Understanding the Implications of the FDA's Black Box Warning on Antidepressant Medication for Youth

by Peg Nichols

IN MID OCTOBER, the U.S. Food and Drug Administration (FDA) mandated "black box" warnings on *all* antidepressant medications prescribed to children and adolescents. The ruling followed a year of public scrutiny of the FDA, re-analysis of previous clinical trial data, widespread media coverage, and several hearings that examined the potential for suicidal thoughts and suicide attempts in clinical trials of selected antidepressants in pediatric patients with major depressive disorder (MDD) and other psychiatric conditions. As this article goes to press, members of the medical community continue to discuss and debate the FDA's ruling. *Attention!*® will apprise its readers of further developments in future issues of the magazine.

1. What is a black box warning?

A "black box" warning is the most serious warning placed in the labeling of a prescription medication. Until now, only 10 drug products approved for children contained a black box warning. The new warning language does not prohibit the use of antidepressants in children and adolescents. Rather, it warns of the risk of suicidal thoughts and encourages prescribers to balance this risk with clinical need. In addition, "reminder ads" (advertisements to health care professionals that promote a medication's availability) are now prohibited. The FDA also has determined that a Patient Medication Guide (MedGuide) highlighting precautions and associated risks must be given to patients (and their parents or caregiver) who take an antidepressant.

2. Why did the FDA take this step?

The FDA received widespread criticism for withholding critical information from physicians and the public about the safety and effectiveness of SSRI (selective serotonin reuptake inhibitor) antidepressant medications in children. Analysis of data revealed that 2–3 percent of pediatric patients in clinical trials showed increases in suicidal thoughts during the early stages of treatment that exceeded the risk from the disease being treated. Last March, the FDA mandated antidepressant manufacturers to include on medication labels a warning that antidepressants could lead some patients, children and adults alike, to have suicidal thoughts. This past September, following two days of testimony by experts, advocates and families whose children committed suicide while taking an SSRI antidepressant, the majority of an advisory committee of 31 independent experts recommended the black box warning.

3. If antidepressants have been shown to increase risks for suicide, how can a parent or caregiver feel safe about putting their child or adolescent on an antidepressant?

All treatments have potential risks and benefits. Parents and caregivers need and deserve access to as much information as possible in order to make fully informed decisions about treatment options. Children and adolescents who are taking antidepressant medication should be monitored closely by a physician, especially early in the course of treatment, or when medications are being changed or dosages adjusted. It is important to note that antidepressant medication usage—when carefully monitored by patient, family and physician—has proven largely effective in the treatment of depression in many patients.

4. How serious is the risk of suicide for depressed children or adolescents who take antidepressants?

For every 100 youth taking antidepressants, about two to three will think about or attempt suicide due to the medication, according to 24 studies of more than 4,600 children who took an antidepressant. There was not a single suicide in the studies. The risk of suicidal behavior associated with an antidepressant is greatest in the first four weeks after a patient begins taking the medication or changes the dose. Caregivers or parents of children or adolescents who begin taking an antidepressant should watch for changes that may signal worsening depression or increased risk of suicide, including anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, uncontrollable restlessness and mania.

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5. By contrast, how serious is the risk of suicide for depressed children or adolescents who *don't* take medication?

Scientists estimate that 2 million children and teenagers may be clinically depressed, yet only 20 percent receive treatment. Left untreated, the consequences can be devastating. Children and adolescents are likely to have ongoing problems in school, at home and with their friends. Forty percent will go on to have a second episode of depression within two years. They are also at increased risk for substance abuse, eating disorders and adolescent pregnancy. Research indicates that over half will eventually attempt suicide, and at least 7 percent ultimately will die as a result.

It is crucial to note that there is concern among physicians, mental health advocates and others that the black box label could discourage the use of antidepressants by adolescents who need them and that the negative risk of treatment is overshadowing the positive effects. Some fear that the black box warning will have a chilling effect on appropriate prescribing, putting seriously ill patients at grave risk. Suicide rates—while still tragically high—are now lower than they were a decade ago. Clinicians believe this is due to the availability and appropriate use of medication for children and adolescents who need it.

6. If I suspect my child has depression, what should I do?

Children and adolescents with signs and symptoms of depression need a comprehensive evaluation and an accurate diagnosis by a trained physician. Depression can sometimes be difficult to recognize. In addition, many youth also have signs and symptoms of a second psychiatric condition. An accurate diagnosis is essential to the development of an appropriate and effective treatment plan. **Critical note:** If you are the caregiver or parent of a child or adolescent currently taking an antidepressant, absolutely do not discontinue the medication on your own, without the input and oversight from the physician of record.

7. Are there alternatives to medication?

Medication is often an important component of treatment, but medication alone is rarely an appropriate intervention for complex child psychiatric disorders like depression. Not all young people with depression need to be treated with medication. In particular, research suggests that many children and adolescents with milder cases of depression respond well to psychotherapy. This is why it is essential to get a comprehensive evaluation and to carefully consider the full range of treatment options. A combination of medicine and talk therapy has been shown to be successful for 70 percent of young patients.

8. What's the bottom line?

Parents and caregivers need to be advocates for their children. Ask questions about the diagnosis and any proposed course of treatment. If you're not satisfied with the answers or the information you receive, seek a second opinion.

Above all, parents and caregivers should not hesitate to seek treatment for children or adolescents who suffer from depression. The good news is that depression is treatable. The greater travesty is the fact that too many children and adolescents aren't getting the appropriate and effective treatment that they need and deserve. ■

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Note: The text within this article reflects statements and statistics issued independently by the U.S. Food and Drug Administration, the American Academy of Child and Adolescent Psychiatry, the American Academy of Pediatrics and the American Psychiatric Association. This article was reviewed for clinical accuracy by Bruce Pfeffer, M.D., CHADD Professional Advisory Board member.