

The Use of Medication in Treating Childhood and Adolescent Depression: Information for Physicians

**Prepared by the
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On October 15, 2004, the Food and Drug Administration directed pharmaceutical companies to label all antidepressant medications distributed in the U.S. with a black box warning that the medications "...increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) or other psychiatric disorders."¹ The warning states that the increased risk of suicidal thinking and/or behavior in a small proportion of children and adolescents is most likely to occur during the early phases of treatment. The FDA did not prohibit use of the medications in youth, but called on physicians and parents to closely monitor children and adolescents who are taking antidepressants for a worsening in symptoms of depression or unusual changes in behavior.

The American Psychiatric Association (APA) and the American Academy of Child and Adolescent Psychiatry (AACAP) represent the majority of the Nation's general psychiatrists and child and adolescent psychiatrists. The APA and AACAP share the concern that the FDA action may limit access to necessary, appropriate, and effective treatment for children and adolescents with depression, anxiety, and other psychiatric disorders.

Two competing issues emerged in the deliberations of the FDA advisory panel: A) a belief that the need for close monitoring of suicidal thoughts and behaviors among child and adolescent patients receiving antidepressant medications is essential and would be underscored by a black box warning, and B) awareness of the risk that a black box would have the unintended effect of limiting access to necessary, appropriate, and effective treatment. The APA and AACAP are concerned that the scientifically proven benefits of treating depression with antidepressants may be under-emphasized or even disregarded in current discussions of the potential risks of these medications.

¹ Food and Drug Administration. FDA public health advisory: suicidality in children and adolescents being treated with antidepressant medications [online]. 2004 Oct 15. Available at URL: <http://www.fda.gov/cder/drug/antidepressants/SSRIPHA200410.htm> [Accessed 2004 Dec 16]

Along with psychiatrists, pediatricians and other primary care physicians play a critical role in the provision of medical care for children and adolescents with depression and related disorders. Yet many physicians are finding that the black box warning is fostering fear and concern in families in which a child or adolescent is currently receiving appropriate and effective medical treatment, including medication, for depression. Such concerns have been intensified by contradictory and often confusing media reports about the purported risks that antidepressant medications pose to young patients.

Antidepressant medications are and will continue to be an important and valuable component of comprehensive treatment of pediatric mental disorders. For this reason, the APA and AACAP collaborated in preparing this Fact Sheet to provide physicians with accurate information on the appropriate use of these medications, as a component of a comprehensive treatment program for child and adolescent patients.

Prevalence and Impact of Child/Adolescent Depression

Depression and suicide are national public health problems for children and adolescents. Major depression affects an estimated 2.5% of children and 8.3% of U.S. adolescents. These rates account for approximately 2.6 million youth ages 6 - 17².

Clinical depression can affect every facet of a young person's life: family and peer relationships, academic performance, and general health through the effects of depression on concentration, eating, sleeping, and exercise patterns. Depression tends to be an episodic, recurrent illness. It frequently is associated with disabling anxiety and with thoughts of suicide experienced by 40- to 80% of youth with the illness³, suicide attempts by up to 35% of

² Birmaher B, Ryan ND, Williamson, DE, et al (1996). Childhood and adolescent depression: a review of the past 10 years. Part I. *J Am Acad Child Adolescent Psychiatry*, 35(11), 1427-39.

³ Haavisto A, Sourander A, Ellila H, Valimaki M, Santalahti P, and Helenius H (2003). Suicidal ideation and suicide attempts among child and adolescent psychiatric inpatients in Finland. *J Affect. Disord.* 76 (1-3), 211-221; Ryan ND, Puig-Antich J, Ambrosini P, Rabinovich H, Robinson D, Nelson B, et al. (1987). The clinical picture of major depression in children and adolescents. *Arch Gen Psychiatry*, 44, 854-861; Patton GC, Coffey C, Posterino M, Carlin JB, Wolfe R. (2000). Adolescent depressive disorder: a population-based study of ICD-10 symptoms. *Aust NZ J Psychiatry*, 34, 741-747; Roberts RE, Lewinsohn PM, Seeley JR (1995). Symptoms of DSM-III-R major depression in adolescence: evidence from an epidemiological survey. *J. Am. Acad. Child Adolesc. Psychiatry*, 34, 1608-1617; Grunbaum JA, Kann L, Kinchen S, Ross J, Hawkins J, Lowry R, et al. (2004). Youth risk behavior surveillance--United States, 2003. *MMWR Surveill Summ.*, 53, 1-96; Hallfors DD, Waller MW, Ford CA, Halpern CT, Brodish PH, Iritani B (2004). Adolescent depression and suicide risk: association with sex and drug behavior. *Am J Prev Med*, 27, 224-231.

depressed youth⁴, and, very rarely, completed suicides. Once a child or adolescent has one period of depression, he or she is likely to get depressed again at some point in the future⁵.

