The Oncology Drug Shortage
Where We Are Today

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National Drug Shortages
January 2001 to September 15, 2011

Note: Each column represents the # of new shortages identified during that year
Source: University of Utah Drug Information Service
Shortages by Drug Class

University of Utah Drug Information Service

Shortages, Chemo Only

Source: UUDIS
Hospital Shortages

Percent of Hospitals Reporting the Number of Individual Drugs For Which the Hospital Experienced a Drug Shortage in the Last Six Months

![Bar Chart]

- 1 to 5: 6%
- 6 to 10: 19%
- 11 to 15: 19%
- 16 to 20: 13%
- 21 or more: 44%


Nearly half of hospitals reported experiencing a drug shortage on a daily basis.

![Pie Chart]

- Daily: 47%
- Weekly: 40%
- Monthly: 13%
- Have not experienced any: 1%

Patient Impact

Percent of Hospitals Reporting the Impact on Patient Care as a Result of a Drug Shortage

<table>
<thead>
<tr>
<th>Impact</th>
<th>Always</th>
<th>Frequently</th>
<th>Rarely</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient treatment was delayed</td>
<td>17%</td>
<td>62%</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Patient received a less effective drug</td>
<td>11%</td>
<td>58%</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>Patient did not receive recommended treatment</td>
<td>10%</td>
<td>52%</td>
<td>63%</td>
<td></td>
</tr>
<tr>
<td>Patient experienced an adverse outcome</td>
<td>3%</td>
<td>32%</td>
<td>35%</td>
<td></td>
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</tbody>
</table>


Three out of four hospitals report rationing or implementing restrictions for drugs that are in short supply.

Percent of Hospitals That Have Implemented Rationing and/or Restrictions for Drugs in Short Supply

- Yes: 78%
- No: 22%

Three of 4 hospitals report that they rarely or never receive advance notice of drug shortages...

Percent of Hospitals Reporting They Receive Advance Notice of Drug Shortages from Drug Manufacturers, Wholesalers, Distributors, Group Purchasing Organizations or the FDA

- Always: 3%
- Frequently: 20%
- Rarely: 63%
- Never: 14%


...and are often not informed of the cause or the expected duration of the shortage.

Percent of Hospitals Reporting They Are Informed of the Cause of the Drug Shortage

- Never: 6%
- Always: 6%
- Frequently: 29%
- Rarely: 61%

Percent of Hospitals Reporting They Are Informed of the Expected Duration of the Drug Shortage

- Never: 5%
- Always: 3%
- Frequently: 41%
- Rarely: 51%

Causes of shortages

- Product Quality issues 42%
- Production/Capacity 18%
- Product discontinuation 18%
- Unavailability of raw material (API) 9%
- Loss of site 5%
- Unavailability of other components 4%
- Other drug shortages 4%

54% (as of 12-2010)

Source: FDA Drug Shortages Program

Supply Chain/Manufacturing Problems

- Single source API or raw materials
- Foreign sites major source of raw material
  - ~1200 NDA's for 2007
  - 13% US, 39% India, 43% China
  - Many interruptions beyond control of firm or unpredictable
- Few manufacturers of sterile injections
- Same production lines for multiple items
- Tighter inventories = less backup
The FDA’s Role in Drug Shortages

The FDA Cannot:

- Require notification from manufacturers of potential or pending shortages, or product discontinuation (tiny exception for sole-source, medically necessary)
- Prevent discontinuation of a medically necessary drug until an alternative is identified
- Require firms to increase production of a drug during a shortage
- Impose an allocation plan when a shortage causes life-threatening conditions
The FDA Can:

- Encourage other manufacturers to ramp up production when a drug is in shortage
- Authorize importation of drugs from ex-US sources
- Allow use of products that fall outside quality specifications (regulatory discretion)
- Help a manufacturer put an allocation plan in place
- Successfully intervene in some cases to prevent shortages when given the appropriate notice

Somewhat Differing Views...

Manufacturers...

