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Veterans Health Administration
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UNDER SECRETARY FOR HEALTH'S INFORMATION LETTER

ANTIDEPRESSANTS AND SUICIDALITY

1. Black Box Warning. This Information Letter reviews the recent United States (U.S.) Food and Drug Administration (FDA) black box warning regarding an apparent increase in suicidality (suicidal ideation or behaviors) in the short term among young adults (18-24 years of age) treated with antidepressant medications. The FDA's warning was released on May 2, 2007, and is directly relevant to providers in the Veterans Health Administration (VHA) who are seeing increasing numbers of young veterans returning from Operation Iraqi Freedom and Operation Enduring Freedom requiring treatment with antidepressant medications for depressive disorders, anxiety disorders, or Post-traumatic Stress Disorder (PTSD). This document presents this information in the context of the broader risks regarding veteran suicide, and gives guidance regarding the clinical management of patients starting antidepressants or changing doses.

2. Background

a. An FDA-commissioned meta-analysis of randomized controlled trials of antidepressant medications among adults with psychiatric disorders was made public in November 2006. This meta-analysis indicated that the risks of suicidal ideation and behavior were increased in adults younger than 25 years of age, but not older adults, following the initiation of treatment with antidepressants.

b. The FDA report states: "When results are analyzed by age it becomes clear that there is an elevated risk for suicidality and suicidal behavior among adults younger than 25 years of age ... The net effect appears to be neutral … for adults between 25 and 64, and to reduce the risk … in subjects 65 years and older. Regardless of the exact mechanism, the observations contained in this review support the idea that antidepressant drugs can have two separate effects, one that promotes suicidality or suicidal behavior, and one that prevents it. The preventive effect may correlate with measures of clinical response. The relative susceptibility to these two effects varies with age. In older subjects, the preventative effect appears to predominate while in younger subjects the opposite is true. It is also likely that these effects vary among individuals of comparable ages. The observed relationship between suicidality, age, and antidepressant treatment appears to be generalized beyond subjects with major depressive disorder to all subjects with psychiatric diagnoses."

c. Suicide is the 11th leading cause of death in the U. S., accounting for 1.3 percent of all deaths. In the U.S., older individuals, whites, and men are more likely to commit suicide. Patients of any age with mental illnesses are at greater risk, and those with co-occurring disorders, such as depression and alcohol abuse, are at still higher risk.

d. The Department of Veterans Affairs (VA) population is at higher risk for suicide than the general U.S. population, by virtue of its demographics (predominantly male and older), and its clinical characteristics. However, it is less clear whether veterans have suicide rates that are higher than age-matched males in the U.S. population.

e. The FDA's recent analyses in adults receiving antidepressants extend findings that led to earlier warnings regarding increased risks for suicidality among children and adolescents. On October 15, 2004, the FDA issued a "black box" warning for antidepressant medications prescribed for youths, and urged close monitoring of children and adolescents in the 12 weeks following antidepressant starts or dose changes. In a separate announcement on June 30, 2005, the FDA urged similar close monitoring of adults with new prescriptions or dose changes. Although the recent FDA meta-analysis suggests that antidepressants may be protective in the short-term among adults older than 65, the FDA product labeling still states that: "Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior."

f. Close monitoring, during the weeks following the initiation of treatment or dose changes, is to facilitate timely detection of suicidality or suicidal behavior, and the early identification of symptoms that may lead to it. Close monitoring is needed to promote early detection of worsening depression, antidepressant induced mania, increased anxiety, dysphoria, restlessness, agitation, or other adverse effects that might follow antidepressant use and subsequently increase suicide risks.

g. In addition to the FDA meta-analysis of controlled clinical trials, there have been reports of an increased risk of suicidal behaviors soon after discharge from a psychiatric hospitalization or the initiation of antidepressant treatment in clinical settings. This effect has been attributed to activation as an early component of treatment response, but may also represent the periods of clinical worsening that occurs as part of patients' illness course and prompted the use of antidepressants. Regardless of the reasons for increased risk, these reports reinforce the need for a high-degree of clinical vigilance, and close monitoring for patients being treated for depression, especially after hospital discharge, after the initiation of treatment, and following dose changes.

3. Evaluation and Treatment

a. Findings suggest that an increase in the risk of suicidality in adults younger than 25 years of age receiving antidepressants should not constitute a barrier to antidepressant treatment for patients who need it. However, they point to the need for care in diagnosis and treatment planning, as well as in monitoring for those receiving these medications.

b. Clinicians should consider recommending evidence-based psychotherapies for depressive disorders, anxiety disorders, or PTSD instead of, or in addition to, antidepressant medications. Before prescribing antidepressants, clinicians need to carefully consider whether patients have disorders in which antidepressant medications are likely to be more effective than a placebo or watchful waiting. For example, patients with moderate to severe major depression clearly have better outcomes when prescribed antidepressant medication, while patients with minor depressive symptoms (depression, not otherwise specified) often do no better when prescribed antidepressants than when they receive a placebo or non-specific treatment. Patients with bipolar disease may deteriorate if they are treated with an antidepressant, but not a mood-stabilizer.

c. When patients are prescribed antidepressants, patients and involved family members need to be advised that antidepressant induced mania, anxiety, restlessness, agitation, dysphoria, or suicidal ideation may follow antidepressant initiation or dose changes. The emergence of these symptoms is to be communicated immediately to the patients' care providers.

d. Close monitoring is needed following the start of antidepressant treatment and after dose changes, especially for adults 25 years of age and younger. For some adults, an increased risk of suicidality or suicidal behavior may be due to antidepressant initiation or changes. For others, risks may be increased at these times as a result of the underlying psychiatric illnesses and symptoms.

e. There is no definitive data on the frequency, types, or content of visits that are adequate to ensure optimal detection of emergent suicidality or medication adverse effects. The current VA-Department of Defense clinical practice guidelines on major depressive disorder recommend that a patient be seen 1 to 2 weeks after starting treatment, then again at 4 to 6 weeks. Depression management programs that include regular, proactive follow-up contacts result in improved clinical outcomes for adults with major depression and anxiety disorders.

4. References. References may be found at website: www.mentalhealth.va.gov

5. Inquiries. Questions regarding this information letter may be addressed to (202) 273-8434.

Michael J. Kussman, MD, MS, MACP
Under Secretary for Health

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