Lessons from cisapride

One evening just over a year ago, 15-year-old Vanessa Young sat chatting with her father in his study. She rose to go upstairs, fell to the floor, and died. Her cardiac arrest was undoubtedly caused by the drug cisapride, which she had been taking for stomach complaints associated with an eating disorder. Her pharmacist testified that he was unaware of any particular risk of cisapride; the information sheet he dispensed with the drug made no mention of the ventricular arrhythmias that, since 1990, had resulted in 80 deaths in Canada and the United States.

Health Canada had reported on severe and fatal adverse reactions experienced by patients taking cisapride through the *Canadian Adverse Drug Reaction Newsletter* in July 1996, January 1998 and January 2000. The US Food and Drug Administration (FDA) started to issue warnings about the drug in June 1998; these culminated in an advisory on Jan. 24, 2000, alerting US physicians to the occurrence of fatal cardiac arrhythmias among patients taking the drug. An equivalent advisory didn't emerge from Health Canada until May 31.[1] Cisapride was off the US market by July 14; Canadians could keep filling their prescriptions until Aug. 7, more than 6 months after the FDA warning.

Warnings to physicians and pharmacists don't necessarily change prescribing practice. A US study showed that FDA regulatory action in 1998 relating to contraindications to cisapride use had virtually no impact on prescribing.[2] Perhaps physicians miss such warnings; perhaps the rarity of catastrophic side effects leaves too much room for complacency. Forty-four cisapride-associated cardiac arrhythmias have been reported in Canada,[1] where 7.7 million prescriptions for the drug have been filled.[3] Most prescribing physicians would have perceived the drug as beneficial.

Three people need information about the risks of a drug: the physician, the pharmacist and the patient. Keeping patients informed is an element of good practice that Canadian pharmacies use as a selling point. But, in providing this service, they rely on patient-targeted information provided by manufacturers or packaged by private companies. This information is sometimes incomplete. Moreover, the twin goals of improving patient compliance (a troubling concept to start with) and ensuring patient safety are not necessarily compatible.

Who should take responsibility for patient information leaflets? The one available to Vanessa was falsely reassuring; if she had obtained the drug in the US, the patient information would have told a different story.[4] In the US, pharmaceutical companies include patient information sheets in the packaging of prescription drugs, and that information is FDA approved. We've argued for parallel regulation in Canada.[5]

Until patients are given better information, alerts directed to physicians are even more vital. This is not the first time we have observed Health Canada's advisory and regulatory actions lagging behind the FDA's. But it is the last time that we will merely observe. Henceforth, we will do 2 things: first (for what it's worth), we'll send copies of this editorial and similar ones to our federal minister of health. Second, we'll monitor FDA physician advisories and inform Canadian physicians through this journal of any warnings of serious adverse drug reactions issued by the FDA. — *CMAJ*

References

1. Health Canada. *Prepulsid to be withdrawn as a result of cardiac complications*. Document no. 2000-56. 31 May; 2000. Available: www.hc-sc.gc.ca/english/archives/warnings/2000/2000_56e.htm. (accessed 2001 Apr 5).
2. Smalley W, Shatin D, Wysowski DK, Gurwitz J, Andrade SE, Goodman M, et al. Contraindicated use of cisapride: impact of food and drug administration regulatory action. *JAMA* 2000; 284(23):3036-9.
3. Owens AM. Dead girl's family not warned about dangers of drug. *National Post* [Toronto] 20 Mar 2000; A:5.
4. Sukkari SR, Sasich LD. Cisapride and patient information leaflets [letter]. *CMAJ* 2001;164(9): 1276-7.
5. Drug interactions: Who warns the patient? [editorial]. *CMAJ* 1999;161(2):117.