Depression is a serious medical illness and may be potentially lethal because of the risk of suicide. However, when recognized and correctly diagnosed, it can be treated successfully, using a combination of therapeutic approaches. These include medication, psychotherapy, or both, individualized to the needs of a child and his or her family.

Overview of Treatment Effectiveness and Suicidality

The effectiveness of treatment was demonstrated recently in a definitive study supported by the National Institute of Mental Health (NIMH). The Treatment of Adolescents with Depression Study (TADS)⁶ showed that a combination of fluoxetine (Prozac[®]) and cognitive behavior therapy (CBT) led to significant clinical improvement in 71% of moderately to severely depressed adolescent patients. Improvement rates for other treatment groups in the study were 61% for fluoxetine alone, 43% for CBT alone, and

⁴ Roberts RE, Lewinsohn PM, Seeley JR (1995). Symptoms of DSM-III-R major depression in adolescence: evidence from an epidemiological survey. *J Am Acad Child Adolesc Psychiatry*, 34, 1608-1617; Kessler R C Walters EE (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depress Anxiety*, 7, 3-14; Wichstrom L (2000). Predictors of adolescent suicide attempts: a nationally representative longitudinal study of Norwegian adolescents. *J Am Acad Child Adolesc Psychiatry*, 39, 603-610; Fombonne E, Wostear G, Cooper V, Harrington R, Rutter M, (2001). The Maudsley long-term follow-up of child and adolescent depression. 2. Suicidality, criminality and social dysfunction in adulthood. *Br J Psychiatry*, 179, 218-223; Haavisto A, Sourander A, Ellila H, Valimaki M, Santalahti P, and Helenius H (2003). Suicidal ideation and suicide attempts among child and adolescent psychiatric inpatients in Finland. *J Affect. Disord.* 76(1-3), 211-221; Ryan ND, Puig-Antich J, Ambrosini P, Rabinovich H, Robinson D, Nelson B, et al. (1987). The clinical picture of major depression in children and adolescents. *Arch Gen Psychiatry*, 44, 854-861; Grunbaum JA, Kann L, Kinchen S, Ross J, Hawkins J, Lowry R et al. (2004). Youth risk behavior surveillance--United States, 2003. *MMWR Surveill Summ*, 53, 1-96.

⁵ Lewinsohn PM, Clarke GN, Seeley JR, and Rohde P (1994). Major depression in community adolescents: age at onset, episode duration, and time to recurrence. *J Am Acad Child Adolesc Psychiatry* 33 (6), 809-818.

⁶ March J, et al (2004). Fluoxetine, Cognitive Behavioral Therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA* 292(7), 807-820

35% for placebo. This finding replicated two previous positive studies in pediatric populations^{7,8}.

A key finding of the TADS concerned the positive impact of treatment on suicidal thoughts and behaviors, or "suicidality," in depressed youngsters. Suicidal ideation is a key symptom of major depression. It is typically present before the start of antidepressant treatment and is one of the major symptoms targeted for treatment. Since mood disturbances often are among the last symptoms to remit in treatment, and because antidepressant medications typically require several weeks to exert a clinical effect, the initial changes in brain functioning brought about by treatment are often not adequate to suppress suicidal thoughts. In the event that worsening might occur, the physician, in collaboration with the child's parents or other family members, must appreciate the importance of intensively monitoring a pediatric patient to assure patient safety during the early stage of treatment. In some instances, hospitalization may be necessary, although the vast majority of patients respond to outpatient treatment.

Against this backdrop, it is noteworthy that in the TADS, 29% of the depressed young patients reported having clinically significant suicidal thoughts at baseline. At week twelve, the number of youth reporting any suicidal ideation had declined to 10%. Because youngsters who were most suicidal were excluded from the TADS sample, the proportion reporting suicidal thoughts when the study began was substantially lower than rates of suicidal ideation found in the community samples cited above (reference #3) of youth with major depressive disorder.

