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Understanding Drug Shortages as a Pharmacist

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Introduction
A drug shortage is an inadequate supply of medication that negatively affects how a pharmacy dispenses, compounds or clinically uses a drug, as defined by the American Journal of Health-System Pharmacy. Drug shortages in the U.S. health care system are more prevalent now than ever, and their impact is very substantial. In 2010, there were 178 reported drug shortages, up from 61 in 2005 according the Federal Drug Administration (FDA) Center for Drug Evaluation and Research (CDER).\(^1\) Our health care system is designed to rely on the availability of safe, effective and cost-efficient medications. When a medication is unavailable, there are significant consequences not only in the quality of care offered to patients but also in the economic viability of such services. Understanding the causes, challenges and impacts of drug shortages can help pharmacists effectively manage this problem. Pharmacists have the opportunity to develop strategies in order to circumvent drug shortages ensuring appropriate patient outcomes. In order for a pharmacist to effectively manage drug shortages, the pharmacist must first understand the causes as well as the impact on patient care, economical effects and enhanced professional responsibilities of this prevalent problem.

Why do Drug Shortages Exist?
Due to the innate complexity of pharmaceutical supply chains, often it is very difficult to pinpoint a reason for a drug shortage. There are many factors that go into the production and distribution of a drug, and a disturbance at any phase may result in a drug shortage. A drug shortage may be the result of insufficient raw materials and may take over a year for a manufacturer to locate a new source of material and obtain FDA approval.\(^2\) More than 80 percent of raw materials are imported from overseas, which makes the process even more challenging. Besides problems with raw materials, a manufacturer may discontinue production of a drug strictly for financial reasons. For example, if a drug does not achieve a certain profit margin, a pharmaceutical manufacturer may elect to stop its production. As a result, other manufacturers are left responsible to meet the demand of the product. Due to antitrust laws, a manufacturer is not permitted to notify competitors before discontinuing a product. The manufacturer does, however, have the ability to notify the FDA if they choose. The FDA will then post information to the public. Informing the FDA is not required unless the company is the sole manufacturer of a life-saving drug. In short, the FDA has no authority to require a manufacturer to make a product. Also, FDA regulation is a major cause of drug shortages. A manufacturer must meet good manufacturing practice (GMP) regulations. If a manufacturer fails to meet these regulations, the FDA will provide the manufacturer with a list of problems and potential corrective actions that need to be taken. Upon subsequent inspections from the FDA, if the manufacturer did not correct the problems, the FDA may take enforcement action. This could lead to the shutdown of manufacturing sites. Furthermore, manufacturers may choose to voluntarily recall a product due to production issues thus leading to temporary shortages. Although preservation of the availability of a drug is always attempted, sometimes it is just not possible.\(^2\)

How are Drug Shortages Handled?
Both manufacturers and health care systems have a large role in drug shortages and availability. For example, manufacturers commonly employ a just-in-time inventory management style due to the lack of available resources. As a result, when a drug shortage arises, manufacturers are unable to meet the increased demand. Similarly, many hospitals also employ the just-in-time inventory management style. However, an institution aims to maximize profits by reducing the cost of inventory. During a drug shortage, the small amount of inventory on hand will result in the unavailability of a medication to patients.\(^3\)

For example, in March 2011, the FDA issued a bulletin regarding the drug shortage of calcium gluconate. Due to the calcium chloride shortage resulting from American Regent, Inc. ceasing its production seven months prior, an increased demand of the therapeutic alternative, calcium gluconate arose. Furthering the gluconate shortage, two other companies were also experiencing manufacturing delays with this product. As a result, other manufacturers of calcium gluconate such as APP Pharmaceuticals, LLC and Lupin Pharmaceuticals, Inc., experienced an overwhelming demand for this drug starting in June 2011. At the time this article was written, calcium gluconate products were either on backorder, currently being allocated, and/or had been discontinued according to the FDA drug shortage list.\(^4\) As of now, supplies are being released in limited quantities as they become available. There are many efforts being made to conserve this limited supply. First and foremost, health care practitioners began restricting the use of calcium within their institutions to the most critically ill patients and those who were experiencing severe symptoms of hypocalcemia.

