Surviving Drug Shortages and Effectively Managing Recalls

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and
Jamie Tharp, PharmD, Inventory & Distribution Manager, University of Michigan HomeMed, Ann Arbor, MI
Top 4 Things to Know for CE

1. Make sure your BADGE IS SCANNED each time you enter a session to record your attendance.

2. Carry your Evaluation Packet with you to EVERY session.

3. Pharmacists, Pharmacy Technicians and Nurses need to track their hours on the Statement of Continuing Education Form as they go *(the 2-page triplicate form, so press firmly!)*.

4. FOR CE: At your last session, total the hours and sign both pages of your Statement of Continuing Education Form.

   ✓ Keep the PINK copy for your records and place the YELLOW and WHITE copies in your CE Envelope.

   ✓ Make sure an Evaluation Form is in your CE Envelope for each session you attended *(extra forms are available at the registration desk if you forgot to pick one up)*.

   ✓ Write your name and unique ID number *(six digit number at the bottom of your name badge)* in the designated area on the outside of the envelope, seal it, and place it in the drop box located near the registration area.
• Don Filibeck and Jamie Tharp declare no conflicts of interest or financial interest in any service or product mentioned in this program.

• Clinical trials and off-label/investigational uses will not be discussed during this presentation.
Drug Shortages – How Did We Get Here and How Do We Fix This?

Donald J. Filibeck, PharmD, MBA, National Director, Pharmacy Services, Critical Care Systems, Dublin, OH
Objectives

• List the factors that contribute to the current drug shortage crisis
• List the challenges posed by drug shortages from a pharmacy operations perspective
• Describe the effort currently under way to address the drug shortage crisis
• Explain the steps an infusion provider should or should not take when coping with drug shortages
Audience Questions

• Who has a clear understanding as to why we are in this current state of affairs?
• Who in the room has NOT been significantly affected by a drug shortage?
• Who has someone (e.g., a technician, pharmacist) who spends at least 50% of his/her time dealing with drug shortages?
• Who has gone to outside providers (e.g., compounding pharmacy, alternate vendors) to obtain drugs that are in short supply?
Recent Headlines

• NYT (12/19/11) – “US Scrambling to Ease Shortage of Vital Medications”¹
• WSJ (02/01/11) – “Drug Shortages Distress Hospitals”²
• USA Today – “Drug Shortages Lead to Price Gouging”³
• FoxNews.com – “Reporter’s Notebook: Hospital Drug Shortages Threaten Patient Health, Prove Costly”⁴
• Pharmacist Activist – Drug Shortages – Pharmaceutical Companies Have Caused This Problem and it is Their Responsibility to Resolve It!”⁵
• Washington Post – “Shortages of Key Drug Endangers Patients”⁶
• Detroit Free Press – “Shortages of Important Drugs Mean Big Problems for Thousands of U.S. Patients”⁷
• Bloomberg (06/21/11) – “Too Much FDA Intervention Equals Too Few Drugs: Ramech Ponnuru”⁸
• AMED News (08/01/11) – Mounting Drug Shortages Delaying Treatment⁹
• AOL News (03/29/11) – “9 Dead After IV Infections at 6 Ala. Hospitals”¹⁰
Key Facts

• The number of drug shortages has tripled from 61 in 2005 to 178 in 2010

• Of the 127 studied drug shortages in 2010-11:
  – 80% were injectable drugs
  – 28% were oncology drugs
  – 13% were anti-infective agents
  – 11% were electrolyte/nutrition drugs
Key Facts (Cont.)\textsuperscript{11, 12}

- Of the 127 studied drug shortages in 2010-11:
  - 50% were generic or “unapproved” drugs
  - 43% were innovator drugs
  - 7% were both

- Also:
  - 171 companies were involved in the 127 studied drug shortages
  - 40% of the 127 shortages were caused by 3 companies
  - 1 company was involved in 27 shortages
  - 1 company was involved in 23 shortages
  - 1 company was involved in 19 shortages
Number of U.S. Drug Shortages, 2005-2010

Ref: 11
Drug Shortages by Route of Administration, 2010-2011

(Based on 127 drug shortages beginning between January 1, 2010 and August 26, 2011)
Drug Shortages by Drug Class, 2010-2011

Drug classes with five or fewer shortages 33%

Oncology 28%
Neuromodulator 9%
Electrolyte/Nutrition 11%
Antibiotic 13%
Hormonal 6%

Based on 127 drug shortages between January 1, 2010 and August 26, 2011

Ref: 11
Drug Shortages of Interest to Home Infusion Pharmacies

- TPN Additives
  - Electrolytes
  - Trace Elements
  - Amino Acids / Fat Emulsions
  - Various Additives
- Chemotherapy Drugs
- Antibiotics

Source: baxterbiopharmasolutions.com
Key Facts

• 71% of the generic injectable market is held by three (3) manufacturers
• Most sterile injectables have one (1) manufacturer that produces at least 90% of the drug
• Dedicated manufacturing lines are often required
• Manufacturing processes are complex and can more easily lead to problems
• Most manufacturers utilize “just-in-time” manufacturing and inventory practices
Reasons for the Drug Shortages\textsuperscript{11,13,14,15}

- Leading primary reasons
  - 43% due to problems at the manufacturing plant
  - 15% due to delays in manufacturing or shipping
  - 10% due to shortages of the active pharmaceutical ingredient (API)
- Manufacturer quality problems have included:
  - Glass shards
  - Metal filings
  - Fungal and other contamination

