

## **Feds Recommend Warnings on ADHD Drugs**

By ANDREW BRIDGES, Associated Press Writer 1 hour, 34 minutes ago

### **WASHINGTON -**

Ritalin and other stimulant drugs for attention deficit hyperactivity disorder should carry the strongest warning that they may be linked to an increased risk of death and injury, federal health advisers said Thursday.

The Food and Drug Administration advisory panel voted in favor of the "black box" warning after hearing about the deaths of 25 people, including 19 children, who had taken the drugs. The vote was 8-7, with one abstention.

One committee member, Dr. Curt Furberg, a professor of public health sciences at the Wake Forest University Baptist Medical Center, said it would be "inappropriate, unethical behavior" not to disclose that there was uncertainty about the safety of the drugs.

The FDA is not required to follow the recommendations of its advisory committees but typically does.

"The committee plainly wanted to tell us certain things ought to be in labeling in a more forceful way," Dr. Robert Temple, director of the FDA's Office of Medical Policy, told reporters after the meeting.

Doctors prescribe the drugs to about 2 million children and 1 million adults a month.

Drugs that would have to carry the warning labels are methylphenidates, which are sold as Ritalin, Concerta, Methylin and Metadate. The labels for Adderall and Adderall XR, both amphetamines, have included the warnings since 2004.

The Drug Safety and Risk Management advisory committee also recommended that the drugs include a medication guide for patients and parents. The vote was 15-0, with one abstention.

Adderall is made by Shire Pharmaceuticals; Ritalin by Novartis Pharmaceuticals Corp.; Concerta by Johnson & Johnson; Methylin by Mallinckrodt Pharmaceuticals; and Metadate by UCB. Various other companies make generic versions of Ritalin.

Novartis said Ritalin, approved by the FDA in 1955, is safe and effective. A company review of more than 50 years of records shows no apparent increase in cardiovascular problems associated with the drug's use, according to Novartis' medical safety director, Dr. Todd Gruber.

He told the committee that the drug's label advises caution in patients with certain pre-existing heart conditions.

The FDA had asked the advisers to consider ways of studying the drugs because agency data suggested the drugs were linked to an increased risk of sudden death and serious cardiovascular problems, including heart attacks.

The committee, however, quickly began debating whether it should consider new warnings for the drugs rather than the need for more studies.

Dr. Steve Nissen, medical director of the Cardiovascular Coordinating Center at The Cleveland Clinic, told fellow committee members they should recommend the black box warning.

Nissen said his suggestion was meant partly to slow what he characterized as the "out of control growth" use of the drugs.

The drugs already carry warnings related to the possible risk they could pose to patients with heart defects.

"We feel this warning is appropriate given our current knowledge of these drugs," said Dr. Gerald DalPan, a division director in the FDA's Center for Drug Evaluation and Research.

The FDA review that found 25 reports of deaths among the drugs' users between 1999 and 2003 also uncovered 54 cases of serious cardiovascular problems, including heart attack, stroke, hypertension, palpitations and arrhythmia. Some of these ADHD drug-treated patients had pre-existing heart conditions or hypertension.

"There's smoke. Does that mean there's fire?" asked Dr. David Graham, a medical officer at the FDA's Center for Drug Evaluation and Research.

"We wouldn't be going through this exercise if we didn't think there was a real possibility of increased risk," Graham told reporters.

The FDA's review found fewer than one reported death or life-threatening injury for every 1 million prescriptions filled for the drugs.

"The decision has been apparently made, and if it's been made, I agree with it, that the reports are not enough to warrant regulatory action," committee member Sean Hennessy said.

Hennessy, an assistant professor of epidemiology and pharmacology at the University of Pennsylvania School of Medicine, ended up voting against recommending additional warnings.

The FDA said the few studies that have looked at longer-term use of ADHD drugs provide little information on those risks.

Also, the agency's analysis of the reports of death and injury only suggests a possible link between the drugs and cardiovascular problems, said Dr. Kate Gelperin, a medical officer in the agency's Office of Drug Safety.

She said the link is not conclusive, nor is it clear whether there is an increased incidence of death or serious injury among people treated with the drugs.

That "is really a question we'd like to have answered," she said.

Sales of ADHD drugs rose to \$3.1 billion in 2004 from \$759 million in 2000, according to IMS Health, a pharmaceutical information and consulting firm.

About 2.5 million children between age 4 and 17 take ADHD drugs, according to federal survey data cited by Dr. Andrew Mosholder, a medical officer in the Office of Drug Safety. The survey found 9.3 percent of 12-year-old boys and 3.7 percent of 11-year-old girls take the drugs, Mosholder said.

Adult use of the drugs alone grew 90 percent between March 2002 and June 2005, he said.