
AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY

AACAP Message from the President

AACAP Statement on FDA Advisory On Methylphenidate February 13, 2006

Dear Colleague:

Last Thursday, the Food and Drug Administration (FDA) Drug Safety and Risk Management Advisory Committee voted (8-7, with one abstention) to require black box warnings on methylphenidate. The committee had reviewed reports of 25 deaths, 19 of them under age 18, and a preliminary analysis of post marketing surveillance reports that suggested that stimulants might increase the risk of strokes, myocardial infarctions, and arrhythmias in children and adults. Sudden death was described, although the rate never exceeded one in a million for any stimulant drug.

The hearing was intended to discuss better ways to predict and identify rare, unexpected, and serious adverse events of sudden death, hypertension, myocardial infarction, and stroke that occasionally appear in post-marketing reports of these medications.

Larry Greenhill, M.D. and Adelaide Robb, M.D., were outstanding representatives of the AACAP at the hearing. Dr. Greenhill testified about the positive benefit to risk ratio that stimulants offer children and adolescents with ADHD. He also stated that although these drugs, like all drugs, are associated with adverse events, most of them are manageable by dosage adjustment or changing the stimulant. Dr. Greenhill suggested that the FDA consider working with existing research programs to gather more definitive information about the risks of these rare adverse events. Such programs include an American Academy of Pediatrics sponsored ADHD registry in the offices of developmental pediatricians, the jointly sponsored, NIMH/AACAP CAPTN large simple trials network, and the NICHD sponsored National Children's Study that will follow 100,000 American children for 25 years.

Dr. Robb discussed the case of a child with cardiovascular abnormalities that she has treated in consultation with a cardiologist. She stated that appropriate monitoring of patients on these medications, even with cardiac abnormalities, can have substantial benefits.

Dr. Gardiner, a member of the FDA advisory panel, asked Dr. Greenhill to comment on the effectiveness and benefits of ADHD medication treatments for children and adolescents with ADHD, based on Dr. Greenhill's experience as one of the principal investigators on the NIMH Multimodal Treatment Study of ADHD (MTA Study).

The effectiveness of stimulants in the treatment of ADHD can be gauged from the results of the MTA Study. Swanson et al. (2001) counted the proportion of "excellent responders" -- those whose ADHD scores on treatment were reduced to the normal range. The MTA investigators found that 25% of ADHD children became responders on community-based treatment as usual, 35% responded to behavioral therapies, 55% responded to methylphenidate, and 65% responded

to a combination of methylphenidate and behavioral treatment. Improvements in the MTA extended from significant decreases in ADHD symptoms to reductions in negative and ineffective parenting, improvements in scholastic achievement scores, improvements in reading scores, and improvements in social status in the classroom. Large effect sizes, averaging over one standard deviation of change, are observed in double-blind, clinical trials of children with ADHD, the standardized amount of change when treatment on stimulants is compared to treatment on placebo.

After listening to the morning comments by experts, some committee members spoke up, saying that they should do more than simply recommend further research. The concern among the committee members was that there needed to be stronger wording to physicians and patients. "I want to cause people's hands to tremble a little bit before they write that prescription," said Dr. Nissen, a panel member. There was also a 15-0 (one abstention) vote for a medication guide for patients and parents.

The committee that met Thursday was made up of drug-safety specialists. Next month, the FDA will ask another advisory group, the Pediatric Advisory Committee, comprised of pediatricians and psychiatrists, to review the same issues. The following day, the Psychopharmacologic Drugs Advisory Committee will meet to discuss a new drug application (SPARLON or Modafinil) from Cephalon. The AACAP will participate in both meetings.

To read Dr Greenhill's testimony and the AACAP press release, please [click here](#).

To assist our members with discussing these concerns with parents and patients, AACAP is developing a set of talking points. We will continue to work with the FDA to provide them with our practice parameters and other information to assist them in making the most informed decisions.

I would like to thank all of our members who commented on our draft ADHD (revised) practice parameter. If you would like a copy of this draft parameter, please call 1-800-333-7636, ext 137.

Sincerely,

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