Ref: 11
Reasons for the Shortage

(Based on 127 drug shortages between January 1, 2010 and August 26, 2011)

Ref: 11
Reasons for the Drug Shortages

• Regulatory and legislative factors
  – Barriers or ambiguities
  – Lack of FDA authority
  – Lengthy and costly approval process
  – Packaging requirements
  – REMS requirements
Other Reasons for Drug Shortages\textsuperscript{11,15,16}

- Voluntary recalls
- Changes in product formulation or manufacturing process
- Unexpected increases in demand and/or shifts in clinical practice
- Natural disasters
- Restricted drug product distribution and/or allocation
Other Reasons for Drug Shortages\textsuperscript{11,15,16}

• Manufacturers’ product decisions and economics
  – Availability of generic products
  – Market size
  – Patent expiration
  – Drug approval status
  – Regulatory compliance requirements
  – Anticipated clinical demand

• Industry consolidation
Other Reasons for Drug Shortages$^{11,15,16,17}$

- Inventory practices
  - “Just-in-time”
  - Poor ordering practices
  - Hoarding (due to rumors)
  - Unexpected delivery delays
- Nontraditional distributors
- Output controls
- Price controls
Some Findings Associated with the Drug Shortages

• Near misses, errors, and adverse outcomes
  – 1 in 3 (35%) experienced a near miss
  – 1 in 4 had actual errors occur
  – 1 in 5 had one or more adverse patient outcomes

• Who’s reporting
  – 21% staff-level practitioners vs. 18% administrative staff

• What discipline is reporting
  – 33% physician
  – 21% pharmacist
  – 16% nurse
## Frequently Encountered Difficulties

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<th>Description</th>
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<td><strong>85%</strong></td>
<td>Little or no information available about the duration of the shortage</td>
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<td><strong>84%</strong></td>
<td>Lack of advanced warning</td>
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<td><strong>83%</strong></td>
<td>Little or no information about the cause of the shortage</td>
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<td><strong>82%</strong></td>
<td>Substantial resources spent</td>
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<td><strong>80%</strong></td>
<td>Difficulty in obtaining alternatives</td>
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<td><strong>78%</strong></td>
<td>Experienced a significant financial impact</td>
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<td><strong>70%</strong></td>
<td>Lack of a suitable alternative</td>
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<td><strong>69%</strong></td>
<td>Substantial resources spent preparing and/or administering the alternative</td>
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<td><strong>64%</strong></td>
<td>Risk of adverse patient outcomes</td>
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<td><strong>58%</strong></td>
<td>Internal hoarding</td>
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<td><strong>55%</strong></td>
<td>Physician anger</td>
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Issues with Alternative Medicines

• Usually have a lower efficacy profile and/or a higher risk profile
• Alternatives quickly become scarce
• Risk of an error or adverse outcome when using unfamiliar alternative drugs
Notification Issues\textsuperscript{18}

• Most learn about a shortage the hard way: failure to receive an order

• Secondarily, internal purchasing, word of mouth, listserves, websites (e.g., ASHP’s drug shortage website)

• Few individuals rely on the FDA’s website for information
Impact of the Drug Shortages

- No clear findings or systematic studies
- Primarily media and anecdotal reports
- ISMP Poll\textsuperscript{18}:
  - 35% reported a near miss
  - 1 in 4 reported a medication error
- AHA Survey\textsuperscript{19}:
  - 82% delays in treatment
  - 69% patients receiving less effective drugs
  - 35% had patients experience an adverse reaction
  - 78% reported rationing or restricting a drug’s use
  - 92% experienced increases in drug costs
Impact of the Drug Shortages

• ASHP Survey\textsuperscript{20}
  – Increase in time spent by personnel managing the drug shortages
  – The larger the hospital, the greater the number of shortages and the impact of those shortages
  – Multiple approaches used to deal with the shortage, including:
    • Changing dispensing practices
    • Allocations
    • Alternative therapies
Impact of Drug Shortages

• Suboptimal outcomes
  – Lack of key antibiotics
  – Lack of first-line chemotherapy drugs

• Deficiencies
  – Trace elements in parenteral nutrition patients

• Product distribution issues
  – Ordering
  – Stocking
  – Order entry
  – Compounding
  – Dispensing / administration
Efforts to Address Current Drug Shortages\textsuperscript{11,22,23,24}

• FDA’s actions to prevent drug shortages
  – Expedited review
  – Regulatory flexibility
  – Increased production

• FDA’s actions in response to a drug shortage
  – Ask manufacturers to increase production
  – Work with manufacturers
  – Expedite review
  – Regulatory discretion
Immediate FDA Actions

- Manufacturer contact
- Guidance and regulations
- Additional FDA staffing
- Legislative support
- Database development
Longer-Term FDA Actions$^{11}$

- Identify factors that contribute to successes and failures in preventing drug shortages
- Identify quality issues
- Work with manufacturers
- Develop a reporting network
- Work with wholesalers
Congressional Efforts$^{25,26}$

