

Drug Shortages are Plentiful

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Have you ever reported to work
and encountered this scenario?



What now?



Objectives

- Explain reasons for medication shortages
- Outline strategies to manage medication shortages
- Discuss financial implications of medication shortages on a health-system
- Recognize potential safety issues resulting from medication shortages
- Describe methods to minimize medication errors as a result of a medication shortage



What is a Drug Shortage?

- Defined as a supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent.

AJHP. 2009;66:1399-406



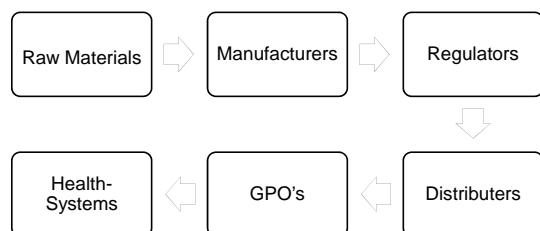
Background

- Drug product shortages...
 - Adversely affect drug therapy
 - Compromise or delay medical procedures
 - Adversely affect health-system finances
 - Result in medication errors
 - Lead to frustration

AJHP. 2009;66:1399-406



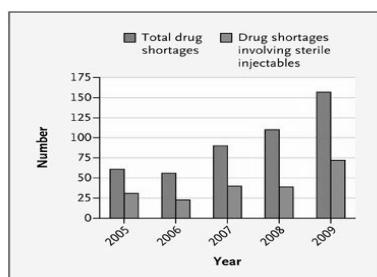
Many Players are Involved



What percent of shortages are injectable medications?

- Less than 10 %
- 15 %
- 30 %
- Greater than 50 %

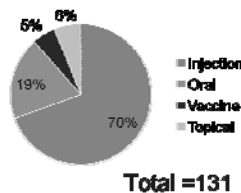
Number of Shortages are on the Rise



Jensen, V. Rappaport, B. Reality of drug shortages-the case of the injectable agent propofol. nejm.org, accessed June 16, 2010

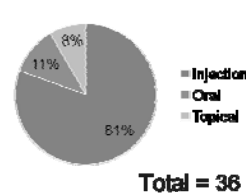
Consider the Source

ASHP Drug Shortages
July 23, 2010



Total = 131

FDA Drug Shortages
July 23, 2010



Total = 36

ashp.org and fda.org
accessed July 23, 2010

Raw Material Shortage

- 80% of raw materials used in pharmaceuticals come from outside the United States
- Problems can occur due to:
 - Political unrest
 - Animal diseases contaminating raw supplies
 - Damage during harvest, storage, or transport
- Example:
 - Aztreonam and Kanamycin

Manufacturing Difficulties and Regulatory Issues

- FDA enforcement action concerning noncompliance with good manufacturing practice
- Closure of a specific manufacturing facility
- Example:
 - Soul source for hyaluronidase production closed leaving no supplier

Voluntary Recalls

- Generally related to manufacturing problems
- Temporary
- Minor issues with manufacturing not subject to FDA legal action
- Affect specific lots
- Example:
 - Sulfamethoxazole/Trimethoprim injection – crimp on vial faulty



Business Decisions

- Generic products
- Market size
- Patent expiration
- Regulatory compliance requirements
- Insufficient financial returns
- Example:
 - Levetiracetam injection



Shortage Example: Propofol

- In 2009 there were 3 manufacturers
 - Teva Pharmaceuticals
 - Hospira
 - APP Pharmaceuticals
- Early October, 2009 Hospira recall due to particulate matter
- Late October, 2009 Teva recall due to possible contamination
- APP is left as the sole supplier



Shortage Example: Propofol

- Late 2009, FDA allows APP to import and distribute Fresenius Propoven
- May, 2010 Teva announces they will exit the propofol market
- July, 2010 Hospira has still not returned to the market



Change in Product Formulation

- Process to change the formulation could create a product shortage
- Examples:
 - Albuterol meter-dosed-inhalers
 - Heparin



Industry Consolidations

- Narrow focus of product lines
- Move to new manufacturing facilities
- Typically result in single source products
- Resiliency in supply chain decreases
- Example:
 - Vaccines



