

Drug Shortages in Health Care Institutions: Perspectives in Early 2014

Isabelle Barthélémy, Denis Lebel, and Jean-François Bussières

INTRODUCTION

The year 2012 was marked by an unprecedented number of drug shortages in Canada. This crisis was due in particular to the publication, in November 2011, of a warning letter from the US Food and Drug Administration (FDA) to Novartis International AG for its Boucherville plant, which was managed by Sandoz Canada.^{1,2} Although Sandoz was not the only drug manufacturer with shortages for some products, the wide range of single-source generic parenteral products affected by this crisis led to a high level of uncertainty in the Canadian health care sector. Since the publication of our most recent analysis of the Canadian drug shortage situation,³ the FDA has issued at least one other warning letter, this time to Apotex, a Canadian generic manufacturer.⁴

In 2012, our research group evaluated the impact of drug shortages in 5 Quebec teaching hospitals and highlighted administrative costs of at least Can\$0.5 million to manage these shortages, mainly at the level of individual pharmacies.⁵ Barthélémy and others⁶ also published a case study of the management of drug shortages in hospitals, illustrating the challenges for pharmacists and the risks for patients.

In response to this crisis, many stakeholders (including the Standing Committee on Health, the Royal College of Physicians and Surgeons of Canada, the Ordre des pharmaciens du Québec, the Canadian Pharmacists Association, and the group purchasing organization SigmaSanté) came together in 2012 and made a set of recommendations to various levels of government, buying groups, supply chains, the pharmaceutical industry, and individual pharmacists.⁷ Surprisingly, only one-third of the 30 recommendations had been implemented 1 year later.⁷

In June 2013, a Member of Parliament from the New Democratic Party of Canada proposed a private member's bill on the mandatory disclosure of drug shortages in Canada,⁸ but this bill was defeated at second reading in February 2014. In September 2013, Health Canada published a drug-shortage protocol and tool kit, based on the work of the Multi-Stakeholder Steering Committee on Drug Shortages.⁹ In its Appendix B, the

protocol establishes a guide for drug-shortage notification and communication and lists the key relevant fields to be completed by drug manufacturers in the Canadian drug shortage database (www.drugshortages.ca). Pharmacists and various stakeholders, such as the Canadian Society of Hospital Pharmacists and group purchasing organizations, found this database to be incomplete and requested the addition of key data (e.g., number of similar commercialized products, links to other relevant information sources). Disappointingly, it took more than 24 months after initial consultations for these key data to be added as fields on the website for complete update by the manufacturers. Before then, these key data were available only on a website known as "FridayPM". The FridayPM website, a voluntary, pharmacist-initiated tool launched in early 2011, was closed in August 2014, as drug manufacturers are now allowed by some group purchasing organizations to declare their drug shortages only on the Canadian drug shortage platform.

DESCRIPTION OF THE PROGRAM

The Pharmacy Practice Research Unit of the Centre hospitalier universitaire Sainte-Justine has been gathering data on drug shortages since 2006.¹⁰⁻¹⁶ For these reports, drug shortage data were extracted from the pharmacist-initiated website (FridayPM). Here, we provide an update on the situation for the period September 1, 2012, to August 30, 2013. For this analysis, data from the 12-month period in 2012–2013 were compared with data from 2006 to 2012.

EVALUATION OF THE PROGRAM

A total of 497 drug shortages were reported in the 12-month period in 2012–2013, which represents a 54% decrease from the 1081 drug shortages reported in a corresponding period in 2011–2012. Before 2011, the annual numbers of drug shortages were 493 in 2006, 400 in 2007, 441 in 2008, 679 in 2009, and 429 in 2010.

The average duration of drug shortages has increased, with a mean (\pm standard deviation) of 168 ± 153 days (range 15–710

days), compared with 141 ± 116 days (range 1–775 days) for 2011–2012, 103 ± 85 days (range 8–363 days) for 2010–2011, and 108 ± 130 days (range 5–1623 days) for 2006–2010. Shortages of parenteral formulations have increased over the years, representing 33% of drug shortages in 2011–2012 and 36% in 2012–2013. In terms of duration, shortages of parenteral formulations represented 37% of the total number of drug-shortage days in 2011–2012 and 47% in 2012–2013.

The number of manufacturers involved in drug shortages declined to 38 manufacturers in 2012–2013, compared with 58 in 2011–2012, 41 in 2010–2011, and 70 over the period 2006–2010. Most of the drug shortages in 2012–2013 involved generic drug manufacturers, which accounted for 85% of the total number of drug shortages and 87% of the total number of drug-shortage days. The main manufacturers involved were, in decreasing proportion of total number of shortages, Apotex (16%), Teva (15%), Pharmascience (15%), Baxter (10%), Sandoz (9%), and Hospira (9%).