There have been several recent examples where supplies of individual medications have been exhausted and health systems were forced to look at alternatives. Several approaches are often employed in concert to be sure that safe and effective care is not compromised. This usually includes convening content experts to determine criteria for using limited remaining drug supplies and identifying any alternatives that might be feasible. At the same time, unnecessary use of the medication is prevented through a variety of mechanisms that include use of electronic health information systems, provider education and direct pharmacist intervention. In the most extreme cases, hospital leadership is involved to determine if elective or other non-urgent procedures or admissions need
to be delayed if sufficient drug supplies are not available to meet the needs of target patient populations.

What Factors are Impacted?
The most significant impact of a drug shortage is compromised patient care. The Institution for Safe Medication Practices (ISMP) conducted a study in 2010 looking at the consequences of drug shortages on patient safety. Of the 1,800 practitioners that responded, 35 percent reported that their facility experienced a near miss that could have resulted in patient harm due to a drug shortage. Additionally, 25 percent reported that the error actually reached the patient and 20 percent testified that the error resulted in an adverse event.4 With such a high incidence of medication errors related to drug shortages, it is important to understand how shortages compromise patient safety in such a substantial fashion. One of the most common ways to deal with a drug shortage is for a physician to prescribe an alternative medication. Many times the physician may not be very familiar with the alternative option. As a result, contraindications and dosing regimens may not be fully understood. Also, some alternative medications may not be as effective as the first-line therapy. Furthermore, therapeutic alternatives may not exist for certain drugs. All of these challenges compromise the care and safety of the patient.

In addition to having a negative impact on patients, the increased labor brought about by drug shortages cannot be ignored. A survey was conducted that included 353 directors of pharmacy from across the nation. It was found that pharmacist and pharmacy technicians spend a considerable amount of time (pharmacist: 9 hours/week, pharmacy technician: 8 hours/week) managing drug shortages as compared to other health care professionals (physicians: 0.5 hours/week, nurses: 0 hours/week).5 This statistic is considerably higher than in 2004 when pharmacists spent 3 hr/wk managing drug shortages. This increased burden results in pharmacists having less time for other high value tasks such as medication therapy management, direct patient care, and enhanced drug delivery. Another very large contributor to increased labor is the extensive use of automation systems in most institutions. Frequently automation systems such as electronic physician ordering, barcode technology, and inventory systems are used in conjunction with one another. Although the increasing use of automation is beneficial within the realm of normal operations, the presence of a drug shortage can cause significant problems. The integration of a new drug and/or protocol into an automated system requires an extensive amount of human resources.6 In contrast, a hospital with a more manual ordering system may present with other challenges such as notifying prescribers of a drug shortage at the time of prescribing.

Not only do drug shortages have a significant impact on patient care and safety, but they have a substantial impact economically as well. As mentioned, one of the most prevalent ways to deal with a drug shortage is through the use of alternative medications. Typically, if an institution is able to purchase an alternative generic, it is attained at an increased cost due to off-contract pricing. A recent study estimated that the purchase of more expensive generics and therapeutic alternatives is at least $200 million annually. When this considerable cost is combined with the $216 million associated with increased labor cost5, the extensive economic impact of drug shortages becomes very clear.

