CE

Antidepressant Use in Children, Adolescents, and Young Adults: 10 Years After the Food and Drug Administration Black Box Warning

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ABSTRACT

Depression in children, adolescents, and young adults can jeopardize health status, well-being, and development. Almost a decade ago, risks and benefits of antidepressant use in this group prompted the Food and Drug Administration (FDA) to ask manufacturers to include black box warnings on antidepressant prescriptions. This article reviews initial FDA decisions related to black box warnings for antidepressants in youth, reviews effects of the warnings, and considers clinical implications of prescribing antidepressants for treatment of youth depression. Health care providers must consider the risks and benefits of initiating antidepressant medication treatment, closely monitoring adherence, patient outcomes, and suicidal ideation.

Keywords: adolescents, antidepressants, black box warning, children, depression, major depression, suicide

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The black box warning is set apart as the most prominent information included in a drug product's insert. A black box warning is indicated in the following 3 situations: (1) there is an adverse reaction so serious in proportion to the benefit from the drug that it is essential to be considered in assessing the risks and benefits of using the drug (including life-threatening or permanently disabling

This CE learning activity is designed to augment the knowledge, skills, and attitudes of nurse practitioners who prescribe antidepressants to children, adolescents, and young adults (CAYA).

At the conclusion of this activity, the participant will be able to:

A. Describe indications for an FDA black box warning for the use of antidepressants in CAYA.
B. Understand evidence for black box warning for antidepressants in CAYA
C. Consider clinical implications of prescribing antidepressants in CAYA

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The authors do not present any off-label or non-FDA-approved recommendations for treatment.

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adverse reactions); (2) there is a serious reaction that can be prevented or reduced by patient selection, careful monitoring, avoiding certain concomitant therapies, or managing a patient in a particular manner; and (3) the Food and Drug Administration (FDA) approved the drug with restrictions on use and distribution to ensure safe use.[1,2]

This article presents a review of the FDA decisions to issue black box warnings for prescription antidepressants for depression in children, adolescents, and young adults; presents a summary of evidence to date related to the effects of the warnings; and presents clinical implications related to initiating treatment of antidepressants and monitoring treatment effects for this population.

In 1906, Congress passed and President Theodore Roosevelt signed into law the Pure Food and Drugs Act.[3] Since then, Congress has enacted various laws regulating that new drugs on the market be safe for consumers. Currently, the FDA is the scientific, regulatory, and public health agency that regulates many products for the federal government of the United States. This agency is responsible for regulating food products, drugs, medical devices, radiating emitting devises, and cosmetics.[4] The mission of the FDA is to ensure that products made and sold to consumers in the US are safe, effective, and pure; today, the FDA's regulatory activity affects items that account for 25% of spending by consumers in the US.[5]

In 1970, the FDA required that the first patient information packet insert (which was for oral contraceptives) contain specific information for patients about their risks and benefits. In 1981, the FDA and the Department of Health and Human Services revised the regulations for human subject protection based on the 1979 Belmont Report.[3] In 1993, MedWatch was launched as a consolidation of several adverse reaction reporting systems designed for the voluntary reporting by health professionals of problems associated with medical products to be filed with the FDA, and in 2005 the Drug Safety Board was founded with the mandate to advise and communicate to health professionals and patients on drug-safety issues.[3]

Antidepressant Use in Children, Adolescents, and Young Adults Selective serotonin reuptake inhibitors (SSRIs) are commonly used psychotropic agents in treating children and adolescents with psychiatric disorders from preschool through early adulthood.[6] The use of SSRIs to address mood concerns/disorders in children began in 1988 when fluoxetine (Prozac) was introduced.[7] The use of SSRIs grew throughout the 1990s[6] despite controversy regarding their safety, efficacy, dosing recommendations, and need for monitoring. An analysis of data from the National Ambulatory Medical Care Survey for the years 1985, 1993, and 1994 revealed a doubling of psychotropic medication visits to psychiatrists for children and adolescents and an expanded use of SSRIs in psychiatry, primary care, and physician practices.[7]

Similar results were replicated in studies examining prescribing practices for stimulants and SSRIs through the North Carolina Medicaid System from 1992 to 1998[6] and in an analysis of health care systems in a Mid-Atlantic state and in a Midwestern state.[8] Despite the lack of FDA approval and methodologic flaws in existing pediatric SSRI trials, by the close of the century, the use of SSRIs in the pediatric population neared the same level of use as in the adult population.[6-8]

Because no non-SSRI medications showed effectiveness in children and adolescents with depression,[9] providers within psychiatry and primary care were generally willing to prescribe SSRIs to children and adolescents during the 1990s.[10] Initially, psychiatrists were the predominant prescribers of SRRIs. Zito et al[11] hypothesized that this practice was secondary to their earlier access to data on psychotropic drugs than their counterparts in primary care. By the end of the century, the majority of prescriptions for SSRIs used in the child and adolescent population were being written by generalists.[10,12]

Today, several other classes of antidepressants are being used to treat depression in youths; these are modifications of the earlier antidepressants. Known as "third-generation antidepressants," these medications include selective norepinephrine reuptake inhibitors, norepinephrine reuptake inhibitors, norepinephrine dopamine reuptake inhibitors, norepinephrine dopamine disinhibitors, and tetracyclic antidepressants.[13] To date, evidence does not clearly answer questions about the effectiveness and safety of these