- **S.296 “Preserving Access to Life-Saving Medications” act of 2011**
  -Introduced 2/7/11
  -Amy Klobuchar (D-MN)
- **HR.2245 “Preserving Access to Life-Saving Medications act of 2011”**
  -Introduced 6/21/11
  -Diana DeGette (D-CO)
- **Attempt to amend the Food Drug Cosmetic Act to provide the FDA with improved capacity to prevent drug shortages**
The White House\textsuperscript{27,28}

- 10/31/11 Presidential Executive Order directing the FDA to:
  - Take action to further prevent and reduce drug shortages
  - Protect consumers
  - Prevent price gouging
  - Promote broader reporting
  - Expedite regulatory review
- Presidential support for S.296 and HR.2245
- Communicated to manufacturers
- Increased staffing resources at the FDA and Drug Shortage Program (DSP)
- 12/15/11 Follow-up to the 10/31/11 executive order:
  - Issued an interim final rule to help prevent prescription drug shortages that requires certain manufacturers to report to the FDA
Other Federal Government Agencies

• CDER (Center for Drug Evaluation and Research)
  – Drug Shortage Program
• CBER (Center for Biologics Evaluation and Research)
• CDRH (Center for Devices and Radiological Health)
• CMV (Center for Veterinary Medicine)
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<th>CDER</th>
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<th>CDRH</th>
<th>CVM</th>
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<td><strong>Product shortage reporting requirement</strong></td>
<td>Required to provide up to 6 months notification of discontinuation of certain sole-source drugs</td>
<td>Similar to CDER for a small proportion of CBER-regulated products</td>
<td>No reporting requirement</td>
<td>No reporting requirement</td>
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<td><strong>Frequency of industry reporting on shortages</strong></td>
<td>Staff estimate under 50% of product discontinuations are properly reported to CDER</td>
<td>Good cooperation and early notification received from manufacturers</td>
<td>Rarely, if ever. CDRH often finds out about shortages from the media. To obtain information, CDRH must contact the manufacturer directly</td>
<td>Rarely</td>
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<td><strong>Description of shortage problem</strong></td>
<td>About 30-40 shortages currently. Number of shortages has increased significantly over last several years</td>
<td>Very few shortages (last reported in 1/2010)</td>
<td>Limited information</td>
<td>6 active shortages currently. Has been experiencing an increase in shortages</td>
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<tr>
<td><strong>Product most often involved in shortage</strong></td>
<td>Sterile injectables</td>
<td>IVIG, vaccines</td>
<td>Unknown</td>
<td>Sterile injectables</td>
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<td><strong>Database of shortages that have occurred?</strong></td>
<td>Yes</td>
<td>No; Access database in development</td>
<td>No</td>
<td>Consolidated internal list of shortages</td>
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<td><strong>List of shortages publicly available? Does it include reason for shortage?</strong></td>
<td>Yes; List includes company/product, reason (general), and related information</td>
<td>Yes. List includes product name, reason for shortage (general), and status</td>
<td>No</td>
<td>No</td>
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<td><strong>Is there a shortage plan in place?</strong></td>
<td>Yes: MAPP</td>
<td>Yes; SOPP 8506. SOPPs for use within OCBQ currently being developed</td>
<td>CDRH has Standard Operating Procedures to address device shortages</td>
<td>No. In process of updating written procedures</td>
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<td><strong>Have you used regulatory discretion in attempting to resolve shortages?</strong></td>
<td>Yes. Through expedited review, discretion with regard to distribution of particular lots, and importation</td>
<td>Yes. Through expedited review and/or inspection of a facility</td>
<td>Yes</td>
<td>Yes, temporary regulatory discretion is considered, but extent of use is unclear</td>
</tr>
<tr>
<td><strong>Have you used importation as a solution to resolving shortages?</strong></td>
<td>Yes; 3 new instances of importation in 2010 and 5 new instances to date in 2011</td>
<td>No</td>
<td>Yes</td>
<td>Yes. While the supplemental approval process is being reviewed</td>
</tr>
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State Legislative Efforts

• Primarily deal with price gouging
• Internet transactions
• Pedigree regulations
Efforts of Professional Societies

- Several key stakeholder meetings
- American Society of Anesthesiologists
- American Society of Clinical Oncology
- ISMP
- ASPEN\textsuperscript{30}
  - www.nutritioncare.org
  - Clinical recommendations and measures
- American Society Health System Pharmacists
Efforts of Professional Societies

American Society Health System Pharmacists$^{31}$

• Published guidelines on managing drug product shortages
  – Monitor for shortages
  – Monitor product usage
  – Report shortages
  – Report errors as a result of shortages
  – Assess appropriate use
Drug Shortage Identified

- Operational Assessment
- Therapeutic Assessment

  Shortage Impact Analysis
  (Estimated impact on patient care)

  Establish Final Plan

  Communicate
  Implement
ASHP’s Phased Approach

- Take a leadership role
- Develop a contingency plan
- Identify a point person
- Plan
  - Identification and assessment
  - Preparation
  - Contingency
ISMP’s Recommendations

• Learn more about drug shortages
• Access inventory of drugs on hand
• Research the drugs in short supply
• Identify potential therapeutic alternatives
• Prioritize patients, place limitations on use
• Conduct a Failure Mode and Effects Analysis (FMEA)
• Do NOT hoard medications
• Establish ongoing communications
• Engage risk management, professional practice
• Establish a drug shortage network
• Establish an organization position on alternate suppliers
• Proactively monitor and report adverse events
**FMEA Approach\textsuperscript{32,33}**

