

Actionable Patient Safety Solutions (APSS) #3F: **Drug shortages**

How to use this guide

This guide gives actions and resources for creating and sustaining safe practices for drug shortages. In it, you'll find:

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Executive summary checklist

Drug shortages are a growing threat worldwide. A drug shortage is a situation in which the total supply of all clinically interchangeable versions of a drug is too low to meet the current or projected demand for use.

- Senior leadership recognize that drug shortages must be treated as a preventable adverse drug event (harm and injury caused by medicine)
- Commit to monitor, prevent, and mitigate drug shortages as outlined by the National Quality Forum (NQF)
- Work on legislation to regulate kickbacks to Group Purchasing Organizations (GPO) from pharmaceutical companies
- Use an effective monitoring and screening system to rapidly identify and mitigate the effects of drug shortages
- Create a rapid response intervention based on the 2018 ASHP Guidelines on Managing Drug Product Shortages (Fox, 2018).
- Review all drug shortages and their impact on patient safety biannually
- Use biannual review to create an improvement plan and as a learning opportunity

What we know about drug shortages

Drug shortages are recurring problem for the US healthcare system (Fox & Tyler, 2003; Baumer & Clark et al., 2004; Kumar, 2006) and around the world (Bochenek, et al., 2018; Iacobucci, 2017; De Weerd & De Rijdt et al., 2017;). The World Health Organization also considers drug shortages as a global problem and has discussed the need for a global notification system (Jarosawski, Azaiez, Korchagina, and Toumi, 2016). Drug shortages happen with all therapeutic classes including:

- Therapeutic products
- Preventive products
- Diagnostic products (Fox, et al., 2009)
- Routinely recommended vaccines (CDC, 2004; CDC, 2002; CDC, 2000; CDC, 2017)
- Biologics (CDC, 2017)
- Parenteral nutrition (Ziesenitz, et al., 2017)
- Saline water (Holcombe, et al., 2017)
- Orphan drugs (Donaldson & Goodchild, 2017)

As of August 28, 2019, the following drug shortages were reported:

- The US Food and Drug Administration (FDA) reported 117 drugs in shortage, including small volume parenteral solutions, electrolytes, sterile water for injection, anesthetics, opioids, and antibiotics, among other drugs
- The European Medicines Agency (EMA) reported 6 drugs in shortage - however, the EMA only reports drug shortages approved using the European centralized system and most shortages are dealt with at a national level. For example, the UK reported 16 new drug shortages in the period January 1-August 28, 2019

The problems with drug shortages

Shortages of drugs, vaccines, and other biological products have an adverse effect on patient outcomes and healthcare costs (Steinbrook, 2009; Hampton, 2007; Kumar, 2006; National Vaccine Advisory Committee, 2003). Current trends show an increase in the health and economic impacts of shortages (Fox & Tyler, 2003; Eggertson, 2010). Pharmaceutical shortages may have a profound effect on patient outcomes (Fox, Tyler, and Caravati, 2002; Hampton, 2007; National Vaccine Advisory Committee, 2003; Lukmanji & Sauro, 2018; Omorodion, et al., 2017).

- Patients may stop the use of an essential product, miss doses, or defer use until the shortage ends (Phuong, et al., 2019; Kumar, 2006; Dorsey, et al., 2009)
- Medicine changes due to pharmaceutical shortages can increase prescribing, dispensing, administration errors, and reduce patient adherence (Fox & Tyler, 2003; Baumer & Clark et al., 2004; Pendergrast, Sher, and Callum, 2004)
- Drug shortages can suddenly change formularies, clinical practice, and clinical decision-support systems, resulting in the disruption of patient care
- Vulnerable populations, including the elderly and patients with rare diseases, bear the highest clinical burden of shortages
- Drug shortages significantly increase drug prices and other health care costs (Flannery, et al., 2017; Fox and Tyler, 2017; Alevizakos, et al., 2016; Iacobucci, 2017)
- Patients often need to switch to more expensive alternatives, (Kumar, 2006; Dorsey, et al., 2009; Pendergrast, Sher, and Callum, 2005; Hampton, 2007; Hendricks and Singha,

2005) increasing health care cost and out-of-pocket expenditures (Phuong, et al., 2019)

Shortages can have negative effects on the financial performance of the industry (Fox). They also create an economic burden to public health programs and health care professionals and providers related to the cost of:

- Tracking inventories
- Complying with recommendations
- Recalling patients when the product is available (Baumer and Clark, 2004; Traynor, 2010)

Stockpiling and other procurement strategies that often follow the reporting of a shortage may amplify its health and cost effect.

