The Oncology Drug Shortage

A Crisis in Care

Michael Link, MD
Annual New Drug Shortages
January 2001 to December 31, 2010

University of Utah Drug Information Service
National Drug Shortages
January 2001 to June 20, 2011

Note: Each column represents the # of new shortages identified during that year
Source: University of Utah Drug Information Service
Shortages by Drug Class
> 10 Shortages in 2010

- Anti-infectives: 19
- Antineoplastics: 20
- Autonomic: 13
- Cardiovascular: 14
- CNS: 28
- Electrolyte: 17
- EENT: 13
- Hormone: 11
Shortages by Drug Class

Comparing drug shortage trends
Then and now…

- **1996 - 2003**
  - Average # of drugs tracked: 60/year

- **2003 – 2011**
  - Average # of drugs tracked: 150/year
Crisis

• Current pace is for >300 for 2011
  – Q1 2010 = 49 shortages vs. Q1 2011= 89
  – Jan 1, 2011 through June 20, 2011 = 156

• Particularly concerning for oncology: 77% of 2010 shortages were of sterile injectables

• Chemotherapy drug shortages
  – 23 in 2010 and 11 so far in 2011 (Q1)
  – No alternatives to these drugs for most indications

• Manufacturing issues are not resolving
Causes of the Drug Shortage

• Manufacturing difficulties/compliance issues
• Corporate decisions/discontinuations
• Market concentration/limited capacity
• Raw materials/API shortage
• Changes in clinical practice
• Emergency situations
• Hospital/pharmacy-based issues

*Source: FDA November 2010
Causes of Drug Shortages 2010

- No reason provided: 47%
- Supply/Demand: 14%
- Regulatory: 1%
- Raw Materials: 3%
- Manufacturing: 28%
- Discontinued: 7%

Source: University of Utah DIS
Shortages of Sterile Injectables: Marketing/Business Causes

For older sterile injectable products
- Fewer firms making these products
- Not enough capacity
- Complex manufacturing process
- Generally not economically attractive; not enough financial return to justify corrective action when problem occurs
- Resources directed to more profitable products

When one firm has problems or discontinues, a shortage almost always occurs.
# Oncology Drugs in Short Supply

<table>
<thead>
<tr>
<th>DRUG</th>
<th>APPLICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin</td>
<td>Lymphoma, testis</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Bone marrow transplantation</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Testis, ovary, lung, sarcoma</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Leukemia, lymphoma</td>
</tr>
<tr>
<td>Daunomycin</td>
<td>Leukemia, lymphoma</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Leukemia, lymphoma, breast, sarcoma</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Leukemia, sarcoma, testis, lung</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>Bowel, sarcoma. lymphoma</td>
</tr>
<tr>
<td>Mechlorethamine</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Leukemia, lymphoma</td>
</tr>
<tr>
<td>Taxol</td>
<td>Breast, lung</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>Bone marrow transplantation</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Many cancers</td>
</tr>
</tbody>
</table>
Consequences of Cancer Drug Shortage

• Treatment delays—never a good idea
• Substitution treatments
  – Less effective therapies
  – Sometimes no effective work-around available
• Increased patient anxiety
• Time and expense of finding drug supply
• Adverse effect on ongoing clinical trials
• Price markup and increase costs of care
Consequences of Cancer Drug Shortage

• Unavailability of Potentially *Curative* Therapy
  – Leukemia
  – Hodgkin disease
  – Non-Hodgkin lymphoma
  – Testis cancer
  – Sarcomas of bone and soft tissue
  – Multiple childhood cancers
Survival Trends in Common Pediatric Cancers

- Hodgkin Lymphoma
- Wilms' tumor
- ALL
- Non-Hodgkin lymphoma
- Brain tumors
- Neuroblastoma
- Bone tumors
- AML

5 Yr Survival [%]
Improvement in Outcome Over Time: Results of COG Studies of ALL

- 1996-2000 (n=3421)
- 1989-1995 (n=5121)
- 1983-1988 (n=3711)
- 1978-1983 (n=2984)
- 1975-1977 (n=1313)
- 1972-1975 (n=936)
- 1970-1972 (n=499)
- 1968-1970 (n=402)
Consequences of Cancer Drug Shortage—Childhood Leukemia

• Acute Lymphoblastic Leukemia (ALL)
  – Most common childhood cancer
  – 5000 cases annually in the USA
  – Currently ~ 85-90% are cured

• Curative therapy for ALL
  
  Vincristine*  
  Prednisone (pills)  
  Asparaginase  
  Daunomycin*  
  Mercaptopurine (pills)  
  Cyclophosphamide  
  Cytarabine*  
  Methotrexate* + leucovorin*

*In short supply
Consequences of Cancer Drug Shortage—Bone Tumors

- Osteosarcoma
  - Most common bone tumor in children and adolescents
  - Currently 65% can be cured with surgery + chemotherapy
  - <10% cured with surgery but without chemotherapy

- Curative therapy for osteosarcoma

  Surgery
  - Doxorubicin*
  - Cisplatin*
  - High dose methotrexate* + leucovorin*

  *In short supply