Unavailability of Outpatient Medications: Examples and Opportunities for Management

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Abstract

Drug shortages create significant challenges for patients and health care providers. Pharmacists play important roles in managing medication therapy during drug shortages. The management of drug shortages by the community pharmacist is an expanding role. Adverse drug reactions and delayed treatments are highlighted in the literature as some of the consequences of outpatient drug shortages; it is likely these harms are underreported. This commentary reviews examples and opportunities for the management of outpatient drug shortages.

Keywords

outpatient, community pharmacy, drug shortage

While the majority of shortages are generic, injectable agents that mostly affect the inpatient population, outpatient drug shortages also create significant challenges for health care professionals and patients.¹ These shortages negatively affect the direct pharmaceutical care provided by pharmacists and other health care providers and require tremendous human resources.² The roles of community pharmacists are expanding in chronic disease management and prevention to ensure effective, safe, and efficient use of medications by establishing ongoing initiatives to improve the quality of prescription drug therapy.³ The role of both outpatient and community pharmacists now includes the management of drug shortages. The American Society of Health-System Pharmacists (ASHP) Drug Shortage Guidelines mainly focus on management of inpatient drug product shortages, and more information is needed regarding the management of outpatient drug product shortages.²

Examples of Outpatient Drug Shortages

Various reasons for drug shortages exist, including the following issues: supply/demand, raw and bulk material, manufacturing, wholesale and distribution, market structure, and regulatory.² In addition, a shortage can occur at any stage of the pharmaceutical distribution chain. Table 1 lists select examples of outpatient drug shortages from the United States that have been collected by the University of Utah Drug Information Service. A few of these examples are highlighted below.

In November 2012, a manufacturer reported a shortage of isoniazid 300 mg tablets due to difficulty in obtaining the active ingredient. In December 2012, the Centers for Disease Control and Prevention encouraged pharmacies to dispense isoniazid 100 mg tablets until the shortage of isoniazid 300 mg was resolved.⁴ In January 2014, the Food and Drug Administration (FDA) announced a national shortage of oseltamivir oral suspension. During that time only oseltamivir 75 mg capsules were available.⁵ Since pediatric patients may not be able to swallow capsules, the FDA reminded health care professionals to use approved compounding instructions available on the FDA website as well as on the product label to compound oral suspension from the 75 mg capsules.⁵

Impact of Outpatient Drug Shortages

There have been several surveys of outpatient pharmacists regarding drug shortages. A prospective study was conducted in Ireland from October 2012 to February 2013, attempting to discover the numbers of drug shortages and the durations of those shortages. The authors found that

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Table 1. Select Outpatient Drug Shortages^a.

Drug on Shortage	Reason	Year	Date Notified	Date Resolved
Albuterol inhalation solution	Supply/demand	2014	09/09/2014	02/13/2015
Albuterol inhalation solution	Unknown	2009	10/26/2009	11/23/2009
Albuterol metered dose inhaler	Raw materials	2012	09/17/2012	10/15/2012
Atovaquone suspension	Unknown	2015	02/20/2015	05/19/2015
Clopidogrel 75 mg tablets	Unknown	2014	02/25/2014	05/13/2015
Dapsone tablets	Unknown	2011	03/28/2011	05/05/2011
Isoniazid tablets	Unknown	2012	12/10/2012	01/22/2015
Itraconazole oral suspension	Manufacturing	2011	05/20/2011	06/10/2011
Methotrexate tablets	Increased demand	2012	08/20/2012	10/20/2014
Mupirocin ointment	Unknown	2009	04/28/2009	06/29/2009
Mupirocin cream	Unknown	2014	12/05/2014	—
Mupirocin nasal ointment	Unknown	2015	08/12/2015	—
Mupirocin cream	Unknown	2005	09/08/2005	6/5/2006
Mupirocin nasal ointment	Unknown	2014	09/11/2014	01/12/2015
Mupirocin nasal ointment	Unknown	2014	04/07/2014	05/08/2014
Mupirocin ointment	Supply/demand	2001	12/06/2001	04/10/2003
Mupirocin ointment	Unknown	2005	3/25/2005	12/2/2005
Ondansetron ODT	Unknown	2012	02/09/2012	08/08/2013
Ondansetron ODT	Unknown	2014	12/01/2014	05/05/2015
Oseltamivir capsule	Manufacturing problems	2001	11/1/2001	11/7/2002
Oseltamivir capsule	Unknown	2009	09/29/2009	03/24/2010
Oseltamivir capsule	Supply/demand	2014	01/06/2014	01/16/2014
Oseltamivir capsule	Supply/demand	2005	10/26/2005	3/13/2006
Oseltamivir capsule	Supply/demand	2014	12/18/2014	04/20/2015
Oseltamivir suspension	Supply/demand	2013	01/02/2013	11/18/2013
Oseltamivir capsule and suspension	Supply/demand	2003	12/18/2003	1/22/2004
Phenytoin (kapseal formulation)	Discontinued	2009	07/28/2009	07/28/2009
Phenytoin 300 mg capsules	Unknown	2014	02/28/2014	08/04/2015
Phenytoin chewable tablets	Manufacturing	2008	11/17/2008	01/07/2009
Phenytoin capsules	Unknown	2011	05/10/2011	10/04/2011
Posaconazole suspension	Unknown	2010	11/01/2010	02/01/2011
Posaconazole suspension	Manufacturing	2014	10/08/2014	08/11/2015

Abbreviation: ODT, orally disintegrating tablets.