Most therapeutic classes were affected by shortages in 2012–2013. In decreasing order of the number of drug shortages, drug classes affected were central nervous system agents (AHFS drug classification 28:00), accounting for 23% of affected products; cardiovascular drugs (24:00), 13%; anti-infective agents (08:00), 11%; skin and mucous membrane agents (84:00), 6%; hormones and synthetic substitutes (68:00), 5%; gastrointestinal drugs (56:00), 4%; antineoplastic drugs (10:00), 3%; and all other classes (35%).

Besides the decrease in drug shortages for the period from September 2012 to August 2013, this update indicates an increase in the proportion of parenteral formulations among the drugs that were in shortage and an increase in the shortages involving generic manufacturers. The same 6 generic drug manufacturers were mainly involved, representing 74% of the total number of drug shortages.

IMPLICATIONS AND SIGNIFICANCE FOR PRACTICE

Should we be reassured that fewer drugs were in shortage in 2013? Perhaps. However, at the same time, the safety of the drug supply chain is being questioned, not only because of drug shortages but also in relation to the safety of drug manufacturing in Asia and other overseas locations.¹⁷ In France, the Académie nationale de pharmacie has recognized that one of the causes of drug shortages is the lack of quality of some imported raw materials.¹⁸ In addition, issues of dishonesty with regulatory authorities have been reported in the press. For example, in May 2013, the generic manufacturer Ranbaxy pleaded guilty to 7 federal criminal counts of selling adulterated drugs with intent to defraud, failing to report that its drugs did not meet specifications, and making intentionally false statements to the government.¹⁹ The grey market is also becoming an issue in Canada,²⁰

and Sandoz is again facing manufacturing and distribution challenges and has almost 50 products on allocation.²¹

Drug shortages represent a complex problem with many potential solutions. At the hospital level, pharmacists could alleviate the effects of drug shortages by revising inventory levels and maintaining a safe buffer of 60 days' worth of critical drugs. Having a buffer stock would make a difference if there is a pandemic, a local catastrophe, or just typical back-orders, as has been the case over the past 7 years in Canada. We also need to better understand this complex problem and evaluate the effects of interventions (or the absence of interventions) by provincial and national authorities.

References

1. Inspections, compliance, enforcement, and criminal investigations: Novartis International AG 11/18/11 [warning letter]. Silver Spring (MD): Food and Drug Administration (US); 2011 Nov 18 [cited 2012 Sep 20]. Available from: www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm281843.htm
2. Lettre aux clients (15-16 février). Boucherville (QC): Sandoz Canada Inc; 2012 Feb 15 [cited 2014 Sep 26]. Available from: www.sandoz.ca/fr/inventaire/letter1_fr.shtml
3. Barthélémy I, Lebel D, Bussi eres JF. Drug shortages in health care institutions: perspectives in early 2013. *Can J Hosp Pharm.* 2013;66(1):39-40.
4. Inspections, compliance, enforcement, and criminal investigations: Apotex Inc. 2/21/13 [warning letter]. Silver Spring (MD): Food and Drug Administration (US); 2013 Feb 21 [cited 2013 Aug 27]. Available from: www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm344476.htm
5. * valuation des cons quences des ruptures d'approvisionnement en 2012 au sein des cinq CHU qu b cois*. Montr al (QC): Programme de gestion th rapeutique des m dicaments; 2013 [cited 2013 Aug 15]. Available from: www.pgtm.org/documentation/FSW/RUPTURES_AD_20130716.pdf
6. Barth el my I, Lebel D, Atkinson S, Bussi eres JF. Ruptures d'approvisionnement de m dicaments : une illustration de la gestion des risques en  tablissement de sant . *Risques Qual.* 2013;10(3):162-70.
7. Barth el my I, Bussi eres JF. Un an apr s la crise des p nuries de m dicaments Sandoz : peu d'avanc es. *Can J Hosp Pharm.* 2013;66(4):257-62.
8. Bill C-523, *An act to amend the Department of Health Act (disclosure of drug shortages)*, 2nd sess., 41st Parl., 2013 [cited 2014 Apr 30]. Available from : www.parl.gc.ca/LEGISInfo/BillDetails.aspx?billId=6251914&Mode=1&View=10&Language=E
9. *Protocol for the notification and communication of drug shortages*. Multi-Stakeholder Steering Committee on Drug Shortages in Canada; 2013 [cited 2013 Sep 13]. Available from: www.drugshortages.ca/CMFiles/MSSC_Notification_Communication_Protocol_EN.pdf
10. Ottino G, Lebel D, Bussi eres JF. Perspective face aux causes de ruptures d'approvisionnement de m dicaments. *Pharmactuel.* 2012;45(3):207-12.
11. Bussi eres JF, Chiveri A, Lebel D. Perspective sur les ruptures d'approvisionnement de m dicaments en  tablissement de sant  de 2006   2010. *Can J Hosp Pharm.* 2011;64(6):426-35.
12. Ottino G, Lebel D, Bussi eres JF. Drug shortages in health care institutions: perspectives in early 2012. *Can J Hosp Pharm.* 2012;65(2):151-2.
13. Barth el my I, Bussi eres JF, Lebel D, Gaudreault P, Prot-Labarthe S, Bourdon O. Drug shortages: What does France do better than Canada? *Can J Hosp Pharm.* 2012;65(5):406-7.
14. Ottino G, Lebel D, Bussi eres JF, Bourdon O. Gestion des ruptures d'approvisionnement de m dicaments : perspectives en France, aux  tats-Unis et au Canada. *Can J Hosp Pharm.* 2012;65(1):37-42.
15. Barth el my I, Lebel D, Bussi eres JF. Quel avenir pour les donn es portant sur les ruptures d'approvisionnement de m dicaments d clar es sur les sites web de surveillance? *Can J Hosp Pharm.* 2013;66(2):135-6.
16. Barth el my I, Lebel D, Bussi eres JF. Drug shortages in health care institutions: perspectives in early 2013. *Can J Hosp Pharm.* 2013;66(1):39-40.