- Some industry representatives blame part of the problem on increased oversight by the FDA, which has made drug safety a higher priority after coming under intense criticism for being too lax.
- “As you know right now, FDA has taken a heightened approach towards drug safety,” said Maya Bermingham, senior assistant general counsel at the Pharmaceutical Research and Manufacturers of America. “FDA has stepped up inspections. The more you look, the more you may discover problems.”
- While acknowledging that the industry needs to do a better job of coordination, some company officials said the agency should coordinate enforcement actions and drug shortage issues more closely to avoid administrative requirements that cause interruptions.
- “They are very focused on taking quick and aggressive action,” Gordon [Hospira] said. “We applaud the agency’s role in assuring quality, but it can slow things down significantly.”

FDA...

- FDA officials dispute that greater government oversight is a major factor, saying manufacturing problems were the cause of most shortages.
- “There has not been a significant increase in domestic enforcement actions (seizure or injunction) for this class of products in recent years,” Jensen wrote in an e-mail.

*Source: The Washington Post “Shortages of Key Drugs Endanger Patients,” May 1, 2011*
Trends in 483s

- Majority issued for violations of:
  - Quality control: not following procedures / unwritten procedures
  - SOP: not followed or documented
  - Discrepancies: failure to investigate
  - Absence of sound scientific controls
  - Manufacturing performance: lack of procedures to validate or monitor

Source: Pink Sheet, June 6, 2011
Gray market

- 3rd party opportunistic distributors
- Specialize in shortages
  - Buys any available product: bombards organizations with faxes, calls
- Expensive!
  - No guarantee of proper storage, pedigree
  - Possible counterfeit / compounded agent
  - Not enough for usual use

A LITTLE MORE ON THE GRAY MARKET…
Gouging?

- Average markup 650%
- Highest markups:
  - Labetalol, 4,533%
  - Cytarabine, 3,980%
  - Dexamethasone, 3,857%
  - Leucovorin, 3,170%

Source: Premier analysis of 1,745 examples of gray market offers recorded from 42 acute care hospitals, April 2011

Average Markup by Number of Unique Drugs Offered
House Oversight and Government Reform Committee Investigation, Gray Market

5 companies being investigated:

Allied Medical Supply, Inc.
Superior Medical Supply, Inc.
Premium Health Services, Inc.
PRN Pharmaceuticals
Reliance Wholesale, Inc.

What the House wants to know:

How do they obtain the drugs?
How much do they pay for them?
How much do they profit?
Requested information on all company gross revenues, net profits, executive compensation, and labor and equipment costs

Responses due October 19th

Source: CQ Today Online News, 10/5/2011

ASCO and other Stakeholder Activity
Drug Shortages Summit
November 5, 2010

• Partner Organizations
  – American Society of Health-System Pharmacists
  – American Society of Anesthesiologists
  – Institute for Safe Medication Practices

• Product of Legislative/Regulatory Working Group efforts formed basis for recommendations presented at the September 26, 2011 FDA Workshop

We Worked to Focus Media Attention…
2010

“I’ve been in practice more than 30 years and this is the first time I’ve encountered shortages that may affect patient care,” said Dr. Michael Link, president-elect of the American Society of Clinical Oncology.

2010

When drugs are made only by a few suppliers, any one manufacturer can have a huge impact, Michael Link, president-elect of the American Society of Clinical Oncology, tells the Health Blog.
Some in Congress say sterner action may be needed to ensure companies are playing a responsible role. "It's a brewing problem," says Sen. Amy Klobuchar (D., Minn.). She plans to introduce a bill that would require companies to contact the FDA as soon as they sense a supply issue, giving the agency more time to find other makers.

While the dearth that has garnered the most public attention is — ironically — for a barbiturate that is hindering prisons trying to execute inmates, the scarcities are having a much broader impact on keeping people alive, especially in emergency rooms, oncology wards and intensive care units.