**Identify Key Vulnerability Points**

- Formulary decisions
- Procurement
- Storage
- Medication ordering
- Order processing
- Drug preparation
- Drug dispensing
- Drug administration

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<tr>
<th>Potential Failure Mode</th>
<th>Yes</th>
<th>No</th>
<th>Methods of Avoidance</th>
<th>Comments</th>
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<tr>
<td>Selection and Procurement</td>
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<td>Prescribing and Ordering</td>
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<td>Order Processing</td>
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<tr>
<td>Preparation and Dispensing</td>
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Conclusions

• Drug shortages will not be going away anytime soon
• You must manage through the shortage using both internal and external resources
• Report shortages and adverse events related to those shortages
• Have a plan!
Resources

• Error Reporting
  – https://www.ismp.org/orderforms/reporterrortoismp.asp

• Shortage Reporting
  – FDA:
    http://www.fda.gov/drugs/drugsafety/drugshortages/ucm142398.htm
  – ASHP:
    http://www.ashp.org/drugshortages/report/
Resources

• General Information
  – ASPEN: http://www.nutritioncare.org
  – ISMP: http://www.ismp.org/
  – FDA: http://www.fda.gov/drugs/drugsafety/drugshortages.htm
  – NHIA: http://www.nhia.org/
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References


Questions
Surviving Drug Shortages with a Focus on Safety

Jamie Tharp, PharmD, Inventory & Distribution Manager, University of Michigan - HomeMed, Ann Arbor, MI
• Single Site Home Infusion Operation
• University Health System Affiliation
  – 925 bed hospital system
• Service Range (Michigan, Northern OH/IN)
• Staffing FTEs (RPh FTE)= 105 (9.1)
• Demographics
  – Active Patients
    • monthly average 1811 (676 HIT)
  – Orders Activity
    • Rx Fills= 54,000 (monthly avg)
    • Patient orders processed =2,750 (monthly avg)
  – TPN Census (average 45-50 active patients)
Drug Shortage Management—It’s Complicated

• Shortage Management involves all areas of a pharmacy
  – Ordering → Billing
  – Expense → Revenue

• Who should care about shortage management
  – Entry level staff → Director/Owner

• Shortage management must include an interdisciplinary team approach
Drug Shortage Management a Collaborative Effort

- **Inventory staff** to lead coordination/communication efforts
- **Cleanroom staff** assist in inventory use monitoring and conservation
- **Clinical staff** collaborate in
  - Supply utilization strategies
  - Coordination of care
  - Patient education
  - Order modifications
- **Management** supports
  - Vendor relations
  - Policy and Procedure review/development
  - Cost analyses
- **Everyone** monitors for new Safety Risk Points
Drug Shortages- Never the Same Ride Twice

- Drug Shortages have been on the rise—Is anyone used to them yet?
- Every shortage is unique
  - Equivalents available -or- not
  - Changes in presentations
    - liquid vs. dry vial, vial vs. ampule, etc
  - Changes in concentrations
  - Patient activity/acuity
    - low vs. high census
    - urgent need vs. elective therapy
  - Limited access programs
    - manufacturer direct, importation
  - Product Completely Unavailable

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Drug Shortages-Managing Risk Points

• Drug Shortages cause new error risk points in all work processes
  – Ordering
  – Receiving/Stocking
  – Order Template Modification
  – Order Transcription/Entry
  – Picking/Compounding
  – Education/Administration
  – Patient Outcomes
Drug Shortage Management: Ordering

• Alternative Product Identification
  – Inventory Staff Education/training
    • Pharmacy Tech Certified?
    • Pharmacy related experience
    • Training on selecting the best equivalent product
      – Consider: manufacturer reliability, cost, reimbursement, etc
  – Resources
    • FDA Orange Book, Facts & Comparisons, etc
    • Wholesaler ordering platform
      – Generic alternatives, product look up (brand vs. generic)
  – Supervision
    • Do inventory staff have easy access to clinical advice?
Drug Shortage Management: Ordering

• Procurement Restrictions
  – Delivery delays due to:
    • Centralized supply source (ie: manufacturer direct)
    • Supply transfers between distribution centers
    • Key: must communicate delivery time estimates with stakeholders (pharmacy staff, prescribers, and patients)
  – Manufacturer and wholesaler allocation programs
    • Key: Understand how to advocate for allocation
Drug Shortage Management: Ordering

– Manufacturer & wholesaler allocation, continued
  • Advocate for allocation with your wholesaler
    – Understand your wholesaler’s allocation program/product availability reports
    – Ask for allocation reports
    – Request allocation transfers
  • Manufacturer Direct allocations
    – Review industry resources (ASHP and FDA shortage resources)
    – Work with local manufacturer representatives- understand limited reserve and back order processes
  • *Time consuming endeavors*
## Drug Shortage Management: Ordering

- **Sample HomeMed Excel® report**
  - Cross references wholesaler allocation & back order lists
- **Staff reference, run daily**
  - Key information (new items/ items removed from the list)

### Sample HomeMed Excel® report

| Item # | User Name | ORL | D.E. | D.SLJN | AL2N | AL2C3 | 168h | ASSO Stat Hex Code | Description | Unit | Year | D.E. | DL Order Issue | DL Date | Allocation Note | Get Ver Ctr/Effective D.
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4/26/12
Drug Shortage Management: Receiving/Stocking

• Receiving/Stocking shortage risk points
  – Auto-substitutions by wholesaler may result in wrong product errors
    • Are staff made aware of substitution?
    • Are staff validating products down to the NDC level?
  – Managing multiple presentations at once
    • Multiple backorders placed to anticipate product release dates
Drug Shortage Management: Receiving/Stocking

Managing multiple presentations at once, continued

– How do you manage multiple reserve products?
  • Consider Look Alike/Sound Alike (LASA)
    – Physical Separation recommended
    – Separating inventory makes logical inventory organization difficult
  • Do you place new inventory in same location as old product?
    – What do you do with the one old vial straggling on the shelf?

