Commentary: Concerns With the Suspension of Adderall XR

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Adderall XR a combination of amphetamine salts, was approved for use in Canada in January 2004 for the management of Attention-Deficit Hyperactivity Disorder in children. Clinicians in the field welcomed the addition of a 12-hour amphetamine product to compliment the other medications which were currently available.

In a news release dated February 9th, 2005 Health Canada suspended the market authorization of this medication, based on issues of safety. They had conducted a review of 20 cases of sudden death in patients taking Adderall or Adderall XR. These data were from the U.S. Food and Drug Administration (FDA). None of the 20 deaths occurred in Canada. The deaths were not associated with overdose, misuse or abuse. Fourteen of the deaths were in children, six were in adults.

A number of these deaths were associated with individuals who had significant pre-existing cardiac abnormalities. The sudden death rate for the other patients was below the sudden death rate for the general population.

The FDA issued a statement on February 9th, 2005 stating, "FDA does not feel that any immediate changes are warranted in the FDA labeling or approved use of this drug based upon its preliminary understanding of Health Canada's analyses of adverse event reports, and the FDA's own knowledge and assessment of the reports received by the agency".

In the past, pharmaceutical manufacturers' who have had their market authorization suspended have simply gone along with this decision. Shire Biochem the makers of Adderall XR, were concerned about the lack of transparency and disputed the decision. Because of this they refused to comply voluntarily with the order, thus triggering an appeal process which has never been tested before. The appeal process consists of a three-person panel, one selected by Health Canada, one selected by the pharmaceutical manufacturer, and a third person agreed to by the other two parties. To date we have not been informed as to the identity of these individuals, the timeline of this review or even the process following the submission of the report of the panel.

On March 7th, 2005 a joint letter from the Canadian Academy of Child and Adolescent Psychiatry and the Canadian Psychiatric Association, was sent to Dr. Robert Peterson the Director General, Therapeutic Products Directorate, Health Canada. The two associations supported Health Canada's mandate to review and assess the risk of medications, particularly in children and youth. Concerns were expressed however, about the manner in which Health Canada's decision was communicated to the public and the medical community. There was an absence of a comprehensive, advanced notice strategy to physicians. Many doctors and patients became aware of this withdrawal through reports in the media. Request was made that Health Canada conduct a review of their communication strategy.

It was also pointed out that Health Canada had not consulted with expert physicians who were associated with either of the two organizations. There was support expressed for a decision of Health Canada to establish a three person expert panel to review the reasons for this suspension. To complicate matters Dr. Robert Peterson retired from Health Canada immediately after making this decision, and to date Health Canada has not responded satisfactorily to this letter.

At the time of this withdrawal, 11,000 Canadians were receiving treatment with this medication. Many of them were on this medication because of a failure on other psycho-stimulants. This withdrawal caused very considerable anxiety on the behalf of these patients and their families. Physicians across the country and particularly centres that were treating large numbers of children and adults with ADHD had no warning, and on short notice had to contact their patients and make alternate arrangements.

In the province of British Columbia, supplies of Dexedrine Spansules became unavailable due to the sudden need to shift patients to alternate medications. Many of the patients who had been treated with Adderall XR had been failures of methylphenidate preparations, and thus there was no other alternative medication that could readily be used to treat these individuals.

A number of serious questions remain concerning this withdrawal:

1) Why was the medication withdrawn in Canada based on data collected by FDA, when a careful review by FDA did not cause particular concern?

2) Health Canada appears to have no mechanism for, or even interest in, timely consultation with treating professionals or their professional Associations. It is uncertain as to how internal decisions are made and a general lack of transparency.

3) It was unacceptable to physicians that they found out about this withdrawal from reports in the media.

We need to continue to urge Health Canada to develop a better communications strategy by supporting our professional associations in this regard and to demand a more consultative and transparent decision-making process.

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