The Drug Distribution Dilemma & Its Impact on Pharmacy Practice

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Disclosures

- This speaker has no disclosures to make
Objectives

• Discuss the causes of the drug shortage crisis
• Discuss the clinical and economic impact of drug shortages.
• Describe the gray market that has emerged
• Identify good practices to implement in the purchase of medications that are in short supply.
Definition

- Drug Shortage is defined as a “period of time when the total supply of such drug available at the user level will not meet the demand for such drug at the user level. “ H.R. 2245.
Drug Shortages Scope of the Problem

• The number of drugs in limited supply is increasing.
  – 2006: 70 shortages
  – 2010: 178 shortages
  – 2011: 210 shortages

• Includes several critical medications
  – Medications used to treat cancer, pain and infections.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278171/?tool=pubmed>.

Medications Vulnerable to Drug Shortages

- Oncology Medications
- Injectable Medications
  - Morphine, electrolytes, propofol, etc...
- Generic Medications
- Single source/ concentrated market share Medications
- Grandfathered Medications
  - FDA’s Unapproved Drugs Initiative


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Drug Shortages
Scope of the Problem
• Continuing increase in shortages

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278171/figure/f1-ptj3611740/

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Drug Shortages Potential Causes

- Quality/Manufacturing Issues
  - Natural disasters
  - Failure to meet GMP Standards
  - Delays in supply of raw materials
  - Recalls of defective lots
  - Company mergers
  - Discontinuation of unprofitable generics

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278171/?tool=pubmed>.
Drug Shortages Potential Causes

- FDA can't require a firm to keep making a drug it wants to discontinue.
- Older drugs are discontinued by companies in favor of newer, more profitable drugs.
  - Example: fewer firms are making older sterile injectable drugs
Drug Shortages Potential Causes

- Industry Consolidation
  - Seven (7) manufacturers make up the large percentage of this market
- There are fewer manufacturers of certain multisource drugs. Therefore when one manufacturer stops making a drug, there is a larger impact.
Drug Shortages Potential Causes

• Generally, shortages are reported on a voluntary basis
  – If sole manufacturer of a medically necessary drug, must give 6 months notice – See 21 U.S.C. 356c

• 38 shortages could have been prevented in 2010 had sufficient notice been given

  <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278171/?tool=pubmed>.

Impact of Drug Shortages

• A study by the Premier Healthcare Alliance in March 2011 suggested the cost of purchasing alternative therapeutic products to those in shortage to be $200 million

• A survey conducted by ASHP and the University of Michigan indicated that hospital pharmacists are spending eight to twelve additional hours per week dealing with shortage
  – Annual labor costs of $216 million


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Impact of Drug Shortages

- Without access to the preferred drug treatment, clinicians must use alternatives, which may be less effective or associated with increased risk of adverse outcomes.
  - 2011 ISMP Study: 1800 respondents reported over 1000 adverse drug events caused by shortages. (25% were medication errors; 20% were adverse drug reactions.)
  - 2011 American Hospital Association Survey: 82% of hospitals reported delayed treatment and more than half said they could not provide some patients with the recommended therapy.
Impact of Drug Shortages

• Sub-optimal patient therapy
  – ↑ MD calls for substitutions
    • Leading to increased 3rd party calls/ PAs
  – ↓ Patient onset of Tx
  – ↓ Customer satisfaction

• Independents/Buying groups disadvantaged
  – Chain/Corporate warehouses/contracts

Government Response to Drug Shortage Crisis

- President Obama signed Executive Order 13588 (Reducing Prescription Drug Shortages) in October 2011
  - Mandatory notification
  - Emphasis on price gouging
    - FDA will work with the Department of Justice (DOJ) to examine whether any secondary drug wholesalers or other market participants have responded to potential drug shortages by illegally hoarding medications or raising prices to gouge consumers.
    - Based on its determination, DOJ, in coordination with other State and Federal regulatory agencies as appropriate, will undertake whatever enforcement actions, if any, it deems appropriate.
  - Increased staffing at FDA
    - FDA will take steps to expand its current efforts to expedite its regulatory reviews, including reviews of new drug suppliers, manufacturing sites, and manufacturing changes
Executive Order 13588

• Modifications to Notification Requirements
  – Federal law requires drug manufacturers to notify FDA when production of critical drugs provided by only one manufacturer is being discontinued. *21 U.S.C. 356c*
    • Drug must be deemed medically necessary by FDA
    • FDA has no enforcement mechanism to penalize a drug maker for failing to report these problems.
  – Executive order directs FDA to broaden reporting of potential shortages of certain prescription drugs.
Prescription Drug User Fee Act

- Prescription Drug User Fee Act
  - Originally passed in 1992, purpose of legislation was to allow the FDA to collect the fees for processing of applications
  - Is re-visited every 5 years
  - Up for renewal in 2012

- Now being considered a vehicle to address drug shortages
  - Draft includes a section that would require drug manufacturers to report to the Food and Drug Administration (FDA) when they experience a production interruption or discontinue making a drug

(S. 296, H.R. 2245)
Prescription Drug User Fee Act

• “Under proposed legislation, Congress would mandate that companies confidentially notify FDA of the interruption in production of any product six months in advance, or as soon as possible in the event of an unplanned stoppage. Manufacturers that fail to report this information would be subject to civil monetary penalties.”
  