Restricted Drug Product Distribution and Allocation

- Market approval requirements
- Post marketing surveillance
- Restrictions on available limited quantities
- Order direct from manufacturer/specialty distributor
- Example: Intravenous Immune Globulin (IVIG)



Inventory Practices

- “Just in time” inventory practices
- Minimize end of quarter/year inventories
- Stockpiling
- Unexpected delivery delays
- Contract expirations
- Pharmacy inventory turns – 11 to 16 per year



Increase in Demand and Changes in Clinical Practice

- New indication
- New therapeutic guidelines
- Substantial disease outbreak
- Examples:
 - Influenza vaccine
 - Oseltamavir



Nontraditional Distributors

- Specialty, licensed distributors
- Obtain products in short supply for the purpose of reselling
- Often have limited quantities
- Substantial markup: 10 to 1000 times
- Inability to ascertain pedigree



Natural Disasters

- Damage to manufacturing or warehouse facilities
- Delay shipment of product
- Inability to obtain supplies
- Example:
 - In 2005, areas affected by hurricanes Katrina and Rita had increased need of medications and an inability to obtain them



What is the most common reason for medication shortages reported to ASHP?

- Raw material
- Regulatory issues
- Manufacturing problems
- Reason is unknown



FDA's Role in Drug Shortages

- Focuses efforts on products that are considered "medically necessary"
- Medical Necessity: a product used to prevent or treat a serious or life-threatening disease or medical condition for which there is no other available source with sufficient supply or alternative drug available



FDA's Role in Drug Shortages

- Manufacturers are NOT required to notify the FDA of potential or current shortages
 - Unless single source or medically necessary
- Cannot force production
- Can expedite review of facilities and drug approvals
- Can allow the importation and use of foreign drugs



Unapproved Drugs

- DESI
 - Drug Efficacy Study Implementation
 - Refers to drugs that were the subject of 1938 to 1962 NDA's (safety only) and drugs that are identical, related and similar to such drugs
 - Not generally recognized as safe and effective



Unapproved Drugs

- Prescription "Wrap up"
 - Drugs on the Market based on claim of being a pre '38 or pre '62 product or identical, related, or similar to such product
- Post '62
 - Drugs initially marketed after 1962



Unapproved Drugs

- December 2009, Amphastar IMS discontinued many emergency syringe products because they were unapproved
- Hospira became the sole supplier of many emergency syringes



Planning for Drug Shortages

- You can't prevent medication shortages, but you can plan for when they happen
- Shortage policy – TJC requirement
- Identify a point person
- Establish a team or committee



Management of Shortages

- Validate details of shortage
- Determine stock on hand and availability from wholesaler or manufacturer
- Identify alternative products or drugs
- Impact analysis
- Establish a final plan
- Implement the plan
- Communicate



Sources for Shortage Information

- Purchasing agent
- Wholesaler
- Manufacturer
- FDA
 - fda.gov
- American Society of Health-Systems Pharmacy
 - ashp.org



FDA Drug Shortages

Drug Name	Company Information	Reason for Shortage	Related Information
Amoxicillin capsules	Boehringer Ingelheim Customer service: 1-800-368-4767	Manufacturing delays reported by both manufacturers.	FDA is awaiting additional information from the firms regarding release dates and will post this information.
Amoxicillin (capsules, phenylephrine and pseudoephedrine) suspension	Unifamed Pharma, Inc. 1-888-828-2883, or 1-800-467-6388 with a payphone Available 24 hours, seven days a week.	See information in Related Information section.	Unifamed supplies continue to be available. Please see attached Dear Letter for important safety information.



ASHP Drug Shortages

The ASHP Drug Shortages website provides a comprehensive overview of drug shortages, including sections for Practice and Policy, Managing Drug Shortages, and a list of current shortages. It also features a sidebar with links to related resources and a search function.



What is the best resource for clinical information regarding drug shortages?