– Inventory Management strategies
  • Temporary item locations
  • Limit physical access to reserve supply
  • Label/map reserve supply locations
Drug Shortage Management—Order Template Modification

- Before modifying patient orders, update your staff references
  - Inventory item files
  - Compounding references
  - Rx order templates (including external forms)
  - Supply order templates
  - Compounder configuration/setup

- Checklists can help *dot every i* and *cross every t*
Drug Shortage Management—Order Transcription/Entry

• This step may be the most time consuming and prone to errors
  – High complexity and variability
  – Large number of steps required
  – Increased number of operational level staff involved (Pharm Techs, RNs, RPhs)

• Key Steps:
  – Prescriber notification & plan approval
    • required for non-equivalent substitutions
  – Document the changes required
    • Suggestion: develop standardized note templates
  – Order modification
    • New order from template vs. modifying old order
    • Duplicate (redundant) data entry points increase error risk
Drug Shortage Management—Order Transcription/Entry

• Order Transcription/Entry Risk points, continued

  – Software limitations may prevent substitution or alter units of measure

  – Staff confusion over current product available
    • E-mail information management risky but common
    • Results in productivity loss and rework

  – Frequent product outages increase workload
    • Significant reports of staff fatigue
Drug Shortage Management—Picking/Compounding

• Key Steps
  – Product selection from inventory
  – Order review
  – Order compounding
  – Final product review

• Picking/Compounding Risk points
  – Selecting inventory
    • New inventory locations hard to locate
    • Look alike/Sound alike products
      – Difficult to get used to new/unexpected items
      – New risks arise as new shortages develop
Drug Shortage Management—Picking/Compounding

• Picking/Compounding Risk points, continued
  – Order Review/Compounding
    • Product identification
      – NDC level confirmation of correct product improves product verification
      – Compounding without updating paperwork may prevent NDC confirmation
    • Concentration changes are High Risk
      – Updating a product without modifying compounding instructions may result in significant over or under dosing
      – Examples:
        » Concentrated Sodium Chloride (23.4% vs. 14.6%)
        » Sodium Acetate (2 mEq/mL vs. 4 mEq/mL)
        » Leucovorin 100 mg vial (10 mg/mL) vs. 350 mg vial (20 mg/mL reconstituted)
Drug Shortage Management–Education/Administration

• Shortage education and communication is key to safe administration of medication during a shortage
  – Develop training materials
    • Informative, succinct, limit technical jargon (grade 6-8 reading level)
  – Key: Patient/Nurse notification prior to the change
  – Ensure new product and supplies are in the delivery
Drug Shortage Management—Outcomes Monitoring

• Develop a monitoring plan
  – Interdisciplinary participation is key
  – Identify at-risk patients
  – Develop staff guidelines

• Follow through on your plan
  – Audit for compliance
Drug Shortage Management—Outcomes Monitoring

• Monitoring Complexities
  – Difficult to track many changes at once
  – Utilization queries for TPN difficult to automate
  – Deficiency monitoring is complex and may require patient referrals
  – Consequences may not be immediate
  – Communication and data collection key to watch for trends
    • Involve prescribers in monitoring plan
Drug Shortages Impacting Home Infusion

• Most Significant Shortages affecting UM-HomeMed practice have been:
  – TPN additives
  – Chemotherapy
    • Fluorouracil
    • Leucovorin
    • Cytarabine
  – Antibiotics
    • Aminoglycosides
    • Sulfamethoxazole/trimethoprim
Drug Shortages Impacting Home Infusion

Shortages have most severely affected Parenteral Nutrition management

- Sample of TPN Rx template with shortage items in 2011 highlighted
- Simultaneous shortages increase complexity and risk for errors
Shortage Strategies-Concentration Changes

• Examples
  – Sodium Chloride 23.4% vs. 14.6%
  – Sodium Acetate 2 mEq/mL vs 4 mEq/mL
  – Magnesium Sulfate 50% concentrate vs premix bags
  – Leucovorin 10 mg/mL vs 20 mg/mL
Shortage Example-Concentration Changes

• Risk points-Ordering
  – Case: Sodium Acetate Shortage
    • Usual (2 mEq/mL) product unavailable at wholesaler
    • Available product (4 mEq/mL) ordered
    • Inventory staff unaware of potential consequences of concentration change
    • Direct order placed with manufacturer for 2 mEq/mL product
    • Eventual temporary conversion to 4 mEq/mL product
Shortage Example-Concentration Changes