Without appropriate treatment, the consequences of depression are extremely serious. Children are likely to have ongoing problems in school, at home, and with their friends. Four of ten will have a second episode of depression within two years⁹. They are also at increased risk for substance abuse, eating disorders, and adolescent pregnancy¹⁰. Research indicates

⁷ Emslie GJ, Rush AJ, Weinberg WA, et al. (1997). A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. *Arch General Psychiatry* 54(11), 1031-37.

⁸ Emslie GJ, Heiligenstein JH, Wagner KD et al. (2002). Fluoxetine for acute treatment of depression in children and adolescents: a placebo-controlled, randomized clinical trial. *J Am Acad Child Adolesc Psychiatry* 41(10), 1205-15.

⁹ Lewinsohn PM, Clarke GN, Seeley JR, and Rohde P (1994). Major depression in community adolescents: age at onset, episode duration, and time to recurrence. *J. Am. Acad. Child Adolesc Psychiatry* 33 (6), 809-818.

¹⁰ Kessler RC, Avenevoli S, Merikangas KR (2001). Mood disorders in children and adolescents: an epidemiologic perspective. *Biol Psychiatry* 49(12), 1002-1014.

that over half of depressed youth will eventually attempt suicide, and an estimated 2- to 5% will die by suicide in the 10 to 20 years following an initial episode¹¹.

What Prompted the FDA Warning?

In 2004, the FDA reviewed 23 clinical trials involving more than 4,300 child and adolescent patients who received any of nine different antidepressant medications¹². **No suicides occurred in any of these studies.** Most of the studies that the FDA examined used two measures to assess suicidal thinking and behavior.

1) All used "Adverse Event Reports," which are reports made by the research clinician if a patient (or their parent) spontaneously shares thoughts about suicide or describes potentially dangerous behavior. The FDA found that such "adverse events" were reported by approximately 4% of all children and adolescents taking medication compared with 2% of those taking a placebo. One of the problems with using this approach to measuring suicidal thinking is that most teenagers do not talk about their suicidal thoughts unless they are asked¹³, in which case no report is filed.

2) In 17 of the 23 studies a second measure was also available. These were standardized forms asking about suicidal thoughts and behaviors completed for each child or teen at each visit. In the views of many experts these measures are more reliable than event reports. The FDA's analysis of the data from these 17 studies found that medication neither increased suicidality that had been present before treatment, nor did it induce new suicidality in those who were not thinking about suicide at the start of the study. In fact, on these measures, all studies combined showed a slight reduction in suicidality over the course of treatment. Although the FDA

¹¹ E. Fombonne, G. Wostear, V. Cooper, R. Harrington, and M. Rutter. (2001). The Maudsley long-term follow-up of child and adolescent depression. 2. Suicidality, criminality and social dysfunction in adulthood. *Br J Psychiatry* 179, 218-23; Rao M, Weissman M, Martin JA, Hammond RW (1993). Childhood depression and risk of suicide: a preliminary report of a longitudinal study. *J Am Acad Child Adolesc Psychiatry* 32(1), 21-27.

¹² T.A. Hammad. Results of the Analysis of Suicidality in Pediatric Trials of Newer Antidepressants. Presentation at the FDA Center for Drug Evaluation and Research (CDER), Bethesda, MD. September 13, 2004. Available at: www.fda.gov/ohrms/dockets/ac/cder04.html#PsychopharmacologidDrugs. Accessed January 5, 2005.

¹³ Gould MS, Velting D, Kleinman M, Lucas C, Thomas JG, Chung M (2004). Teenagers' attitudes about coping strategies and help-seeking behavior for suicidality. *J Am Acad Child Adolesc Psychiatry*, 43(9), 1124-33.

reported both sets of findings, they did not comment on the contradiction between them.

Hence, the 2% and 4% spontaneous report rates need to be understood in the context of findings from community samples cited previously in which as many as half or more of teenagers with major depression are thinking about suicide at the time of diagnosis and some 16% to 35% have made a previous suicide attempt.

Although only nine medications were re-examined in the analysis, the FDA applied the labeling changes to all antidepressant medications. This was done on the basis of the advisory committee's perception that currently available data are inadequate to exclude any single medication from being potentially associated with the same increased risk for spontaneous reports of suicidal thinking and/or behavior found in the 23 studies.

Suicidality in Adolescence

Suicidal ideation and suicide attempts are common in adolescence and do not have the same prognostic significance for completed suicide as those behaviors in later life.