- Wholesaler
- Manufacturer
- FDA
- ASHP




Identification and Assessment


- Details and duration of shortage
- Wholesaler's situation
- Inventory on hand
- Special purchasing requirements
 - Allocations
 - Direct from manufacturer
- Impact Analysis
 - Threat to care
 - Costs




Preparation

- Engage impacted clinicians for input
 - Therapeutic alternatives
 - Patient safety implications
 - Networking – What are others doing?
 - Patient prioritization
 - Stockpiling restraint
- 


Stockpiling

- Can cause artificial shortage when health-systems drain the supply chain and exceed manufacturing capacities
 - Increased inventory is costly and may not be absorbed by normal usage if shortages do not occur as anticipated
- 


Shortage Example: Propofol

- Engaged Anesthesia and Critical Care Services
 - Assessment of inventory
 - Identified what patients would benefit most from receiving propofol and restricted use
 - Limited quantities that could be obtained from the OR Pharmacy Satellite
 - Therapeutic alternatives: fentanyl, midazolam, lorazepam, dexmedetomidine for ICU sedation
- 


Shortage Example: Propofol

- Anesthesia Services in the Operating Room:
 - Sign out of propofol will be limited to 400 mg (40 ml).
 - Propofol use should be limited to:
 - Outpatient surgery cases
 - Inpatient cases for patients with a history of severe postoperative nausea and vomiting
- 

Shortage Example: Propofol

- Criteria for Propofol Use Across All ICU's:
 - Propofol should be reserved for the following patients:
 - Pregnant
 - Require frequent neuro checks
 - Alternatives to Propofol
 - Fentanyl, midazolam, and lorazepam will be the primary agents used for ICU sedation.
 - Dexmedetomidine use reserved for those patients where narcotics and benzodiazepines are not appropriate alternatives
- 

Pharmacy Actions

- Consolidate Inventory
 - Remove from automated dispensing cabinets
 - Remove from non-essential sites
 - Decrease waste – i.e. draw up doses
 - Alternatives
 - Clinical Impacts – adverse drug reactions
 - Alternative sources
 - Identify alternatives – guidelines, reference books, primary literature, physicians
 - Temporary guidelines/procedures
- 

Pharmacy Actions

- Conservation
 - Prioritization of patients
 - Decrease par levels
- Communication

DRUG	SHORTAGE INFO.	MANAGEMENT/ ALTERNATIVES	STOCK STATUS	MANU INFO	NOTES
Epinephrine 1 mg syr	Sole source Manuf. delays	Epi kits are being made to refill ADC	0 syr 1 mg amp Available	Release Mid-Aug	
Furosemide	Unknown	Bumetanide 0.5mg = Furosemide 40mg	Out of 100 mg vials		Alt alert added to CPOE

Impact on Finance

- Off-contract purchases
- Alternate products
- Compounding and repackaging services
- Raw materials
- Personnel costs
 - Management of shortages
 - Updating technology
 - Compounding and repackaging

Financial Impact of Heparin Shortage



Impacts on Medication Safety

15th Anniversary Educating the healthcare community about safe medication practices. A tribute to Patient Safety Organizations.

ISMP Medication Safety Alert! Acute Care

July 20, 2010 • Volume 15 Number 15

Drug shortages threaten patient safety

It's just, and it's not just the rising temperature and humidity that's making this a summer of discontent. Healthcare providers are also feeling the heat from an alarming number of drug shortages of critically important medications. Drug shortages can compromise or delay important drug therapy and result in medication errors. According to reports submitted to ISMP, healthcare practitioners are concerned more than ever before about how frequent drug shortages are adversely affecting patient care and exhausting a tremendous amount of hospital resources to address the growing problem.

LOVENOX unit-dose syringe alert. ISMP posted a Special Alert late last week about the manufacturer's label coming loose from certain Lovex (enoxaparin) unit-dose syringes, a problem identified by several hospitals. In one case, a medication error resulted when a nurse's glove stuck to the label when she was withdrawing the syringe from the patient and before the protective needle shield could be engaged. For more information, please visit: www.ismp.org/alerts/enoxaparin.

Lidocaine "without" EPINEPHRINE. An order for lidocaine

care. This increases the risk of serious errors, especially when the drugs in short supply are high-alert medications.

The HYDROcortisone shortage is a prime example. As recommended in our article on special safety (www.ismp.org/alerts/enoxaparin), many organizations changed from a 2 mg/mL (1 mL) ampul or syringe to a 1 mg/mL (1 mL) ampul or syringe to limit the risk of an overdose. In some hospitals, the switch was initially met with resistance, but perseverance led to success. Then the 1 mg/mL (1 mL) ampuls were unavailable, so hospitals

My organization has experienced a medication error related to a shortage.

