Drug Shortages – Causes, Progress, and Strategies

EMS Drug Shortages Summit
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Disclosure

• This presentation represents my own opinions.
National Shortages and University of Utah Drug Information Service

• UU DIS provides drug shortage content to Novation and ASHP

• Public website at www.ashp.org/shortage
  – Partners since 2001
  – Receive voluntary reports submitted via web
  – Collaboration is key to success
  – Frequent communication with FDA drug shortage team
Shortage Website Differences

**ASHP**
- [www.ashp.org/shortage](http://www.ashp.org/shortage)
- Drugs impacting clinical practice (biologics, devices, dosage forms)
- What is available at NDC level
- How to access
- Frequent updates
- Alternatives

**FDA**
- [www.fda.gov/cder](http://www.fda.gov/cder)
- Medically necessary drugs
- Information from manufacturer
Current Trends
National Drug Shortages
New Shortages by Year
January 2001 to February 28, 2014

Note: Each column represents the number of new shortages identified during that year. University of Utah Drug Information Service
National Drug Shortages –
Active Shortages by Quarter

Note: Each column represents the number of active shortages at the end of each quarter. Q1-14 are data through 2/28/14.

University of Utah Drug Information Service
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Active Shortages
By Selected Drug Classes

Active Shortages 2/28/14

- Antimicrobials: 36
- Chemotherapy: 33
- Cardiovascular: 24
- CNS: 43
- E-Lytes, Nutrition: 33
- EMS drugs: 14

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Common Drug Classes in Short Supply – 2010 - 2013

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What do these numbers mean?

• The rate of new shortages has decreased
• The ongoing shortages are not resolving
• Continued daily impact for patients, clinicians, health systems, health care

http://www.gao.gov/products/GAO-14-194
Why is this happening?
Cascade of Events

Early 2000’s
“Find efficiencies in drug production”

Dr. Hamburg
FDA increases scrutiny

Irvine plant closes
New York plant closes
30% manufacturing capacity is closed

Heparin
Warning letters, 483’s begin to document serious quality problems

Ohio plant closes
Fragile Supply Chain - Sterile Injectables

• Few suppliers (4 to 7)
• Lack of redundancy
  – Concentrated, “just in time” production, at capacity
  – Multiple products made on single line
• Complex manufacturing process
  – No simple fixes for quality problems
  – Problems typically affect multiple products
  – “Quality systems of manufacturing” – key cause identified by ISPE

http://www.ispe.org/drug-shortages-initiative
Economic Drivers

- Quality
- No Incentive
- Not Transparent

Law of Supply and Demand???

• Manufacturers produce on an ultra lean, just in time production schedule
• Number of products increased without additional capacity
• No suppliers to step in when others can’t produce
• Patients, not suppliers
Example – Fragile Supply Chain
Electrolyte / Nutrition Shortage

Key supplier
Warning letter 2011
Closed in 2012
Trace elements*
Zinc, Selenium*
Sodium phosphate
Potassium phosphate
Calcium gluconate
Calcium chloride
Sodium bicarbonate

• Zinc shortage results in dermatitis at Children’s National

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6207a5.htm
Shortages of EMS Basics

• Frequent fliers
• 10 medications short > 50 times between 2001 and 2013
  – Dextrose, diazepam, epinephrine, fentanyl, lorazepam, morphine, ondansetron, nalbuphine, naloxone, promethazine
IV Fluids Shortage

• 3 suppliers
• All suppliers state “increased demand”
• “Real story” remains unclear
• Rolling shortages, unclear allocations (expect problems at least until June)
  – Available fluid type, volume will vary
  – FDA working on imported product
Minimizing Impact
National Level
Summits

• ASA, ASCO, ASHP, ISMP – Invitation Shortage Summit – November 2010
• FDA Public Workshop on Drug Shortages – September 2011
• ASHP Drug Shortage Summit 2.0 – April 2013
GAO Report - 2011