The federal Centers for Disease Prevention and Control, or CDC, reports that 17% of adolescents think about suicide in a given year¹⁴. Among high school students, 12% of girls and 5% of boys attempt suicide in a given year. Ultimately, 2 per 100,000 girls and 12 per 100,000 boys die as a result of such attempts — a ratio of attempts to completed suicide that is 6,000 to 1 among girls and 400 to 1 among boys. In the U.S., this translates into approximately 2000 young people who die each year as a result of suicide.

Fortunately, the overall rate of suicide in the 10-19 year age range has declined by 25% over the past decade. Since this decade has been associated with a dramatic increase in the prescription rates of the newer SSRI antidepressants, a recent study has demonstrated that a 1% increase in prescription of antidepressant medication was associated with a 0.23 per 100,000 decrease in adolescent suicides¹⁵.

It is important to consider clinical trial data in the context of these population-based data. In its review of 23 clinical trials involving child and adolescent subjects who received any of nine different antidepressant

¹⁴ Available at www.cdc.gov/HealthyYouth/YRBS/pdfs/trends-suicide.pdf. Accessed 12/29/2004

¹⁵ Olfson M, Shaffer D, Marcus SC, Greenberg T. (2003). Relationship between antidepressant medication treatment and suicide in adolescents. Arch Gen Psychiatry 60, 978-982.

medications, the FDA combined the rates for suicidal thoughts and suicide attempts under the general term “suicidality.” This has fostered a public impression that there is a high rate of suicide attempts or even completed suicides in children and adolescents that can be attributed to taking antidepressant medication; in fact, suicidal thoughts and actions decline with medication and psychotherapy treatments, and there were no completed suicides in the studies reviewed by FDA. *Suicidal thoughts or attempts do not equal suicides.*

Every suicide is a personal tragedy that may be linked to inadequate treatment monitoring or severe adverse side-effects of a medication. Yet the rise in overall population treatment rates with antidepressant medication has not been associated with a rise in completed suicides in the larger population — in fact, there has been a substantial decrease in completed suicides over the past decade. Likewise, the higher spontaneous reports of suicidal ideation and attempts (referred to by the FDA as “adverse events”) in children on antidepressants compared with placebo, has not been correlated with systematic assessments of suicidal ideation or attempts increasing with these medications. Research is needed to determine how the relatively low rate of spontaneous reports of adverse events is related to the much higher systematically assessed rates of suicidal ideation and attempts, and which more clearly indicate a risk for completed suicide.

In an illness where unwanted and spontaneous suicidal thoughts are integral symptom components, treatment that increases communication about these symptoms can lead to more appropriate monitoring and decreased risk for the adverse event of greatest concern — i.e. completed suicide.

Recognition and Diagnosis of Childhood/Adolescent Depression

Extensive research has identified the signs and symptoms of major depression¹⁶. In children, these classic symptoms often may be obscured by other behavioral and physical complaints – features such as those in the right column of the table below. At least five symptoms must be present to the extent that they interfere with daily functioning over a minimal period of two weeks.

¹⁶ American Psychiatric Association (2004). Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR). Washington, DC: American Psychiatric Association.

DSM-IV Symptoms of Major Depressive Disorder	As Frequently Seen in Youth
Depressed mood most of the day	Irritable or cranky mood; Preoccupation with nihilistic song lyrics
Decreased interest/enjoyment in once-favorite activities	Loss of interest in sports, video games, and activities with friends
Significant weight loss/gain	Failure to gain weight as normally expected; anorexia or bulimia; frequent complaints of physical illness, e.g., headache, stomach ache
Insomnia or hypersomnia	Excessive late-night TV; refusal to wake for school in the morning
Psychomotor agitation/retardation	Talk of running away from home, or efforts to do so
Fatigue or loss of energy	Persistent boredom
Low self-esteem; feelings of guilt	Oppositional and/or negative behavior
Decreased ability to concentrate; indecisive	Poor performance in school; frequent absences
Recurrent suicidal ideation or behavior	Recurrent suicidal ideation or behavior

The diagnosis of depression or other psychiatric disorders should be made only in the context of a complete medical examination to identify and/or eliminate any comorbid and/or confounding psychiatric or somatic conditions. More than half of all youth with MDD have other psychiatric disorders, with a significant proportion having two or more disorders¹⁷.