  - e.g. Under H.R. 2245 manufacturers who do not comply with the reporting requirements would be subject to civil monetary penalties of up to $10,000 for each day the violation continues. The penalty amount is capped at $1.8 million.

(S. 296, H.R. 2245)

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FDA Action

- Work with companies to address quality/production issues
- Encourage remaining companies to ramp up production.
- Expedite issues related to addressing shortages (e.g. new manufacturers, increased expiry, increased capacity, new raw material source, changes in specifications).
- Drug Shortage Program (DSP) began in 1999
  - Collaborating with FDA experts, industry, and external stakeholders
  - Communicate information to public
FDA Action

• In 2010, 38 shortages were prevented by FDA
  – 16 prevented through regulatory discretion (risk of quality/manufacturing issue able to be mitigated and was outweighed by benefit of the drug)
  – 13 prevented through expedited review (new manufacturing sites, suppliers, changes in specification or other changes)
  – 8 prevented through encouraging other firms to ramp up
  – 1 prevented through communication with DEA regarding firm’s report to FDA regarding need for quota increase


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Other Solutions

- ASHP has created a list of all medications that have been reported to be in shortage
  - Only lists current shortages, not ones that will occur.
- FDA to release a new Track and Trace system by 2013
  - Allow an providers to see exactly where the drug has been and where it was made


NJ Laws Governing Prescription Drug Wholesale

- Most states have regulations governing prescription drug wholesale practices
- New Jersey: If a company is domestic and/or foreign and is shipping wholesale into or out of the state of New Jersey, it is required to be registered with the New Jersey Department of Health and Senior Services Food and Drug Safety Program.
- The regulations require that all manufacturers, whether contract or virtual, and wholesalers, distributors, re-labelers and brokers register
NJ Laws Governing Prescription Drug Wholesale

• Establish standards for wholesale distribution
• Implement requirements of Federal Prescription Drug Marketing Act (21 C.F.R. 205)
• Violations can result in criminal, civil, and/or administrative penalties.
NJ Laws Governing Prescription Drug Wholesale

• A person is guilty of a crime of the third degree if the person:
  – Engages in the wholesale distribution of prescription drugs and, with intent to defraud or deceive, fails to deliver to another person a complete and accurate pedigree, when required, prior to transferring the prescription drug to another person;
  – Engages in the wholesale distribution of prescription drugs and, with intent to defraud or deceive, fails to acquire a complete and accurate pedigree, when required, concerning a prescription drug prior to obtaining the prescription drug from another person;
  – Engages in the wholesale distribution of prescription drugs, and knowingly destroys, alters, conceals or fails to maintain a complete and accurate pedigree concerning any prescription drug in the person's possession:
NJ Laws Governing Prescription Drug Wholesale

- A person is guilty of a crime of the third degree if the person:
  - Engages in the wholesale distribution of prescription drugs and possesses pedigree documents required by the department, and knowingly fails to authenticate the matters contained in the documents as required, but nevertheless distributes or attempts to further distribute prescription drugs;
  - Engages in the wholesale distribution of prescription drugs and, with intent to defraud or deceive, falsely swears or certifies that the person has authenticated any documents related to the wholesale distribution of prescription drugs;
  - Engages in the wholesale distribution of prescription drugs and knowingly forges, counterfeits or falsely creates any pedigree, and falsely represents any factual matter contained on any pedigree or knowingly omits to record material information required to be recorded in a pedigree;
NJ Laws Governing Prescription Drug Wholesale

- A person is guilty of a crime of the third degree if the person:
  - Engages in the wholesale distribution of prescription drugs and knowingly purchases or receives prescription drugs from a person not authorized to distribute prescription drugs in wholesale distribution;
  - Engages in the wholesale distribution of prescription drugs and knowingly sells, barters, brokers or transfers prescription drugs to a person not authorized to purchase prescription drugs, under the jurisdiction in which the person receives the prescription drugs in a wholesale distribution;
  - Knowingly possesses, actually or constructively, any amount of a contraband prescription drug and knowingly sells or delivers, or possesses with intent to sell or deliver, any amount of the contraband prescription drug;
NJ Laws Governing Prescription Drug Wholesale

• A person is guilty of a crime of the third degree if the person:
  – Knowingly forges, counterfeits or falsely creates any label for a prescription drug or falsely represents any factual matter contained in any label of a prescription drug; or
  – Knowingly manufactures, purchases, sells, delivers or brings into the State, or is knowingly in actual or constructive possession of any amount of a contraband prescription drug.