Preventing drug shortages

Currently, hospitals lack a standardized methodology to assess the incidence and prevalence, causes, predictors, and effects of drug shortages.

Public and private pharmaceutical shortage programs take a short-term approach, reacting to shortage outbreaks rather than anticipating them. Recent shortage outbreaks justify the need for prevention. Once a shortage happens, mitigation strategies are difficult, costly and fail to address the health and economic effects of the shortage (Baumer and Clark, 2004; Pendergrast, Sher, and Callum, 2005; Kumar, 2006).

In the US, the FDA Safety and Innovation Act (FDASIA) of 2012 requires that manufacturers provide early notification to the FDA of a permanent discontinuance or a temporary interruption of manufacturing of certain medically important prescription drugs. Early notification from manufacturers about possible shortages has enabled FDA to work with manufacturers to restore production of many life saving therapies. If notified of a potential disruption in production, the FDA can help to prevent or mitigate a shortage if other manufacturers are able to increase production by:

- Expediting inspections and reviews of submissions
- Exercising temporary enforcement discretion for new sources of medically necessary drugs
- Working with manufacturers to ensure investigation into the root cause of shortages
- Reviewing possible risk mitigation measures for the remaining inventory

Group Purchasing Organizations (GPOs) could increase the risk of drug shortages (Bruhn, Fracica, and Makary, 2018). Hospital contracts with GPOs should include provisions aiming to reduce the risk of drug shortages. GPOs are excluded from the Social Security Act anti-kickback statute and are allowed to obtain undisclosed fees paid by pharmaceutical companies in exchange of exclusionary contracts. As a result, GPOs have been credited to favor suppliers that pay the largest fees instead of negotiating contracts that lower the risk of market supply disruptions (Kantarjian, 2014).

The EMA and the Heads of Medicines Agencies (HMA) of the European Union created the Task Force on the Availability of Authorised Medicines for Human and Veterinary Use in December 2016 to provide support and advice to tackle disruptions in the supply of human and veterinary medicines and ensure their continued availability. The Task Force priorities include:

- Looking at ways to minimize supply disruptions and avoid shortages
- Facilitating approval and marketing of medicines using the existing regulatory framework
- Developing strategies to improve prevention and management of shortages caused by

disruptions in the supply chain

- Encouraging best practices within the pharmaceutical industry to prevent shortages
- Improving the sharing of information and best practices among EU regulatory authorities to better coordinate actions across the EU
- Fostering collaboration with stakeholders and enhancing communication of supply problems to EU citizens

The Task Force has released guidance for reporting drug shortages (HMA & EMA, 2019) and for communicating drug availability issues (HMA & EMA, 2019b).

Leadership plan

Hospital governance, senior administrative leadership, clinical leadership, and safety and risk management leadership need to work collaboratively to reduce drug shortages.

To achieve a goal of zero preventable deaths, leaders need to commit to taking these key actions.

Show leadership's commitment to reducing drug shortages

- Hospital governance, senior administrative leadership, and clinical and safety leadership must commit to a comprehensive approach to monitoring, preventing, and mitigating the effects of drug shortages. The approach must include:
 - Fundamentals of change outlined in the National Quality Forum (NQF) endorsed set of safe practices
 - Creation of GPO resources and networks
 - Establishment of 503B relationships
- Treat drug shortages as preventable adverse drug events, and a drug shortage leadership plan should be included as part of the medication errors leadership plan (APSS #3A Medication Errors)
- Work on legislation to regulate kickbacks from GPOs
- Hospital governance should provide the resources needed to implement the drug shortage monitoring, prevention, and mitigation plan