• Risk points- Order Modification
  – Case: Magnesium Sulfate Shortage
    • Usual (50%, 4 mEq/mL) product unavailable in any size
    • Only available commercial product in premix bags
      (i.e. 4 g/100 mL, 0.325 mEq/mL)
    • Home use includes: Parenteral nutrition, IV hydration supplementation
    • Substituting from concentrate to premix bags took significant administrative preparation
Shortage Example-Concentration Changes

• Risk points- Order Modification
  – Case: Magnesium Sulfate Shortage cont...
    • IV Hydration orders: 9 order templates updated
    • TPN orders:
      – 3 TPN ordering templates created
      – 20 Rx templates updated
      – New compounding configuration created
Shortage Example-Concentration Changes

• Risk points- Order Transcription/Entry
  – Case: Magnesium Sulfate Shortage cont...
    • IV Hydration orders:
      – Old orders could not be copied (contained concentrated compounding volumes)
    • TPN orders:
      – 2 Clinicians devoted to converting active orders to new ordering templates (spreadsheet)
        » Templates saved in patient file as “temporary” to draw attention to product shortage
      – Spreadsheet double checked by primary RPh before entry into ordering system
      – Higher volume for micronutrient, altered the Ca X Phos precipitation factor used by HomeMed → lower allowable Ca, Phos doses
Shortage Example-Concentration Changes

• Risk points- Compounding
  – Case: Magnesium Sulfate Shortage, continued
    • IV Hydration orders:
      – Premix bags used
    • TPN orders:
      – Premix bags placed on the compoudner
      – Limited supply of concentrated product reserved to patients with low volume TPN orders
        » Required manual addition of concentrated product
Shortage Example- Presentation Changes

• Examples
  – Sodium Chloride 23.4%
    • Bulk vial → Bag (outsourced)
  – Multivitamins
    • Adult
    • Pediatric
  – Octreotide
    • Vial → Ampule
  – Milrinone
    • Premix → concentrated vials
Shortage Example-Presentation Changes

• Risk points-Receiving/Stocking + Compounding
  – Case: Sodium Chloride 23.4%
    • Usual (bulk vial, 250 mL) product unavailable
    • Outsourced Compounded product obtained (250 mL mini bag)
    • Literature Review identified Look-alike/Sound-alike risk for compounded products
Shortage Example-Presentation Changes

Sample HomeMed Staff Memo

- Safety Intervention from Literature Reviews
  - ISMP published warning about compounded concentrated sodium chloride 23.4% in mini bags.
  - LASA with manufactured mini bags (i.e. Sodium Chloride 0.9%, Dextrose 5% Water)
  - Education/Intervention:
    - All staff called into break room and shown look alike products (non-present staff attested to written instruction)
    - Separated inventory, limited access bins
    - Additional auxiliary labels added after delivery
Shortage Example-Presentation Changes

• Risk points-Ordering
  – Case: Milrinone Shortage
    • Usual (premix, 0.2 mg/mL) product unavailable
    • Concentrated product (1 mg/mL) available
    • Pharmacist review for stability and appropriateness before ordering

• Risk points-Order Modification
  – Case: Milrinone Shortage, continued
    • New mixing templates created
    • Preparation staff reference updated
Shortage Example-Presentation Changes

• Risk points-Order Entry
  – Case: Pediatric Multivitamins
    • Usual product (dry vial) unavailable
    • Available product (2 vial system)
      – Product dispensed in multi-dose boxes (5 x vial 1 + 5 x vial 2)
      – Lot number on box different than lot number on vials
    • In order to track lot numbers, boxes must not be broken
      – Required dispensing in 5 day increments instead of daily
      – Ordering staff required to alter usual weekly dispensing doses to
        (alternating 10 day → 5 day → 10 day supply quantities)
    • Supply orders must be updated
      – Delete SWFI to dilute dry vial
      – Increase number of syringes to draw up dose
Shortage Example-Presentation Changes

• Risk points-Education/Administration

  – Case: Pediatric Multivitamins, continued

    • Verbal notification at time of refill
    • Notification flyer written (back with mixing instructions)
    • Nursing visit coordinated as needed
ATTENTION!
Drug Shortage Alert

HomeMed will be changing your MVI Pediatric multivitamin to Infuvite Pediatric multivitamin.

- The new product is packaged as a liquid in two separate vials.
- You will withdraw 4ml from vial #1 and 1ml from vial #2 to equal your 5ml dose.
- You will not need sterile water to dissolve powered multivitamins, as before.
- The vitamin content of MVI Pediatric and Infuvite Pediatric (both vials) is the same.

Please call 1-800-862-2731 if you have any questions or concerns.

Turn page over for mixing instructions

---

PEDIATRIC INFUVITE- PARENTERAL NUTRITION (PN) MIXING PROTOCOL

SUPPLIES:
- One PN bag. Make sure the ingredients listed on the label matches your prescription.
- INFUVITE® Pediatric (2 vials) as per labeled dose
- One 10 mL syringe with needle
- One 2 mL syringe with needle
- Alcohol wipes
- Additional additives as prescribed

