Communication about an Ongoing Safety Review of Stimulant Medications used in Children with Attention-Deficit/Hyperactivity Disorder (ADHD)

This information has been updated in the November 1, 2011 FDA Drug Safety Communication: Safety Review Update of Medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in children and young adults and the December 12, 2011 FDA Drug Safety Communication: Safety Review Update of Medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in adults.

Products involved include: Focalin, Focalin XR (dexmethylphenidate HCl ); Dexedrine, Dexedrine Spansules, Dextroamphetamine ER, Dextrostat (dextroamphetamine sulfate); Vyvanse (lisdexamfetamine dimesylate); Desoxyn (methamphetamine); Concerta, Daytrana, Metadate CD, Metadate ER, Methylin, Methylin ER, Ritalin, Ritalin-LA, Ritalin-SR (methylphenidate); Adderall, Adderall XR (mixed salts amphetamine); Cylert (pemoline) and generics

4/2011
FDA has received and is currently reviewing preliminary results of the studies sponsored by FDA and AHRQ to research potential cardiovascular risks associated with medications used to treat ADHD in children and adults.

Because the review is ongoing, FDA does not recommend that patients, caregivers, or healthcare professionals change their use or prescribing patterns of stimulant medications for ADHD. At this time, no conclusions have been made and FDA has not decided if the drug label will need to be updated. The drug labels and Medication Guides for stimulant medications already contain warnings about the potential risk of serious cardiovascular events.

FDA will update the public after the results of the final analyses are evaluated.

8/2010
The results of the ongoing study sponsored by FDA and AHRQ to research potential serious cardiovascular risks associated with medications used to treat ADHD in children and adults has been further delayed. The results of both studies are now expected in the first quarter of 2011. This delay is due to the logistical challenges of obtaining approximately 2,000 medical charts to confirm medical claims diagnoses, as well as the technical challenges associated with pooling and analyzing data from approximately 1.5 million patient records across 12 health plans. Program officials from FDA and AHRQ continue their close contact with the investigators and will provide updates once results are obtained and reviewed.

11/2009
The results of the study sponsored by the FDA and AHRQ to research potential cardiovascular risks associated with ADHD medications in children and adults will be delayed. The child study results are now expected by August 2010 and the adult study results are expected by October 2010. The study, called the Multicenter Observational Cohort Study to Assess the Cardiovascular Risks of Medications Prescribed for Attention Deficit and Hyperactivity Disorder (ADHD), is delayed due to technical challenges and logistic difficulties. Data is being assembled from more than 500,000 ADHD medication users and 1,000,000 non-
users across 12 different health plans, and approximately 2,000 medical records from hundreds of hospitals are being reviewed. FDA and AHRQ officials are in close contact with the investigators, and will update this communication with the results of these studies upon their completion.

6/23/2009

The U.S. Food and Drug Administration is providing its perspective on data published today in the American Journal of Psychiatry on the potential risks of stimulant medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in children.1,2

Given the limitations of this study’s methodology, the FDA is unable to conclude that these data affect the overall risk and benefit profile of stimulant medications used to treat ADHD in children.

Therefore, the FDA believes that this study should not serve as a basis for parents to stop a child’s stimulant medication. Parents should discuss concerns about the use of these medicines with the prescribing healthcare professional. The FDA’s summary of the study and its limitations, and our recommendations for healthcare professionals are provided below.

Study Summary

This study, funded by the FDA and the National Institute of Mental Health (NIMH), compared the use of stimulant medications in 564 healthy children from across the United States who died suddenly to the use of stimulant medications in 564 children who died as passengers in a motor vehicle accident. Use of stimulant medication was determined from parents, medical examiners, and toxicology reports. These two groups of children were compared because the children all died suddenly and the cause of death was not a known health problem.

Findings of the study

- Out of 564 healthy children who died suddenly, 10 were reported to be taking a stimulant medication at the time of death.
- Out of 564 healthy children who died in a motor vehicle accident, 2 were reported to be taking a stimulant medication at the time of death.
- The study authors concluded that there may be an association between the use of stimulant medications and sudden death in healthy children.

Limitations of the study data

- A child’s use of a stimulant medication for ADHD was determined many years after each child’s death. The deaths occurred between 1985 to 1996, but the data on medication usage were collected from March 1997 to January 2008. This time lag may have resulted in reporting errors.
- The differences in cause of death (sudden death versus death from a motor vehicle accident) could have influenced the family or caregiver’s recall of information on stimulant medication use at the time of death, creating an elevated rate of stimulant drug use in the group of children who died suddenly, as compared to the children who died in a motor vehicle accidents.
- The sudden unexplained death of a child, in comparison to a death of a child from a motor vehicle accident, may have increased the likelihood of a post-mortem inquiry into medication use.
- The low frequency of stimulant use in both groups, as well as possible differences in the type of post-mortem inquiry, could have a profound biasing effect on the results.

Ongoing FDA Review:

The FDA is continuing its review of the strengths and limitations of this and other epidemiological studies that evaluate the risks of stimulant medications used to treat ADHD in children. The Agency for Healthcare Research and Quality (AHRQ) and the FDA are sponsoring a large epidemiological study that will provide further information about the potential risks associated with stimulant medication use in children. The data collection for this study will be complete later in 2009.

Recommendations for Healthcare Professionals:

http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/drugsafetyinformationforhealthcareprofessionals/ucm165858.htm
Follow all the current prescribing information for use of these medications, including:

- Take a medical history for cardiovascular disease in the child and his or her family.
- Perform a physical exam with special focus on the cardiovascular system (including examination for the signs of Marfan syndrome).
- Consider obtaining further tests such as a screening electrocardiogram and echocardiogram if the history or examination suggests underlying risk for or the presence of heart disease.

The FDA intends to update this advisory when additional information or analyses become available.

Adverse reactions or quality problems experienced with the use of this Product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax, using the contact information at the bottom of this sheet.

Any child who develops cardiovascular symptoms (such as chest pain, shortness of breath or fainting) during stimulant medication treatment should immediately be seen by a doctor.

Prescription stimulant medications are indicated for the treatment of ADHD as part of a comprehensive treatment plan. ADHD is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more severe than expected for a child’s developmental age. Although estimates vary, ADHD is diagnosed in about 4% to 10% of children in the United States (more boys than girls). Children with untreated ADHD may have significantly higher rates of behavioral, mood and anxiety disorders, often resulting in problems with family, school and friends. Refer to Drugs@FDA\(^3\) for further information on, product labeling, and Medication Guides regarding medications for ADHD.

This information reflects FDA’s current analysis of available data concerning these drugs. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug products and the emerging safety issue. Nor does it mean that FDA is advising healthcare professionals to discontinue prescribing these products. FDA is considering, but has not reached a conclusion about whether this information warrants any regulatory action. FDA intends to update this document when additional information or analyses become available.


2 Study included children and adolescents.

Related Information

- Information about Medications Used to Treat Attention-Deficit/Hyperactivity Disorder (ADHD)\(^6\)
- FDA Issues Safety Communication about an Ongoing Review of Stimulant Medications Used in Children with ADHD\(^7\) [ARCHIVED]
  FDA press release (6/2009)
- FDA Asks Attention-Deficit Hyperactivity Disorder (ADHD) Drug Manufacturers to Develop Patient Medication Guides\(^8\) [ARCHIVED]
  2/21/2007

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