Major depression, or clinical depression, is one form of the larger group of mood disorders. These include *dysthymia*, a mood disorder in which symptoms generally are less severe than in major depression, but the illness is marked by a more chronic and persistent course. Another form of the illness is *bipolar disorder* in which periods of depression alternate with periods of mania, the hallmarks of which are unnaturally high levels of energy, grandiosity, and/or irritability. Bipolar disorder may first appear as a depressed episode. Research has shown that treating unrecognized bipolar depression with antidepressant medications may trigger the manic phase of the illness. Children who have a family history of bipolar disorder will require special treatment considerations that should be addressed in any comprehensive treatment plan.

¹⁷ American Academy of Child and Adolescent Psychiatry (1998), Practice Parameters for the Assessment and Treatment of Children and Adolescents with Depressive Disorders. *J Am Acad Child Adolesc Psychiatry*, 37(10suppl), 63s-83s.

Clinical experience suggests that depression in younger children may be a heterogeneous disorder with multiple etiological factors. Adolescent depression appears to demonstrate greater continuity with major depressive disorder in adults.

Risk Factors for Suicide

Most patients with a depressive disorder do not plan, attempt, or complete suicide; however, an estimated 60% of people who die by suicide have had a mood disorder; among younger patients, comorbid substance use disorders are also common¹⁸.

Suicidal behavior is complex. Some risk factors vary with age, gender and ethnic group and may even change over time. Risk factors for suicide frequently occur in combination. Adverse life events in combination with other strong risk factors, such as depression may lead to suicide. However, suicide and suicidal behavior are not normal responses to the stresses experienced by most people. Many people experience one or more risk factors and are not suicidal.

Research evidence and clinical experience are generally in concurrence that the two key risk factors for suicide are a) the presence of one or more diagnosable mental disorders – particularly a depressive disorder or an aggressive/disruptive disorder – occurring alone or comorbid with an alcohol or other drug use disorder, and b) a prior suicide attempt.

Research has identified an array of more general factors associated with suicide. These include, but are not limited to, impulsivity; a family history of mental or substance abuse disorder; a family history of suicide; family violence, including physical or sexual abuse; the presence of a firearm in the home; incarceration; and exposure to the suicidal behavior of others, including family, peers, or in the news or fiction stories. Clinicians have found that the immediacy of the threat posed by these general risk factors may be influenced by the two key factors listed above, that is, the presence of mental and/or substance abuse disorders and history of a prior suicide attempt.

It is important to note, however, that none of these risk factors are linked specifically to use of antidepressant medications by children and adolescents.

¹⁸ Pfeffer CR (2001). Diagnosis of childhood and adolescent suicidal behavior: unmet needs for suicide prevention. *Biological Psychiatry*, 49, 1055-1061.

Does Talking About Suicide Signal Increased Likelihood That A Child Will Hurt Him/Herself?

Any expression of suicidal thoughts or feelings by a child or adolescent is a clear signal of distress and should be taken very seriously by health care professionals, parents, family members, and others.

Psychiatrists and other mental health specialists have found that when a young person verbalizes suicidal thoughts, it often opens the door to communication regarding the need to take special safety precautions or protective measures; thus any therapeutic intervention that increases discussion of latent, or hidden, suicidal thoughts or impulses is helpful. Much more worrisome and potentially dangerous is a young person with depression who successfully hides the fact that he or she is having suicidal thoughts.

Treating Childhood and Adolescent Depression

The physician, in consultation with the patient and parents/guardians, should develop a comprehensive treatment plan. This typically will include individual psychotherapy, medication, or combined psychotherapy and medication, and work with the child's family and/or school. Several months of treatment may be necessary before depressed mood and accompanying suicidal thoughts and feelings begin to improve.

Evidence-based strategies for comprehensive treatment plans for major depressive disorder are available in AACAP's Practice Parameter on Depressive Disorders¹⁷ and the APA Practice Guideline on the Treatment of Patients with Major Depressive Disorder¹⁹.

Medication alone and/or psychotherapy alone are efficacious in the treatment of depression, but the combined treatments are the best and, when possible, they are preferred. Moreover, not all young people with depression need to be treated with medication. Many children and adolescents with uncomplicated major depressive disorder respond well to psychotherapy^{20,21,22}. Cognitive behavioral therapy (CBT), and interpersonal

¹⁹ American Psychiatric Association (2000). Practice Guideline for the Treatment of Patients with Major Depressive Disorder (Revision). *Am J Psychiatry* 157(4), suppl:1-45.

