Alert for Healthcare Professionals

Adderall and Adderall XR (amphetamine)

FDA ALERT [08/05]: Health Canada Announces Return of Adderall to the Canadian Market.
Adderall will return to the Canadian market for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) (see alert of 02/09/05 below). The Canadian Product Monograph will be revised to include warnings about the misuse of Adderall, and that Adderall generally should not be used in patients with structural cardiac abnormalities.

FDA ALERT [02/05]: Health Canada Suspends Marketing of Adderall
Health Canada has suspended marketing of Adderall products from the Canadian market due to concern about reports of sudden unexplained death (SUD) in children taking Adderall. SUD has been associated with amphetamine abuse and reported in children with underlying cardiac abnormalities taking recommended doses of amphetamines, including Adderall. 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, Adderall products should 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).

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TABLE 1A – Amphetamine

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

Age:	7-16 years (mean 12.5 years)
Gender:	12 male, 0 female
Suspect drug:	Adderall or Adderall XR(12)
Total daily dose:	10mg (1), 20mg (5), 30mg (1), 40mg (1), 50mg (1), NR (3)
Duration of therapy:	1 day – 8 years (range)
Autopsy:	yes (11), not mentioned or not done (1)
Cardiac risk factors:	aberrant origin of coronary artery (1), idiopathic hypertrophic subaortic stenosis (1), bicuspid aortic valve (1), unexplained increase or toxic amphetamine level (3), cardiac hypertrophy (3), positive maternal history of ventricular arrhythmia (1), history of heart murmur (3), none mentioned (4)
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

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, and 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 is an issue that deserves continued evaluation. SUD as a possible effect of amphetamines, even if primarily in patients with structural heart disease, and 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.