"We can't put patients' lives at risk simply because there's some snafu in a process or a manufacturer decides it's less profitable to make a certain drug," said Sen. Amy Klobuchar (D-Minn.). "Patients deserve better than that."
Legislative Efforts
Congressional Action

- Senate Bill introduced by Sen. Amy Klobuchar (D-Minn)
- Co-sponsored by Sen. Robert Casey (D-PA)
- Co-Conveners of the shortage summit joined, provided input
- Currently 16 cosponsors
  - 15 Democrats, 1 Republican
  - Cosponsors include Feinstein, Blumenthal, Collins, Mikulski, Schumer

Preserving Access to Life-Saving Medications Act S.296

- Would require manufacturers to notify FDA of any drug discontinuance, interruption in production, or adjustment; at least 6 months in advance, or ASAP.
  - Adjustments here mean items related to supply of raw materials, including active pharm ingredient, production capabilities, business decisions impacting output, other
- The bill would require FDA to develop an enforcement mechanism—likely fines for not complying.
Shortage Bill (cont’d)

• FDA would develop evidence-based criteria for drugs vulnerable to a shortage.
  – Vulnerabilities include: # of manufacturers, sources of raw materials or API, supply chain characteristics and therapeutic alternatives

Shortage Bill (cont’d)

• FDA would collaborate with manufacturers of drugs vulnerable to a shortage to establish continuity of operations plans for medically necessary drugs
• The bill would revise FDA’s medically necessary definition to include the prevalence of use of a drug as a factor in determining medical necessity.
Other Key Issues

• Not included:
  – Importation
  – Biologics
• No additional resources for FDA

More Congressional Action

• House bill introduced by Rep. DeGette (D-Co 1\textsuperscript{st})
• Co-sponsored by Rep. Rooney (R-Fl 16\textsuperscript{th})
• Currently 40 cosponsors
  – 30 Democrats, 10 Republicans
  – Cosponsors include Eshoo, Cummings, Slaughter, Moran, Connolly
H.R. 2245

- Adds more protection for manufacturers
- Clarifies that “average historic demand” is the individual manufacturer’s average monthly volume of sales of the drug during the last calendar year
- Includes biologics

Recent and Ongoing Activity
As Presented at the NCCS Cancer Policy Roundtable
October 18-19, 2011

ASCO Briefings on the Hill

Dr. Michael Link presents to a full house at an ASCO briefing on the Hill in July.

ASCO Testifies Before Congress

Dr. Charlie Penley presented testimony at an Energy and Commerce Subcommittee on Health hearing September 23, 2011.
ASCO/ASA/ISMP/AHA/ASHP/Hospira Recommendations Presented at FDA Meeting

1. Reallocate FDA resources to Drug Shortage Program and other activities that facilitate resolution of shortages; authorize and appropriate funding for FDA activities that prevent or mitigate drug shortages.
2. Require manufacturers to report product discontinuations and interruptions 6 months in advance or upon determining production will not meet average historic demand; establish communication methods to provide accurate and timely information on drug shortages to providers; establish methods to better predict the seriousness and duration of drug shortages.

- But problem is multifactorial…

3. Establish criteria for determining whether a drug is vulnerable to shortage and designate such drugs as part of the FDA approval process; establish appropriate incentives for manufacturing redundancies or other means of producing emergency supplies for drugs deemed vulnerable to shortages.
4. Require collaboration between the FDA CDER and Research divisions and the Attorney General to establish a process to expedite the increase in manufacturing production quotas when needed in response to shortages of controlled substances.
5. Leverage current FDA pathways to expedite the approval process for medically necessary unapproved drugs vulnerable to shortages without compromising quality and safety of the drug.

- …so will this be enough?
More From the FDA Meeting

• Some believe that:
  – Recent facility shutdowns at heart of problem, caused recent spike in shortages
  – We may be “on our way to recovery” - $$100s of millions being invested in facilities

Other Activities

• Capitol Hill - ASCO staff and volunteers have met with multiple Congressional offices and the HELP and E&C Committees; held briefings
• Meeting with Sec. Sebelius, Commissioner Hamburg 9/9/11
• Senate Working Group: Bipartisan, Cross-Jurisdictional
• GAO Report – promised by end of year
• Federally mandated drug pedigrees (Bennett)?
• House investigation of gray market led by Rep. Cummings (D-Md, ranking member of House Oversight and Government Reform Committee)
Summary

• ASCO working with stakeholders to pursue legislative and policy solutions
• Outcomes of FDA meeting, E&C hearing uncertain
• GAO report still pending