The Role of the FDA
As discussed, drug shortages are more prevalent and severe in today's society. Not only do they compromise patient safety, but they increase the workload of the pharmacy staff and have a substantial economic impact. Due to the severity of these consequences, the FDA works to minimize the effects of drug shortages. When a product that is considered a medical necessity becomes unavailable, the FDA follows a series of steps within the CDER to help resolve the situation. A medical necessity, as defined by American Society of Health-System Pharmacists (ASHP), is a medication that "is used to treat or prevent a serious disease... or condition, and there is no other available source of that product...or an adequate substitute."4 Cost and inconvenience to the manufacturer and/or patient does not qualify the substance as a medical necessity. Therefore, if a drug is considered a medical necessity, the FDA will work with pharmaceutical manufacturers to help acquire additional raw material, technology, or machinery needed to produce the medication. Although the FDA cannot require companies to increase production, it can expedite the review of manufacturing practices.7 This could include extending the product's expiration date, licensing distributors or using materials from different sources. More specifically, if a medication is available but is not identical to the needed product, the FDA can conduct a health hazard evaluation to determine the drug's risk profile.8 Based on these findings, the drug may be used in some protocols. In severe drug shortage cases, the FDA has the authority to temporarily allow the import of non-FDA approved therapy equivalents.9 Throughout these practices, however, maintaining patient safety is of upmost importance. The federal government is taking steps to regulate drug shortages as evidenced by the Executive Order on Reducing Prescription Drug Shortages, which was ordered by President Barack Obama on October 31, 2011.10 Along with collaborating with manufacturers, the FDA also provides continuous updates to the community about the shortage. In 1999, the FDA created the Drug Shortage Program (DSP) as part of the CDER. One of the components of this program is to act as a
liaison between health care professional organizations and manufacturing companies. Working closely with pharmaceutical distributors allows the FDA to provide accurate and timely information to patient groups. Therefore, if a manufacturer decides to discontinue a product and eventually cause a shortage, the FDA can notify important stakeholders and prepare accordingly. As a result, health care professionals are able to identify other treatments for their patients. However, there are additional considerations when utilizing alternative medications. Higher risk profiles, sub-therapeutic results and adverse events are only a couple of examples. Nonetheless, the FDA’s open communication allows health care organizations adequate time to prepare for a drug shortage.

**ASHP Guidelines**

American Society of Health-System Pharmacists (ASHP) developed guidelines for health care professionals, specifically pharmacists, to use when faced with a drug shortage. These guidelines are divided into a process that has three main phases: the assessment phase, the preparation phase and the contingency phase. It is important to note that pharmacists have a vital role in each of these phases.

Throughout the first phase (assessment phase) the duration of the shortage must be determined. Depending on the length of the shortage, institutions may respond differently to the situation. For example, a lack of raw material may cause multiple manufacturers to be unable to produce a drug. As a result, pharmacists and therapeutic committees must find a therapeutic alternative. Before beginning the preparation phase, it is also important for institutions to determine the amount of medication on hand. Based on the quantity and usage history, a measurement of how long a shortage can be endured can be determined.

In order to maintain optimal patient care, the second phase (preparation phase) is vital for pharmacists to utilize in the management of drug shortages. This phase involves preparing for a shortage before its effects are actually seen. For instance, a medication substitution must be considered. Since pharmacists are the drug experts, they have a crucial role in selecting the most ideal alternative. Though a pharmacist should lead this selection, collaborating with doctors, nurses and residents is crucial. While determining drug alternatives, patient safety must also not be forgotten. Therefore, pharmacists are responsible for implementing plans for medical professionals so that patient safety is not compromised. Finally, during the preparation phase, other supply sources of the drug must be researched. If located, availability, contract agreements and payment terms should be discussed. It is crucial for pharmacists not to stockpile a medication. This could lead to a misidentified drug shortage and reduce patient care.

The last and third phase (contingency phase) encompasses therapies that are nontraditional. These medications do not have any therapeutic alternatives nor can they be prepared by a traditional manufacturer. When this happens, institutions should work closely with the FDA. Pharmacists can counsel patients and their families if a delay or compromise in care will occur. Additionally, communicating with the media and other health care organizations can raise awareness of the shortage. As a result, nontraditional companies that produce the drug may be discovered or manufacturers may be motivated to formulate the medication. Throughout the three phases outlined by ASHP, pharmacists have an integral role. From communication advantages to determining therapeutic alternatives, utilization of pharmacist knowledge is vital when faced with a drug shortage.

**Conclusion**

Understanding the contributing factors and consequences of drug shortages is critical for a pharmacist to provide optimal patient care. This is especially important in today’s society due to the fact that drug shortages have reached an all time high. Though the causes of shortages are complex, some contributing factors are lack of resources and manufacturing regulations. One of the major implications of drug shortages is increased labor for the pharmacy staff. As a result, both patient care and health system economics are compromised. Fortunately, the FDA has a major role in preventing, regulating and promoting awareness of drug shortages. Despite the FDA’s efforts, the ultimate responsibility of managing drug shortages falls upon the pharmacist. By applying the phase model created by ASHP, a pharmacist can effectively manage this prevalent problem.

**References**