²⁰ Elkin I, Gibbons ID, Shea T, et al. (1995). Initial severity and differential treatment outcome in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *J Consult Clin Psychol*, 63, 841-847.

²¹ Brent DA, Holder D, Kolko D, et al (1997). A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. *Arch Gen Psychiatry* 54, 877-885.

therapy (IPT) have been shown to be effective in treating milder forms of depression as well as anxiety and OCD.

- The aim of CBT is to help a patient recognize and change negative patterns of thinking that may contribute to depression.
- Depression and other mental disorders frequently affect interpersonal relationships and roles in those relationships. The aim of IPT is to help an individual to address issues such as interpersonal disputes or conflicts, role transitions, or other events that seem to be most important in the onset and/or maintenance of depression.

Simply seeing a skilled health professional regularly for several weeks will result in a reduction in the symptoms of depression in about a third of teenagers. Although this is sometimes confused with a "placebo effect," the interest and support of a health care professional does have a more positive impact on symptom response than neglect or denial of the patient's condition²³.

At the initial diagnostic assessment and every subsequent clinical encounter, the physician should ask a patient directly about the occurrence of suicidal thoughts or behaviors in the current episode of illness.

General strategies for suicide prevention should be employed if a child, or any member of a family, has depression. Lethal means, such as guns should be removed from the house, and large quantities of dangerous medications, including over-the-counter medications, should not be left in an accessible location. The physician should work with families to develop an emergency action plan, including access to a 24-hour number available to deal with crises.

Parents should be advised to contact the supervising physician immediately if a child voices new or more frequent thoughts of wanting to die or to hurt him- or herself, or takes steps to do so.

When used in combination with a medication, interventions such as CBT may have a significant protective effect against suicidal ideation and/or behaviors⁵.

²² Geller B (1994). Should tricyclic antidepressants be prescribed to depressed children and adolescents? *Curr Opin Psychiatry* 7, 301-303.

²³ Fawcett J et al (1987). Clinical management-imipramine/placebo administration manual: NIMH Treatment of Depression Collaborative Research Program. *Psychopharmacology Bulletin*, 23, 309-324.

Suggestions for Physicians When Prescribing Antidepressant Medication to Pediatric Patients

Among the antidepressants, one – fluoxetine, or Prozac® – is formally approved by the FDA for treating depression in pediatric patients – based on evidence of greater effectiveness than placebo in carefully designed clinical trials. Prozac and three other medications – sertraline (Zoloft®), fluvoxamine, and clomipramine (Anafranil®) – are approved for treating obsessive-compulsive disorder (OCD) in children and youth.

Off-label prescribing of antidepressants to child and adolescent patients is common and consistent with general clinical practice. Of the approximately 30% to 40% of children and adolescents who do not respond to an initial medication, a substantial number will respond to an alternate medication.

The physician should describe and discuss with parent/guardian and with the child or adolescent patient the risks and benefits of any treatment, including treatment with medication.

If no clinical response is evident in 6-8 weeks, the physician should reevaluate the treatment plan and consider modifications, as appropriate. Consideration of an alternative treatment is not limited to youth who are being treated with medication, but also to those receiving psychotherapy or other interventions.

Monitoring A Child/Adolescent Receiving Antidepressant Medication

Careful monitoring by physicians and parents of children's mental health and behavioral status upon initiation of antidepressants and changes in medications and/or dosages is critically important.

The FDA recommends that "ideally" a child receiving antidepressants will be seen by the prescribing physician once a week for the first four weeks of treatment; biweekly for the second month of treatment; and at the end of the 12th week on medication. The APA and AACAP believe that rather than requiring adherence to a prescribed schedule, the frequency and nature of monitoring should be individualized to the needs of child and family.

The physician should enlist parents/guardians in the responsibility of monitoring. Family members should contact their child's physician if the child or adolescent patient:

- expresses new or more frequent thoughts of wanting to die, or engages in self-destructive behavior;
- shows signs of increased anxiety/panic, agitation, aggressiveness, or impulsivity;

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- experiences involuntary restlessness (akathisia), or an extreme degree of unwarranted elation or energy accompanied by fast, driven speech and unrealistic plans or goals.

Adverse reactions to antidepressant medication are most likely to occur early in the course of treatment. It may be appropriate to adjust the dosage, change to a different medication, or stop using medication. In a small number of instances, a child or adolescent might have extreme reactions to antidepressants or other commonly used medications such as penicillin or aspirin as a result of genetic, allergic, drug interaction, or other unknown factors.

