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FDA Panel Recommends Warnings of Rare Reports of Aggressive Behavior or Psychotic Symptoms By Todd Zwillich

WebMD Medical News Reviewed By Louise Chang, MD
on Thursday, March 23, 2006

March 23, 2006 -- Government advisors urged new warnings and information for parents of children using drugs to treat attention deficit hyperactivity disorder (ADHD), though they avoided strong safety alerts backed by a separate panel last month.

A committee of mostly pediatric experts urged the FDA to warn doctors and parents about reports linking popular stimulant drugs to aggressive behavior, manic episodes, and psychotic symptoms like hallucinations.

The reports remain rare among the estimated 2 million American children who fill stimulant prescriptions each month. But experts said that events appeared often enough that parents and their doctors should be alerted so that they can stop the drug if such problems arise in their children.

They recommended that warnings be included in medication guides distributed to parents along with children's prescriptions.

"[Parents should] be aware that this could happen, and it may be a justification for stopping the drug," says Robert Nelson, MD, a critical care specialist at the Children's Hospital of Philadelphia and the panel's chairman.

Psychiatric Effects

Some reports of suicidal thoughts or behaviors have cropped up in children and adolescents taking some stimulant medications. Those reports were most common with the ADHD drug Strattera, which is not a stimulant and already carries a "black box" alert warning of potential suicide risk. The committee concluded that further suicide warnings for stimulant drugs, including Ritalin, Concerta, and Adderall XR, are not warranted at this time.

The agency received hundreds of reports of aggressive behavior during the last five years in children taking stimulant drugs. Most of the events were reported as mild, though up to 20% resulted in a significant injury or hospitalization, the agency says. The labels of most stimulant drugs don't warn of a potential for aggressive behavior.

Aggression is a common symptom of ADHD, so some outbursts would still be expected in patients taking medication, researchers say.

But reports in the studies appeared to be significantly more common in children taking active drugs than in those who took placebos, and experts urged the FDA to add new warnings alerting parents and doctors to consider withholding treatment if new aggressive behavior arises with the drug.

"Take the child off of it, see what happens. Those are messages we don't give out enough," says Lauren L. Leslie, MD, a member of the panel and a researcher at the Child and Adolescent Services Research Center in San Diego.

Experts also recommended new labels warning of a possibility of hallucinations and mania amid dozens of reports that such symptoms can arise for the first time in children taking ADHD drugs.

Tom Laughren, MD, head of the FDA's division of psychiatric products, says the committee appeared "unimpressed" by more than 350 reports of suicidal thoughts or behaviors in treated children over the last five years. Up to 20% of middle and high school students already report such thoughts, and it was unclear that drugs other than Strattera led to increased risk, he noted.

But Jacqueline Bessner, of Ishpeming, Mich., told the committee in a tearful statement that she and her husband were never told to be on the lookout for suicidal behavior in their daughter, Leanne. The 15-year-old committed suicide last October 2.5 months after starting treatment with Concerta.

"There was no warning to us that this could have psychiatric behaviors" as side effects, Bessner tells WebMD.

Cardiovascular Risks

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A separate expert panel last month surprised regulators by urging new "black box" warnings of cardiovascular risks in the growing number of adults taking stimulant ADHD drugs.

The drugs are known to increase blood pressure and pulse, and the recommendation came after preliminary reports suggesting that heart attacks and strokes were far more common in adults taking the drugs than in individuals who don't.

Experts said that such a warning was not warranted in children, since reports showed little sign that the drugs increase cardiovascular risk in otherwise healthy kids.

"In the general run-of-the-mill kid I think they're generally well tolerated. I don't see much risk at all if they don't have a heart condition," said John W.M. Moore, a pediatric cardiologist at the Mattel Children's Hospital at UCLA and a member of the panel.

Four sudden heart deaths were reported in children taking Adderall XR. Panelists said the events were most likely due to undiagnosed heart disease in the children. The risk of stimulant medications in such children should be added to labels, experts said.

Matthew Cabrey, a spokesman for Adderall manufacturer Shire Pharmaceuticals, said that the company "agrees with and is supportive" of calls to highlight adverse events that can occur with use of the drug.

The FDA has not yet issued a decision on last month's call to add black box heart warnings for adults.

"We have some work to do in adults," said Robert Temple, MD, the FDA's director of medical policy.

SOURCES: Robert Nelson, MD, Children's Hospital of Philadelphia Department of Critical Care, chair, FDA panel. Lauren Lesley, MD, Child and Adolescent Services Research Center, San Diego. Jacqueline Bessner, of Ispeming, Mich. John W.M. Moore, Mattel Children's Hospital at UCLA; member, FDA panel. Matthew Cabrey, spokesman, Shire Pharmaceuticals. Robert Temple, MD, director, medical policy, FDA.

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