FDA on the Defensive:
Do Antidepressants Harm Children?

The U.S. Food and Drug Administration (FDA) finds itself in a real pickle on the subject of drugs for depression. On the one hand, there have been anecdotal reports that children in particular are vulnerable to the side effects of 10 antidepressants. These drugs were the subject of the FDA’s Public Health Advisory, issued on March 22, 2004. Claims that the drugs were inducing suicides were taken seriously and led to warnings from the United Kingdom’s Department of Health, beginning in the summer of 2003, against prescribing any selective serotonin reuptake inhibitors (SSRIs) except fluoxetine (Prozac®, Eli Lilly) for depressed youths under 18 years of age.

On the other hand, these 10 drugs may be life bearable for probably hundreds of thousands of patients suffering from the otherwise debilitating effects of mental illness. That explains the FDA’s “go slow” approach, with its Public Health Advisory being the latest manifestation.

The advisory asked physicians to “closely monitor all patients” taking antidepressants for “worsening depression and suicidal thinking, which can occur during early periods of treatment.”

The FDA also asked the manufacturers of the 10 drugs to include “stronger cautions and warnings” about the need for patient monitoring in their labels. The warning label request was directed at the makers of bupropion (Wellbutrin®, GlaxoSmithKline), citalopram (Celexa™, Forest), fluoxetine, fluvoxamine (Luvox®, Solvay), mirtazapine (Remeron®, Organon), nefazodone (Serzone®, Bristol-Myers Squibb), paroxetine (Paxil®, GlaxoSmithKline), sertraline (Zoloft®, Pfizer), escitalopram (Lexapro™, Forest), and venlafaxine (Effexor®, Wyeth). Only fluoxetine has been approved for depression in children. Several of these drugs, such as sertraline, fluoxetine, and fluvoxamine, have been approved for the treatment of obsessive-compulsive disorder in pediatric patients.

Jennifer Yoder, a spokesperson for Eli Lilly and Company, said that Lilly would change the Prozac® label to support the FDA’s “efforts to increase awareness of mood changes in depressed patients who are inherently at risk of suicidal thinking.” However, she emphasized that the FDA has not linked antidepressants to suicide in children and that patients, regardless of their age, should not stop taking medication without first talking with their physicians.

Statements such as this one from Lilly might sound self-serving, but at least one major report from a credible medical group has emphasized the benefits of antidepressants over their costs in terms of potential adverse drug effects. Lawrence Greenhill, MD, chair of the American Academy of Child and Adolescent Psychiatry (AACAP) Pediatric Pharmacology Initiative and Ruane Professor of Clinical Psychiatry at Columbia University, appeared before two FDA advisory committees on February 2, 2004. He praised a report that had been produced by a Task Force of the American College of Neuropsychopharmacology (ACNP). He said that the report, dated January 21, 2004, showed “that the evidence for the benefits of SSRIs—as a treatment for depression—outweigh their risks.” He added that the Task Force “did not find evidence for a link between SSRIs and increased risk of suicide in children and adolescents.”

Two months before the FDA issued its advisory asking for additional labeling, Dr. Greenhill argued that the current labeling already carries precautionary language on the possibility of suicide attempts. His implication—that psychiatrists are well aware of the possible risk—was echoed by Suzanne Vogel-Scibilia, MD, who appeared before the advisory committees on behalf of the National Alliance for the Mentally Ill (NAMI), a nonprofit support group.

“NAMI is concerned that any limitations on the ability of knowledgeable practitioners to treat children with SSRIs, when needed, could be damaging to children in our country—especially those with serious, life-altering illnesses,” she told the advisory committees.

Given the important timeline that antidepressants represent, no one wants to pull them from the pharmacy shelves prematurely or without “cause.” The question remains: is there cause? No one has the foggiest idea of how many children might have been driven to suicide by the SSRIs. Moreover, we do not know the converse: how many children who might have otherwise harmed themselves were prevented from doing so by antidepressant therapy?

More answers should be forthcoming from a study now under way at Columbia University. One critic of the antidepressants, Vera Hassner Sharav, MLS, the whirlwind force behind the Alliance for Human Research Protection, has raised conflict-of-interest objections to the psychiatrists at Columbia who are conducting the study. Columbia University is a major psychiatric drug research center. Its psychiatrists and the institution receive millions of dollars from pharmaceutical companies to test their psychotropic drugs in adults and children. The same argument could be made for the psychiatrists on the ACNP’s Task Force.

That is a reasonable concern. Questions about the link between antidepressants and adverse effects are much too important to have any answers sullied by doubts over the impartiality of investigators.