- 1190 shortages between 1/1/01 – 6/20/11
- Average duration 286 days
- 64% of shortages were frequent fliers
- Strengthen FDA’s ability to respond
  - Congress should require manufacturers to report to FDA
  - FDA should enhance ability to respond
GAO Report - 2014

• Ongoing drug shortages remain a problem.
• FDA is working to prevent shortages
• FDA should enhance data analysis to focus on early identification of risk factors.

www.gao.gov/products/GAO-14-194
Limited capacity will take years to resolve

Pricing

- For 44 oncology products short since 2008, prices decreased by a mean of 26.5% between 2006 and 2008. Oncology products not impacted by shortages showed no price decreases.

Government Action

• Executive Order – 10/31/11
• FDA Interim Final Rule – December 2011
• Senate and House Bills provide basis for language included in FDASIA / PDUFA

FDASIA

• Drug shortage language around notifications
• Requires FDA Strategic Plan
• President signed into law July 9, 2012
FDA Strategic Plan

• Mandated as part of FDASIA law (2013)
• 2 key goals
  – Enhance mitigation efforts
  – Develop long-term prevention
• Suggestions for external stakeholders
  – Manufacturing incentives
  – Use quality data when purchasing
  – Capacity, redundancy

Making a Difference?

+ FDA prevents hundreds of shortages
+ More suppliers choose to work with FDA early
+ Decreased rate of new shortages

- Ongoing shortages not resolving
- Manufacturing problems
- Continued patient impact
Coping
Strategies for EMS Shortages

• Make different purchasing and inventory decisions
• Use alternatives
• Consider compounded product
• Use expired product
Purchasing / Inventory

• Purchase from more than 1 source
  – Direct accounts?
• Can you buy a different form? (vials vs. prefilled syringes)
• Inventory strategies may minimize waste
• Consider quality?
Form 483 & Warning Letters

• 483 - documents inspection findings
• Warning letters – significant issues
• Worth reading!
  – Metal particles, mold, contamination
  – Insects, animals
  – Urine
  – Manipulating data, mixing failed API with passing API

http://www.fda.gov/ICECI/EnforcementActions/ucm256377.htm
Alternatives

• Check [www.ashp.org/shortage](http://www.ashp.org/shortage) for suggestions
• IV fluids shortage – may need to substitute a variety of products for NS, LR
• May require education, training, protocol reviews / adjustments
• Beware of dosing errors
Compounded Product

• Dating or refrigeration requirements may be a problem – will require logistics around inventory

• (Must) purchase from a registered outsourcing facility (check at FDA)

• Quality matters – poorly compounded product can be deadly

[Website link] www.fda.gov/drugs/guidancecompliance/regulatoryinformation/pharmacycompounding/ucm378645.htm
FDA and Compounding

- Summary page provides links to actions, recalls, Med Watch alerts, inspections

CDER Statement: FDA alerts pharmacies to concerns with testing conducted by Front Range Laboratories

[8/21/13] The U.S. Food and Drug Administration is advising pharmacies of concerns about the adequacy of testing performed by Front Range Laboratories, Inc., in Loveland, Colo., a testing laboratory used by more than 100 pharmacies in 32 states, to verify quality, sterility, and expiration dating.

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm
Med Watch Trends – Reports Related to Safety, Medication Quality, and Compounding Quality

http://www.fda.gov/Safety/MedWatch/default.htm
Use Expired Product

• Last resort option
• Efficacy – may or may not be potent
• Consider each product, no blanket exceptions
• Standard approach
Crystal Ball Predictions
It’s going to get worse before it gets better…

- FDA increasing inspectors in India
  - Many generic houses moving production
  - Ranbaxy, Wockhardt bans
  - Falsified data, shoddy product
- No new large suppliers (Ben Venue)
- Focus on biosimilars
- Who will make the basics that we need?
But there is some hope

• Trend of decreasing new shortages is real
• Some manufacturers are stepping up, new production models for quality
• Action is moving towards prevention, early identification of manufacturing issues