Alert for Healthcare Professionals

Adderall and Adderall XR (amphetamine)

FDA Alert [02/09/05]: Sudden Death in Children

Health Canada has suspended marketing of Adderall XR (extended release) from the Canadian market due to concern about reports of sudden unexplained death (SUD) in children taking Adderall and Adderall XR. SUD has been associated with amphetamine abuse and reported in children with underlying cardiac abnormalities taking recommended doses of amphetamines, including Adderall and Adderall XR. In addition, a very small number of cases of SUD have been reported in children without structural cardiac abnormalities taking Adderall. At this time, FDA cannot conclude that recommended doses of Adderall can cause SUD, but is continuing to carefully evaluate these data.

Recommendations

FDA is currently examining the data on these cases occurring in children who are using Adderall as recommended. As a precaution, FDA recommends that Adderall products not be used in children or adults with structural cardiac abnormalities.

Data Summary

A review of the data from the FDA's Adverse Event Reporting System database for the years 1999 through 2003 identified 12 cases of sudden death in pediatric patients (1 to 18 years of age) who were being treated for ADHD with Adderall or Adderall XR (see table for description of cases).

Characteristics of domestic pediatric sudden death cases reported during past five years (n=12)*

Age:	7-16 years (mean 12. years)
Gender:	12 male, 0 female
Suspect drug:	Adderall or Adderall XR
Total daily dose:	10 mg (1), 20 mg (5), 30 mg (1), 40 mg (1), 50 mg (1) , NR (3)
Duration of therapy:	1 day – 8 years (range)
Autopsy:	yes (11), not mentioned or not done (1)
Cardiac structural abnormalities:	aberrant origin of coronary artery (1), idiopathic hypertrophic subaortic stenosis (1), bicuspid aortic valve (1), cardiac hypertrophy (2)
Other risk factors:	unexplained increase or toxic amphetamine level (2), family history of ventricular arrhythmia (1), extreme exercise and dehydration (1)
Concomitant meds:	none mentioned (9), 1 med (3)
Year reported	1999 (0), 2000 (2), 2001 (6), 2002 (2), 2003 (2)

*numbers in parentheses represent count of cases

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Five of the 12 pediatric sudden death cases described cardiac risk factors including undiagnosed cardiac abnormalities (e.g., aberrant origin of coronary artery, bicuspid aortic valve, idiopathic hypertrophic subaortic stenosis). Seven occurred in children without such abnormalities, including 1 with a positive family history of ventricular arrhythmia. Several of the cases were complicated by other illness, and very rigorous exercise. Unusual and unexplained accumulation of drug resulting in toxic levels during usual therapeutic dosing also appears to have played a role in several of the pediatric sudden death cases. The rare occurrence of sudden death during stimulant therapy of ADHD deserves continued evaluation. SUD as a possible effect of amphetamines should be considered in the assessment of benefit versus risk during therapeutic decision-making for individual patients. In the pediatric population, potential risk factors include cardiac abnormalities that may be undiagnosed, positive family history for ventricular arrhythmias, and as yet unidentified factors that may cause excessive levels of stimulant to accumulate in children who are taking apparently normal doses.

An update and further analyses of the data are currently in progress.

Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
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