PROCEDURE:
1. Wash your hands thoroughly with an antimicrobial soap
2. Gather your supplies and place in a corner of the room
3. Prepare your work surface by placing a clean paper towel or other clean cloth in a container with clean, unsterile hand soap. Let it dry.
4. Arrange the PN bag and vials on the work surface in the same order as listed under "supplies". Place the appropriate syringe and needle to the right of each vial.
5. Place the syringe holder on the vial.
6. Remove the PN bag from the sterile pack and remove the rod from the injection port. Wipe the injection port of the bag with an alcohol wipe.
7. Pull down the vial by grasping the neck of the vial with a needle, remove the syringe and place it on the work area. Avoid touching the syringe plunger.
8. Check to be sure that the needle is securely attached to the syringe by rotating the needle assembly. Keep the presentation vials away from the needle.
9. Now that you are ready to inject the additives into your PN bag. Wipe the stopper of the vial and rubber injection port of the bag with an alcohol wipe and inject the appropriate amount into the bag. All additives should be injected through the same central port on the injection port of the PN bag.
10. INFUVITE® Pediatric (2 vials)
    - Remove cap from vial #1 and wipe the vial top with an alcohol wipe. Using the 10 mL syringe, insert the needle into the vial and remove it from the vial.
    - Remove cap from vial #2 and wipe the vial top with an alcohol wipe. Using the 2 mL syringe, insert the needle into the vial and remove it from the vial.
11. Hold the bag up over a light source. The bag should be clear without any floating material, no color changes, no floating material or layers on the date.
12. ALWAYS check the accuracy of your compounding by comparing what you used versus the prescripton.
13. Throw away the used syringes and needles in your sharps container. You may throw away your outcome vials in the garbage.
Shortage Example-Presentation Changes

• Risk points-Product Selection/Compounding
  – Case: Octreotide
    • Usual product (vial) unavailable
    • Available product (ampule)
    • When Order entry staff copied old order
      – Filtration instructions were missing
Shortage Example- Non-equivalents

- Example-Amino Acids
- Risk points- Order Modification
  - Usual Product (phosphate free) unavailable
  - Alternate product contains different electrolyte additives

<table>
<thead>
<tr>
<th>Amino Acid Bulk Formulation</th>
<th>Sodium (mEq/L)</th>
<th>Chloride (mEq/L)</th>
<th>Acetate (mEq/L)</th>
<th>Phosphate (mmol/L)</th>
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<td>Substitute</td>
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- Significant Ordering Template modifications required to calculate electrolyte alterations and suggest individual dose adjustments
Shortage Example- Non-equivalents

• Risk points- Order Transcription/Entry
  – Case: Amino Acids continued
    • Prescriber notification/approval
      – Standardized Memorandum written to share with prescribers
      – Explained issue with approximated electrolyte doses and Cl:Acetate ratios
    • 2 Pharmacists dedicated to order conversion, orders double checked by team pharmacists
Shortage Example- Non-equivalents

• Risk points- Ordering/Compounding
  – Case: Calcium Gluconate unavailable
    • Calcium Chloride only alternative calcium source
      – Not recommended for combination with phosphorous in TPN. Summary Reference:
        » Calcium and phosphate compatibility: Revisited again (DW Newton, DF Driscoll Am J Health-Syst Pharm. 2008; 65:73-80)
    • Obtaining the necessary beyond use dating (BUD) information
      – Limited product extended stability information for individual IV administration
      – References:
        » Handbook on Injectable Drugs (LA Trissel)
        » Extended Stability for Parenteral Drugs (CM Bing)
Shortage Example- Non-equivalents

• Risk points- Ordering/Compounding
  – Case: Calcium Gluconate unavailable, continued
    • Calcium Chloride extended stability conundrum
      – Concentrated Electrolytes are considered High Alert, must avoid patient admixture
      – Extended stability studies for multisource generics are not likely to be funded
      – HomeMed performed 14 day physical and chemical stability study
      – Publishing the data is time consuming and difficult for non-academic clinicians
      – Without shared information, each pharmacy will have to complete own internal BUD testing.
Shortage Example- Limited availability

• Examples
  – Amino Acids- 2010
  – Lipids- 2010
  – Calcium Gluconate-2011
  – Trace-minerals 2011/2012
    • Selenium
    • Chromium
    • Copper
Shortage Example- Limited availability

• Risk points- Order Transcription/Entry
  – Case: Lipids
    • Limited supply on hand, no estimate of future supply availability
    • Dose minimization initiated
    • Supply diverted to pediatric patients
    • All long term patients identified at risk for essential fatty acid deficiency
    • Staff decision tree developed
Shortage Example- Limited availability

Example:
Lipid Allocation Plan- 2010

- Weight > 30 kg
  - Oral/Enteral intake?
    - Yes
      - Determine extent of oral/enteral intake
        - If eating significant portion of calories from foods or oral/enteral supplements containing fat, consider eliminating lipids or decreasing to max of 100g/week
          - Contact physician for order for lipid dose decrease and authorization to change to Intralipid® 20% if HomeMed is able to obtain supply from Baxter in the next week
    - No
      - Assess patient’s current TPN lipid dose (Closest to prevent IFAD is a total of 720g/pw week)
        - If oral intake limited to liquids or a low-fat diet follow the decision pathway for NPO patients
          - Is patient’s current lipid dose greater than the dose to prevent IFAD?
            - Yes
              - Contact physician for order for lipid dose decrease and authorization to change to Intralipid® 20% if HomeMed is able to obtain supply from Baxter in the next week
            - No
              - Seek prescription approval to reduce the patient’s weekly lipid dose to ≤30g/week. Also seek authorization to change to Intralipid® 20% if HomeMed is able to obtain supply from Baxter in the next week
      - If eating significant portion of calories from foods or oral/enteral supplements containing fat; consider eliminating lipids or decreasing to 0.5 to 2 g/kg/day
        - If oral intake limited to liquids or a low-fat diet follow the decision pathway for NPO patients
          - Is patient’s current lipid dose greater than the dose to prevent IFAD?
            - Yes
              - Contact the prescriber and discuss possibility to decrease the TPN lipid content to a dose of ≤3g/kg/day (which should prevent IFAD in a pediatric patient). Also seek authorization to change to Intralipid® 20% if HomeMed is able to obtain supply from Baxter in the next week
            - No
              - No lipid dose reduction is required, seeking authorization to change to Intralipid® 20% if HomeMed is able to obtain supply from Baxter in the next week
  - Weight < 30 kg
    - Oral/Enteral intake?
      - Yes
        - Determine extent of oral/enteral intake
      - No
        - Assess patient’s current TPN lipid dose (Closest to prevent IFAD for a pediatric patient is 0.5-1g/kg/dk)
Shortage Example- Limited availability