N.J.S.A. 24:6B-29

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NJ Laws Governing Prescription Drug Wholesale

• Definitions
  – Wholesale distribution means the distribution of prescription drugs in or into the State by a wholesale distributor to a person other than a consumer or patient, and includes the transfer of prescription drugs from one pharmacy to another pharmacy if the value of the goods transferred exceeds 5% of total prescription drug sales revenue of either the transferor or transferee pharmacy during any consecutive 12 month period. N.J.S.A. 24:6B-14
  
  • Determining whether a pharmacy falls within the definition of a wholesaler can be a fact sensitive process
NJ Laws Governing Prescription Drug Wholesale

- Pedigree: a statement or record identifying each previous sale of prescription drug, from the sale by a manufacturer through acquisition and sale by a wholesale distributor, including each distribution to an authorized distributor, starting with the last authorized distributor, or the manufacturer if the prescription drug has not been purchased previously by an authorized distributor or is a prescription drug on the specified list of susceptible
NJ Laws Governing Prescription Drug Wholesale

- Misbranded: a prescription drug with respect to which the label is:
  - False or misleading in any particular
  - Does not bear the name and address of the manufacturer, packer or distributor and does not have an accurate statement of the quantities of the active ingredients
  - Does not show an accurate monograph for legend drugs
  - Is misbranded based upon other considerations as provided in the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. s.301 et seq.
Drug Shortages & The Emergence of a Gray Market

- U.S. Representative Elijah Cummings is investigating the “gray market” sales of drugs in short supply.
- As part of this investigation, Cummings obtained confidential information relating to companies that allegedly charge prices many times higher than those negotiated with authorized manufacturers and distributors.
- The investigation has included wholesalers, pharmacies, and other healthcare providers.

Drug Shortages & The Emergence of a Gray Market

- Drugs reviewed by Congressman Cummings include:
  - Cytarabine
  - Paclitaxel
  - Leucovorin
  - Fluorouracil
  - Magnesium Sulfate

Gray Market

• Specially licensed brokers who seek out supplies of medication in short supply, secure the remaining supplies and remarket them with significant markups

• Price increases: 200% to 4500%
  – Average Increase: 650%
    • Cytarabine normal price: $12/vial
    • Increased to $990/vial

Gray Markets Cont.

- Institute of Safe Medication Practices conducted a survey of 549 hospitals in 8/11
  - 52% purchased from gray market vendors in the past 2 years
  - 80% say that purchases from gray market vendors have increased due to recent shortages

Drug Pedigree

- Gray Market medications can exchange hands many times
- Only about $\frac{1}{2}$ the states have drug pedigree laws
  - Enforced at the state level so every law is different
- Creates uncertainty about authenticity, the proper storage and handling, and the viability of the drug

Online Pharmacies

- Desperate patients and hospitals may turn to online sources
- NABP surveyed over 8,000 websites
  - 96% provide prescription drugs from questionable sources
  - 6,812 (>85%) do not require valid prescriptions
  - 3,687 offer foreign/non FDA approved Rx
  - 2,100 have physical addresses outside the US
  - 2,878 have server locations in foreign countries

Online Pharmacies

- Verified Internet Pharmacy Practice Sites (VIPPS)
- VIPPS certified by the NABP
  - Only 30 online pharmacies are certified
- To be VIPPS accredited, a pharmacy must
  - Comply with the licensing and inspection requirements of their state and each state to which they dispense pharmaceuticals.
  - Have demonstrated to NABP compliance with VIPPS criteria including
    - patient rights to privacy
    - authentication and security of prescription orders,
    - adherence to a recognized quality assurance policy
    - provision of meaningful consultation between patients and pharmacists.
Drug Shortages Good Practices

- Recognize that the drugs may be counterfeit, stolen, diverted, mishandled, and/or adulterated
- Develop an institutional policy on how to deal with gray vendors
- Purchase only from authorized distributors or a verified-accredited wholesale distributor
- Be wary of deep discounts

Drug Shortages Good Practices

- Require non-authorized distributors to provide pedigree
- Keep a list of suspect distributors
- Compare with original manufacturer’s product to see if there are differences
- Report suspect medications and pedigree violations to the BOP, FDA, and FTC