Action plan

Ensure accountability

- Create an interdisciplinary healthcare team to design and implement a drug shortage prevention and mitigation plan, and assess the risk of drug shortages and their potential effect on patient care
- Create a surveillance system to rapidly identify drug shortages and respond with interventions to mitigate the effect of drug shortages. The surveillance system should include continuous real-time monitoring and assessment of drug shortages reported by:
 - The US Food and Drug Administration (FDA)
 - The American Society of Health-System Pharmacists (ASHP)
 - pharmaceutical companies and suppliers
- Create a technology system to provide real-time report of the drug inventory in the hospital, impact analysis, and internal resources that are available for compounding and repackaging

- Use the informatics or information technology team need to develop a streamlined process to accommodate drug changes in the electronic health record system, barcode validation, and the infusion pump library
- Negotiate with GPOs, wholesalers, and pharmaceutical companies' contractual clauses to:
 - o Set up prevention programs
 - o Reduce the incidence and duration of shortages
 - o Establish responsibilities for the effects of drug shortages

Find areas for improvement

- Review all drug shortages and their impact on patient care and health outcomes for opportunities to learn and enhance planning.
- Formally assess opportunities to reduce the incidence of drug shortages with a comprehensive self-assessment process.
- The self-assessment must identify risk factors for drug shortages including:
 - Purchasing strategies
 - Inventory management
 - Formulary management
 - Drug use strategies

Create protocols and provide staff training

- Understand the medicine safety gaps actually and potentially caused by drug shortages included in one's formulary
- Consider the risk of drug shortages as one of the factors in drug formulary decision-making
- Promote adequate inventory practices for prevention and mitigation of drug shortages
- Create a process for rapid response interventions to mitigate the effect of drug shortages according to the 2018 ASHP Guidelines on Managing Drug Product Shortages (Fox and McLaughlin, 2018).
- The process for managing drug shortages should include:
 - o Assess the details and potential duration of the shortage
 - o Assess and manage inventory hand and potential drug supply sources
 - o Approve alternative therapies
 - o Define alternative clinical pathways for care of patients affected by drug shortages
 - o Address ethical considerations related to the allocation of drugs in short supply
 - o Communicate with staff, patients, the FDA, and the AHSP

Technology plan

These suggested practices and technologies have shown proven benefit or, in some cases, are the only known technologies for certain tasks. If you know of other options not listed here, please complete the form for the PSMF Technology Vetting Workgroup to consider:

patientsafetymovement.org/actionable-solutions/apss-workgroups/technology-vetting/

System or practice	Available technology
All settings	
ONC Meaningful Use Certified EHR system Electronic Health Record (EHR) System with the following capabilities: <ul style="list-style-type: none"> • Computerized Provider Order Entry (CPOE) • Drug-drug interaction check • Drug-allergy interaction check • Electronic Prescribing (eRx) • Electronic Prior Authorization (ePA) 	
Electronic Medication Administration Record (eMAR) system with pharmacy and bedside barcoding capabilities	
FDA-approved clinical decision support solution for medication therapy recommendations	
Infusion pumps that wirelessly communicate data back to the electronic eMAR	
Patient and medication barcoding system	<ul style="list-style-type: none"> • Single Use Injection Vials and Kits
CPOE simulation tool to quantify the risk of serious ADEs with one's current system CPOE (Metzger, Welebob, Bates, Lipsitz, & Classen, 2010).	
Drug libraries	
Drug libraries	
Pharmacy Workflow Manager	

Surgery environment	
<ul style="list-style-type: none"> • IV injectable doses • Audible and visual feedback for each syringe attached with measurement of dose • Allergy alerts • More accurate and timely wireless documentation to the anesthesia information system 	
Pharmacy environment	
Pharmacy robots to reduce safety problems associated with providers drawing up their own medication stations, and risks associated with contamination from outsourced compounders.	
Utilize Single Use Injection Kits or Pre-mixed sterile solutions	
Other considerations	
"End-to-end" smart pump system, or other electronic pump systems	

Conflicts of interest disclosure

The Patient Safety Movement Foundation partners with as many stakeholders as possible to focus on how to address patient safety challenges. The recommendations in the APSS are developed by workgroups that may include patient safety experts, healthcare technology professionals, hospital leaders, patient advocates, and medical technology industry volunteers. Some of the APSSs recommend technologies that are offered by companies involved in the Patient Safety Movement Foundation. The workgroups have concluded, based on available evidence, that these technologies work to address APSS patient safety issues. Workgroup members are required to disclose any potential conflicts of interest.

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