• Risk points- Outcomes Monitoring
  – Case: Lipids, continued
    • Deficiency monitoring required
      – Staff educated with review of signs/symptoms
    • Lab monitoring plan established
    • Compliance with monitoring plan validated
Shortage Example- Product Unavailable

• Alternative Product Procurement Pathways
  – When we are desperate to provide patient care we may feel the need to turn to:
    • Gray Market
      – Questionable drug pedigree
      – High cost
    • Borrowing
      – Chain of custody documentation difficult
      – Contract pricing and own-use contract restrictions
    • Outsourced Compounding
      – Risk of product contamination and compatibility issues
      – High Cost
Shortage Example- Product Unavailable

• Questions we asked about High Risk Compounding/Outsourcing:
  – Can we do this ourselves?
    • Formulation, supplies, facilities, staffing, education, etc
  – How to find a reliable compounding pharmacy?
    • Local compounding pharmacy toured
  – What Quality assurance tests to request?:
    • Potency, Endotoxin, Sterility (USP <71> filtration +/- Rapid Scan)
  – To wait or not to wait that is the question?
    • Compounded products may take 14+ days to be released from quality hold

• Examples of unavailable products we have outsourced
  – NaCl 23.4% 250 mL bags
  – Sodium Phosphate
  – Selenium
  – Copper
Improving your Shortage Management Processes

• No man is an island
  – Develop a plan that brings people/ideas together
  – Distribute workload
  – Cross train employees
Improving Your Shortage Management Processes

- Staff Education/Communications
  - Primary communication method: Email
- Standardize Communication Templates
- Easily overlooked and forgotten
Improving Your Shortage Management Processes

• Create Additional Staff References
  – Shortage Resources
    • Website to archive shortage communications
      – Accessible to offsite staff
    • Active TPN component list
  – Checklists
    • Key elements of shortage planning and workload distribution
Example Staff References:
Internal Shortage Web page & Shortage Checklist

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Shortage Safety Management Plan

• Shortage Monitoring
  – Wholesaler shortage list
  – Manufacturer websites and representative contacts
  – Product use monitoring
    • Weekly/monthly inventory counts
  – Internal Summary Reports
    • Monitor for new items to list and expected recovery dates
  – Industry Websites (see next)
Shortage Safety Management Plan

• Staffing modifications
  – Pull staff offline to manage complicated shortages

• Inventory Considerations
  – Look Alike/Sound Alike considerations
  – Temporary vs. Permanent storage locations
  – Where do you store reserve products or stragglers
  – Limit access to products not in active use
    • Virtual and physical inventory
Shortage Safety Management Plan

• Limited access and patient allocation planning
  – Involve Medical Director, prescribers, patients
  – Prescribers & Home Infusion Providers work in collaboration to monitor for adverse effects or signs of deficiency
Shortage Safety Management Plan

• Involve Staff
  – Parenteral Nutrition Taskforce
    • Multidisciplinary committee (RPh, RN, RD representation)
    • Evaluates shortages and develops utilization and monitoring plans
    • Act as staff resource for education and shortage expertise
  – Patient Safety Committee
    • Multidisciplinary committee (RPh, RN, PharmTechs, Shipping/Inventory, Management)
    • Errors and near misses tracked via internal reporting tool
    • Errors summarized and trended monthly, quarterly, annually
      – Trends over time often more insightful than isolated incidents
    • Lead process improvements and information sharing to all functional areas.
    • Results: Increased Staff engagement in error reporting since committee development and focus on culture of safety
Shortage Safety Management Plan

• Literature and Industry Information Sources
  – ISMP http://www.ismp.org/
  – ASPEN http://www.nutritioncare.org
  – NHIA
    • Website http://www.nhia.org/
    • List serve
Our Contribution to Industry Information Sources

• Error Reporting
  • https://www.ismp.org/orderforms/reporterrortoismp.asp
Our Contribution to Industry Information Sources

- Shortage Reporting
Conclusion

- Drug Shortages are numerous and increase system complexity
  - Increase risk of medication errors
  - Lead to staff fatigue and lower job satisfaction
  - Require coordination plan
  - Safety plan should include multidisciplinary approach to error reviews and information sharing with staff
Learning Assessment Questions & Answers

Please refer to the NHIA Annual Conference & Exposition 2012 On-Site Program for a brief post-test.

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