^aDescription of outpatient medications on shortage with the reason and date the shortage occurred as well as the date it was resolved.

65/1232 (5.3%) of the dispensed drugs were unavailable with a median 13 days of unavailability. After the authors spoke with the manufacturers and wholesalers, they discovered that reasons for the shortages could be categorized into the following: parallel (unauthorized) exportation (11/65, 17%), manufacturing/licensing issues (16/65, 25%), excess demand (10/65, 15%), and unknown causes (28/65, 43%).⁶

In Finland, pharmacists from 195 randomly selected pharmacies were asked to fill out forms regarding medicines on shortage.⁷ One hundred twenty-nine pharmacies (66%) responded, and 79.8% of those pharmacists reported experiencing daily shortages or almost daily shortages. The reason for the shortage was provided to 11.2% of those pharmacists. Most of the medications on shortage were commonly used medications needed for the nervous

system (30.8%) and cardiovascular indications (17.5%). Approximately half of the cases had available alternative medications. Of all the medicines on shortage, 44.8% were less expensive than most medications, and 39.3% were the least expensive alternative. The study highlighted the increased workload for the pharmacists when experiencing a drug shortage, which ultimately leads to patient dissatisfaction.⁷

There have also been several cases illustrating the unintended consequences outpatient drug shortages have on patients. In 2012, the Canadian supply of trimethoprim-sulfamethoxazole (TMP-SMX) was jeopardized when 2 major manufacturers experienced backorders of the drug.⁸ A case report detailed a highly immune-suppressed 54-year-old patient who developed a brain abscess from *Nocardia* after being switched to dapsone from

TMP-SMX. Unfortunately, most alternative agents have little or no activity against *Nocardia* species infections.⁸ In France, a shortage in 2012 led to the substitution of 100 mg phenytoin with 100 mg phenytoin sodium.⁹ The results of the substitution were detailed in a case series and included the following: hospitalizations, increases in epileptic attacks, memory issues, thymic disorders, and one death.⁹ A case was reported in which a 75-year-old woman self-discontinued ticlopidine for her dual antiplatelet therapy because of its lack of availability from the pharmacy.¹⁰ Fortunately, the alternative therapy was well tolerated by the patient.¹⁰

Role of the Community Pharmacist in the Management of Drug Shortages

As the majority of the published evidence is linked to inpatient drug shortages, there is considerable need for appropriate management strategies for outpatient drug shortages. For patients, pharmacists are usually the first resource to help with drug shortage issues. In general, the FDA Drug Shortages or ASHP Drug Shortage websites are the starting point to determine the extent and nature of a drug shortage.

When a drug is backordered or discontinued, the pharmacy team should contact the patient to explain the situation and advise of any delays in medication access. If an alternative manufacturer is to be used, the patient should be counseled that the medication will have a different appearance. Other courses of action include proposing a list of appropriate alternatives to the physician for substitution, contacting other community or mail order pharmacies (if the patient is eligible for mail order service through their insurance) to check for inventory, and contacting the pharmacy wholesaler for updates. The pharmacy team can also help reduce out-of-pocket costs by notifying third party payers and advising them of the shortage and alternative products that may need to be added to their formulary.

Potential Role of Pharmacy Benefit Managers in the Management of Drug Shortages

Pharmacy Benefit Managers (PBMs) also play a role in managing drug shortages.¹¹ They efficiently distribute medications throughout all 50 states via mail order and specialty dispensing operations; capabilities that can be used during life-threatening shortages to properly manage remaining inventory. PBMs may play a role in preventing shortages from worsening by (1) providing advance notice to suppliers if the PBM intends to prefer one product over another, (2) preventing active shortages from intensifying by allowing patients to access alternatives or nonpreferred agents at the

patient's usual co-payment rate, and (3) giving access to those with the highest priority by using "prior authorization" programs.¹¹ PBMs could possibly merge their resources with larger health care organizations such as public and private integrated health care systems, national health insurance carriers and managed care organizations, national pharmacy chains, prescription drug wholesalers, and comprehensive care networks to extend these capabilities and provide access to potentially lifesaving therapies.¹¹

The appropriate management of drug shortages is imperative. As such, the role of the outpatient and community pharmacist regarding drug shortages will continue to evolve. Many cases have been reported highlighting the harms that outpatient drug shortages have caused, and it is likely that these harms have been underreported. All clinicians should continue to advocate for a global solution for the drug shortages issue and continue to research the consequences of these shortages. For pharmacists and health care professionals, improving communication among all stakeholders regarding medications will be needed as drug shortage issues continue to occur.

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