17. Cassels A. Most of our prescription drugs are manufactured overseas—but are they safe? *CMAJ*. 2012;184(14):1648.
18. *Recommandations. Médicaments : ruptures de stock, ruptures d'approvisionnement*. Paris (France): Académie nationale de pharmacie; [cited 2013 Dec 10]. Available from: www.acadpharm.org/dos_public/Recommandations_ruptures_de_stocks_et_appro_VF_2013.04.24.pdf
19. Eban K. Dirty medicine. *Fortune Magazine* 2013 May 15 [cited 2013 Aug 27]. Available from: <http://features.blogs.fortune.cnn.com/2013/05/15/ranbaxy-fraud-lipitor/>
20. Teisceira-Lessard P. Un pharmacien a créé des pénuries de médicaments pour son profit. *La Presse* 2013 Aug 27 [cited 2013 Aug 27]. Available from: www.lapresse.ca/actualites/sante/201308/26/01-4683457-un-pharmacien-a-cree-des-penuries-de-medicaments-pour-son-profit.php
21. Breton P. Sandoz : médicaments en quantités limitées. *La Presse* 2013 Aug 13 [cited 2013 Aug 27]. Available from: www.lapresse.ca/actualites/sante/201308/13/01-4679355-sandoz-medicaments-en-quantites-limitees.php

Isabelle Barthélémy is a Research Assistant in the Pharmacy Practice Research Unit, Centre hospitalier universitaire Sainte-Justine, Montréal, Quebec. She is also a DPharm student at Université Claude Bernard Lyon 1, Villeurbanne, France.

Denis Lebel, BPharm, MSc, FCSHP, is Assistant Director of the Pharmacy Practice Research Unit, Centre hospitalier universitaire Sainte-Justine, Montréal, Quebec.

Jean-François Bussièrès, BPharm, MSc, MBA, FCSHP, is Director of the Pharmacy Practice Research Unit and the Pharmacy Department, Centre hospitalier universitaire Sainte-Justine, Montréal, Quebec. He is also Professor with the Faculty of Pharmacy, Université de Montréal, Montréal, Quebec.

Competing interests: None declared.

Address correspondence to:

Jean-François Bussièrès
Pharmacy Department
Centre hospitalier universitaire Sainte-Justine
3175, chemin de la Côte Sainte-Catherine
Montréal QC H3T 1C5

e-mail: pfu@providencehealth.bc.ca

SPECIAL INTEREST COMMUNITIES OF PRACTICE
Connecting pharmacists across Canada
FOR IMPROVED PATIENT CARE



PHARMACY SPECIALTY NETWORKS
NETWORK PSN
communicate

CSHP has more than 20 PSNs to join! Check out www.cshp.ca for a complete list.

Join the Pharmacy Specialty Network! CSHP membership will connect you with what's important – people and information.

PSNs:

- connect members with others who share a passion for a particular facet of pharmacy practice
- facilitate the quick exchange of ideas, developments, methods, experiences, knowledge to improve practice
- support collaboration on projects, research, and educational programs to address the needs of the members of a PSN
- provides additional opportunities for members to serve as both opinion leaders and key resources for CSHP Council on professional specialty issues, including development of relevant position statements, guidelines, and information papers

Participation in PSNs is free of charge to CSHP members

Visit MY.CSHP.ca and sign up today!



Canadian Society of Hospital Pharmacists
Société canadienne des pharmaciens d'hôpitaux