning in its labeling would not be approved by the FDA for availability without a prescription from a pharmacist. I would contend that the boxed warning should be removed from the labeling for varenicline. However, even if the present or revised boxed warning is continued in the labeling, there are already situations in which boxed warnings address a concern with a medication that is available without a prescription. For example, the prescription product Vicodin contains a combination of hydrocodone and acetaminophen, and its labeling includes a boxed warning. The boxed warning does not address a concern with hydrocodone, but rather a risk of hepatotoxicity with acetaminophen – the most widely used of

*(Continued on Page 4)*

# New Drug Review

## Cariprazine hydrochloride (Vraylar – Allergan) Antipsychotic Agent

**New Drug Comparison  
Rating (NDCR) = 2**  
*(significant disadvantages)  
in a scale of 1 to 5 with 5 being  
the highest rating*

### Indications:

Treatment of patients with schizophrenia, and in the acute treatment of manic or mixed episodes associated with bipolar I disorder.

### Comparable drugs:

Aripiprazole (e.g., Abilify).

### Advantages:

- May be effective in some patients who have not experienced an adequate response with other agents;
- Is less likely to be implicated in drug interactions involving the CYP2D6 metabolic pathway;
- Labeling does not include warning regarding a risk of suicidal thoughts and behaviors.

### Disadvantages:

- Has not been directly compared with comparable drugs in clinical studies;
- Labeled indications are more limited (aripiprazole also has labeled indications for adjunctive treatment of patients with major depressive disorder, the treatment of patients with Tourette's disorder, and the treatment of irritability associated with autistic disorder);
- Has not been evaluated in pediatric patients (whereas aripiprazole is indicated for use in patients as young as 6 years for certain conditions);
- May be more likely to cause extrapyramidal reactions;
- May accumulate with continued use and increase the possibility of late-occurring adverse events;
- Dosage forms are more limited (aripiprazole is also available in an oral solution formulation, and in a parenteral formulation for intramuscular injection).

### Most important risks/adverse events:

Increased risk of death in elderly patients with dementia-related psychosis (boxed warning), and a higher incidence of cerebrovascular events (e.g., stroke) in these patients; neuroleptic malignant syndrome; tardive dyskinesia; seizures; orthostatic hypotension and syncope; body temperature dysregulation; dysphagia; metabolic changes (e.g., hyperglycemia/diabetes, dyslipidemia, weight gain); leukopenia, neutropenia, and agranulocytosis; potential for cognitive and motor impairment (patients should be cautioned about operating hazardous

machinery); late-occurring adverse events (cariprazine and its major metabolites may accumulate over time, and adverse events may not be evident, or worsen, over a period of several weeks after initiating treatment and dosage increases); is a substrate of the CYP3A4 metabolic pathway and activity is increased by the concurrent use of a strong CYP3A4 inhibitor (e.g., clarithromycin; dosage of cariprazine should be reduced); action is reduced by the concurrent use of a strong CYP3A4 inducer (e.g., carbamazepine; concurrent use is not recommended); may cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure.

### Most common adverse events:

In patients with schizophrenia – extrapyramidal symptoms (19%), akathisia (13%); in patients with bipolar mania – extrapyramidal symptoms (26%), akathisia (20%), nausea (13%), vomiting (10%).

### Usual dosage:

Recommended starting dosage is 1.5 mg once a day on Day 1; in patients with schizophrenia, the dosage can be increased to 3 mg once a day on Day 2, and the recommended dosage range is 1.5 mg to 6 mg once a day; in patients with manic or mixed episodes associated with bipolar I disorder, the dosage should be increased to 3 mg once a day on Day 2, and the recommended dosage is 3 to 6 mg once a day; in patients being treated concurrently with a strong CYP3A4 inhibitor, the dosage should be reduced and the product labeling should be consulted for the specific recommendations.

### Products:

Capsules – 1.5 mg, 3 mg, 4.5 mg, 6 mg.

### Comments:

Cariprazine is an atypical antipsychotic agent with activity that is most similar to that of aripiprazole and brexpiprazole (Rexulti). It exhibits partial agonist activity at dopamine D<sub>2</sub> and serotonin 5-HT<sub>1A</sub> receptors, and antagonist activity at serotonin 5-HT<sub>2A</sub> receptors. It has been demonstrated to be more effective than placebo in reducing the occurrence of symptoms of schizophrenia and bipolar disorder. It is converted to two major active metabolites, one of which has a long half-life.

Daniel A. Hussar

all medications. My recommendation that varenicline be available without a prescription from a pharmacist, as distinct from general nonprescription availability, continues to provide the involvement of a health professional in assuring optimum safety and effectiveness.

Because many prescription benefit plans provide coverage only for prescription medications, a question exists as to whether the availability of varenicline without a prescription from a pharmacist could be reason for such plans to deny coverage of this medication. I am confident that the smoking cessation benefits that result from the greater availability of varenicline will be recognized to be sufficiently important to warrant coverage at the same or higher level, and that appropriate procedures can be developed and implemented to provide such coverage.

It is my hope that Pfizer will be strongly supportive of pharmacists being given the authority to provide varenicline without a prescription, and I am forwarding a copy of this letter to Mr. Ian Read, the CEO of Pfizer. The fact remains, however, that it is the FDA that has the authority to determine whether a medication may be available without a prescription.

I recognize that there are policies and procedures that would be typically observed in considering a change in the availability of a medication in the manner that I have recommended. However, I consider efforts that will help individuals stop smoking to be so important and urgent that they warrant special action. Indeed, I would urge you to make an executive decision to implement this recommendation that will significantly increase the availability of the medication that is most effective in addressing the most important public health challenge faced in our country. We must no longer accept the paradox in which toxins (cigarettes) are readily available requiring only proof of age to purchase, whereas the availability of the potential cure is restricted.

It is my expectation that there are some individual states in which there would be strong support for the recommendation I have made. However, it is my opinion that consideration of this matter by the FDA provides the best opportunity for effective, efficient, and timely action.

Thank you for your consideration of this recommendation.

Sincerely,

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Remington Professor of Pharmacy  
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cc: Mr. Ian Read, CEO, Pfizer  
Dr. Thomas Menighan, Executive Vice President, American Pharmacists Association  
Mr. Steven Anderson, President and CEO, National Association of Chain Drug Stores  
Mr. Douglas Hoey, CEO, National Community Pharmacists Association

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