If a child/adolescent pediatric patient is being treated with a medication and is doing well, he or she should continue with the treatment.

No patient should abruptly stop taking antidepressant medications because of the possibility of adverse withdrawal effects such as agitation or increased depression. The physician should convey to parents the importance of consulting with the physician before changing or terminating their child's antidepressant treatment.

Which Medications Will Carry The Warning Label?

• Anafranil (clomipramine HCl)	• Paxil (paroxetine HCl)
• Aventyl (nortriptyline HCl)	• Pexeva (paroxetine mesylate)
• Celexa (citalopram HBr)	• Prozac (fluoxetine HCl)
• Cymbalta (duloxetine HCl)	• Remeron (mirtazapine)
• Desyrel (trazodone HCl)	• Sarafem (fluoxetine HCl)
• Effexor (Venlafaxine HCl)	• (Nefazodone HCl)
• Elavil (amitriptyline HCl)	• Sinequan (doxepine HCl)
• Lexapro (escitalopram oxalate)	• Surmontil (trimipramine)
• Limbitrol (chlordiazepoxide/amitriptyline)	• Symbyax (olanzapine/fluoxetine)
• Ludiomil (Maprotiline HCl)	• Tofranil (imipramine HCl)
• (fluvoxamine maleate)	• Tofranil-PM (imipramine pamoate)
• Marplan (isocarboxazid)	• Triavil (Perphenazine/Amitriptyline)
• Nardil (phenelzine sulfate)	• Vivactil (protriptyline HCl)
• Norpramin (desipramine HCl)	• Wellbutrin (bupropion HCl)
• Pamelor (nortriptyline HCl)	• Zoloft (Sertraline HCl)
• Parnate (tranylcypromine sulfate)	• Zyban (bupropion HCl)
	All antidepressant medications under development now and in the future

Treatment of Depression Outcome Measures

The American Academy of Pediatrics recommends tools such as the Beck Depression Inventory and the Children's Depression Inventory-Revised for use in monitoring a child's response to treatment. While rating scales are

not definitive for diagnosing depression, they can help guide questions during follow-up monitoring appointments.

Additional depression screening and severity measurement tools developed specifically for adolescents are currently in development. The APA and AACAP will disseminate information on these instruments as it becomes available.

Future Directions

The controversy and conflicting information surrounding the prescribing of antidepressant medications to children and adolescents has underscored the importance of ongoing discussions regarding need for a comprehensive national registry of clinical trials that is readily accessible to physicians, researchers and the general public. The AACAP and APA were at the forefront in calling for the development of such a registry.

The APA and AACAP also will continue to participate in and monitor important ongoing research that will shed additional light on questions surrounding antidepressant medications and pediatric patients. The National Institute of Mental Health [see <http://www.nimh.nih.gov/studies/index.cfm>] is currently funding three potentially informative projects. These include:

- the Treatment of Resistant Depression in Adolescents, or TORDIA study, designed to determine how to best treat adolescents with depression that is "resistant" to the first SSRI antidepressant they have tried. Participants receive one of three other antidepressant medications, either alone or in combination with cognitive behavioral therapy.
- the Treatment of Adolescent Suicide Attempters, or TASA study, in which participants are randomly assigned to receive carefully monitored antidepressant medication with routine support and management, cognitive behavioral therapy (CBT), or a combination of antidepressant medication plus CBT.
- Finally, data derived from the extended phase of the year-long TADS – only results of the first 12 weeks have been published, as discussed in this Fact Sheet – are being analyzed and promise to significantly enhance our understanding of long-term outcomes associated with the treatments under study.

The APA and AACAP will update this Fact Sheet as additional information becomes available from these sources as well as investigator-initiated and industry-sponsored studies.

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Endorsers

Depression and Bipolar Support Alliance, (www.dbsalliance.org)
Families for Depression Awareness (www.familyaware.org)
American Society for Adolescent Psychiatry (www.adolpsypch.org)
National Association of Psychiatric Health Systems, (www.naphs.org)
Society for Adolescent Medicine (www.adolescenthealth.org)
American Association of Suicidology (www.suicidology.org)
American Foundation for Suicide Prevention (www.afsp.org)
Suicide Awareness Voices of Education (www.save.org)

Disclaimers:

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