Warning Urged for ADHD Drugs

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Several drugs widely used to treat attention-deficit hyperactivity disorder should carry a prominent "black box" warning because of reports that they may have caused sudden deaths or serious complications, a federal expert advisory panel recommended yesterday.

The proposal to require a warning on medications such as Adderall and Ritalin took the Food and Drug Administration, pharmaceutical companies and advocates by surprise. The panel voted 8 to 7 to call for the labelling change after reviewing reports of several dozen patients who suffered cardiac arrest, toxic reactions or sudden death while using the medications.

Members of the board said the recommendation was driven as much by worries that the drugs are being overused in the United States as by the possible side effects: About 10 percent of 10-year-old American boys are taking such medications, and there have been recent sharp increases in the number of adults taking them.

"On the surface, it is hard to believe," said Curt Furberg, professor of public health sciences at North Carolina's Wake Forest University Medical School, who voted for the black-box warning. "What is also interesting is this condition is not really recognized in other countries -- you wonder what we are treating. I am sure there are patients who need these drugs, but it is not 10 percent of all 10-year-old boys."

FDA officials, who convened the panel to discuss how best to assess the risks of the drugs, said they would weigh the recommendation. The panel called for warning labels on methylphenidate drugs, sold under the brand names Ritalin, Concerta, Methylin and Metadate, and on the amphetamines Adderall and Adderall XR.

The FDA usually follows the advice of advisory panels but is not required to do so. How the agency will act in this case is especially uncertain because the recommendation clearly went further than the agency had thought necessary.

"The committee plainly wanted to tell us that certain things ought to be in labeling in a more forceful way," said Robert Temple, director of the FDA's Office of Medical Policy. Asked whether the panel's action surprised him, he said, "I don't know if taken aback is quite the word . . . it does not astonish me, but it wasn't the primary matter for what we went to them for."

Yesterday's action came 16 months after the FDA called for black-box warnings on several antidepressant drugs, including Prozac, Paxil and Zoloft, because of indications that they triggered suicidal thinking in some patients.

Black-box warnings are intended to alert physicians and patients that a drug may carry significant risks; fewer than 10 percent of prescription drugs carry them, according to a 2002 study.

Matthew Cabrey, spokesman for Shire Pharmaceuticals, which sells Adderall, said the company stands by the safety of its product. He said 8.7 million prescriptions for the drug were written last year, generating $700 million in sales. Novartis Pharmaceuticals, maker of Ritalin, said it saw no evidence of a higher rate of heart problems in patients taking its drug.

IMS Health, which tracks the industry, said sales of all ADHD drugs totaled $3.1 billion in 2004, the Associated Press reported.

ADHD is characterized by inattention and restlessness and has been associated with poor performance in school, conduct problems and drug abuse. While diagnosis is most common in children, especially boys, physicians have recently started writing more prescriptions for adults.

Cardiologist Steven Nissen of the Cleveland Clinic, who was one of the committee members who pushed for the warning label, said the growing use of ADHD drugs in adults is a serious concern because the risk of heart attack rises among adults older than 50.

Much as in the debate over antidepressants, Nissen and Furberg said the committee was not just weighing uncertain signals of risk but broader questions, such as how often the drugs are used and the impact of drug industry marketing. A black-box warning would probably curb direct-to-consumer advertising.

While the FDA is traditionally responsible only for regulating drugs and is not supposed to get into the practice of medicine, Nissen and Temple indicated that concerns about medical practice are playing a role in their discussions. Temple said he is concerned that a warning on ADHD drugs might drive away patients and scare physicians, while Nissen said something must be done to curb spiraling prescription rates.

"I felt strongly we need to slow the growth of utilization," Nissen said, adding that about 2.5 million children and 1.5 million adults are taking the drugs. "When you have that kind of exposure for drugs that are suspicious, that does create a major public health concern."

Ginny Thiersch, a spokeswoman for the advocacy group Children and Adults With Attention-Deficit/Hyperactivity Disorder, cautioned that patients should not be alarmed by the warning. "They should definitely not stop taking their medications," she said. "They should consult with their clinician if they have questions, but for so many people these medications are an important part of a very effective treatment."