- Yes
- No

Potential Safety Issues

- Different strength
- Change in concentration
- Different packaging
- Unfamiliar with alternative agent
- Pharmacy compounding or repackaging
- Delays in therapy

Same Drug Different Strength

- Morphine 2 mg prefilled syringe is not available and the hospital is out
- Decide to substitute with morphine 4 mg prefilled syringe
- Both strengths are in same size prefilled syringe



Same Drug Different Packaging



Same Drug Different Concentration

- Prior to shortage only carried cisatracurium **2mg/ml**
- Decision made to purchase **10mg/ml** to make infusions for ICU's
- Computer system updated to reflect new product



Same Drug Different Concentration

- Eventually the **10 mg/ml** is in shortage, but **2mg/ml** supply has recovered
- Main pharmacy runs out of 10 mg/ml concentration
- Computer system changes were reversed
- Cisatracurium **10 mg/ml** still in stock in a pharmacy satellite
- ERROR occurs and reaches the patient



Unfamiliar with Alternative Agent

- Furosemide is in critical short supply
- Bumetanide is chosen for an alternative for use as continuous infusion
- Furosemide 40 mg = Bumetanide 0.5 mg
- CPOE system changes made to facilitate choosing bumetanide
- Physician orders bumetanide 20 mg/hour
- Near Miss – caught by pharmacist



Minimizing Error

- Consult other healthcare providers
- Carefully consider the alternatives
- Perform an FMEA
- Evaluate technology
- Consider using compounding services for high risk drugs
- **Communicate!**



Technology

- Pharmacy systems
- Computerized order entry systems
- Automated dispensing cabinets (ADC)
- Barcode
 - Medication administration
 - ADC refill
- Infusion pump drug libraries



The Checklist

- | | |
|--|--|
| <ul style="list-style-type: none">• Details of shortage• Quantities on hand• Alternative sources• Determine use• Time to impact• Patient population affected• Therapeutic alternatives | <ul style="list-style-type: none">• Impacts on patient care• Establish a plan• Technology changes• New procedures• Communicate<ul style="list-style-type: none">– Shortage– Effective date– Alternatives– Guidelines/Procedures |
|--|--|



What can you do?

- Be on the look out!
- Stay informed
- Be part of the team
- Communicate with healthcare providers
- Identify potential safety issues
- Report medication errors and near misses



ICHP Annual Meeting 2010
Drug Shortages are Plentiful
121-000-10-049-L04-P
121-000-10-049-L04-T
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New England Journal of Medicine. The reality of drug shortages – the case of the injectable agent propofol. Available at: <http://www.nejm.org>. Accessed June 16, 2010

Useful Websites:

US Food and Drug Administration, Drug Shortages:

<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm>

American Society of Health-Systems Pharmacists, Drug Shortages:

<http://www.ashp.org/shortages?WT.ac=hp%5FPopLinks%5FDrug%5FShortages>

Institute for Safe Medication Practices: <http://www.ismp.org>

Post Test Questions

1. Which one below is NOT a contributing factor to drug shortages?
 - a. Raw material is not available
 - b. Change in product formulation
 - c. Hurricane
 - d. New drug product receives FDA approval
2. Which of the following is NOT a good strategy for managing drug shortages?
 - a. Stockpiling
 - b. Assessing current inventory
 - c. Networking with other health-systems
 - d. Carefully choosing therapeutic alternatives
3. Who should be notified of drug shortages?
 - a. Food and Drug Administration (FDA)
 - b. FDA MedWatch
 - c. American Society of Health-Systems Pharmacists (ASHP)
 - d. FDA and ASHP
4. The following negatively impact finance during drug shortages, EXCEPT?
 - a. Off contract purchases
 - b. Use of outside compounding services
 - c. Use of less expensive alternative agents
 - d. Increase personnel time to manage shortages
5. All of the following are threats to patient safety during a drug shortage, EXCEPT?
 - a. Same drug, different concentration
 - b. Same drug, different packaging
 - c. Use of an unfamiliar agent
 - d. Use of a compounding service for high risk medications
6. Which of the following is NOT a method used to minimize medication errors due to drug shortages?
 - a. Review alternatives for potential SALAD errors
 - b. Performing a failure modes effects analysis (FMEA)
 - c. Not consulting other healthcare providers
 - d. Effective communication