What Every Nurse Needs to Know About Drug Shortages

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Speaker Disclosure Statement

- The speakers have no industry relationships to disclose

Learning Outcomes

The learner will be able to:

- Describe the current state, including significance, causes and strategies to manage drug shortages that affect pediatric hematology oncology patients.
- Apply ethical principles to the allocation of drugs to patients during a critical drug shortage
- Describe interventions that the hematology oncology nurse can use in the care of patients and families during an era of drug shortages

Drug Shortage Overview

PREVALENCE, CAUSES, AND SIGNIFICANCE OF DRUG SHORTAGES

Headline News

U.S. Blames Drug Shortages on Low Prices and a 'Broken Marketplace

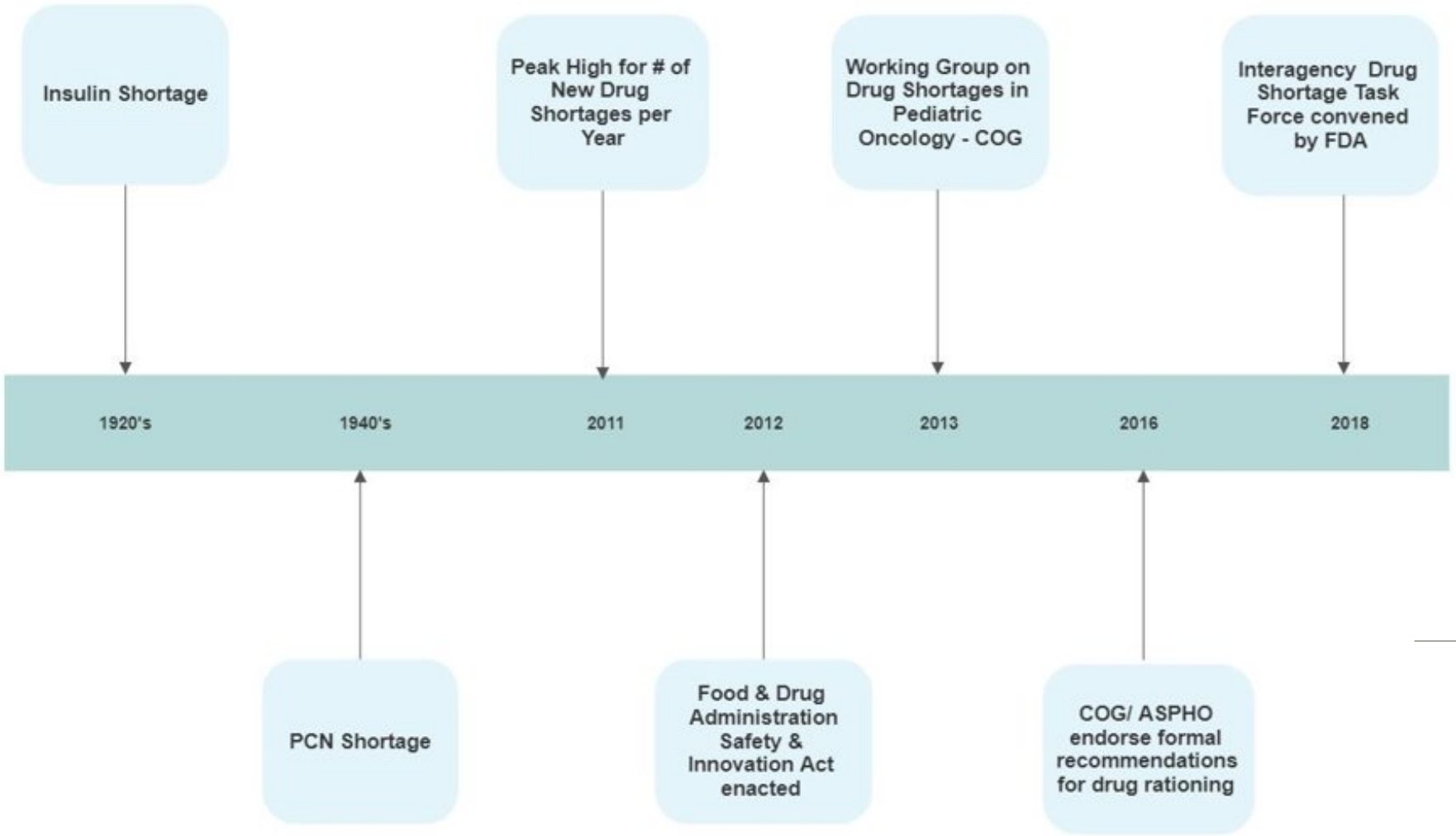
Vincristine shortage underscores vulnerability of 'fragile market' for crucial treatments

Emergency Rooms Run Out of Vital Drugs, and Patients Are Feeling It

Faced With a Drug Shortfall, Doctors Scramble to Treat Children With Cancer

Background

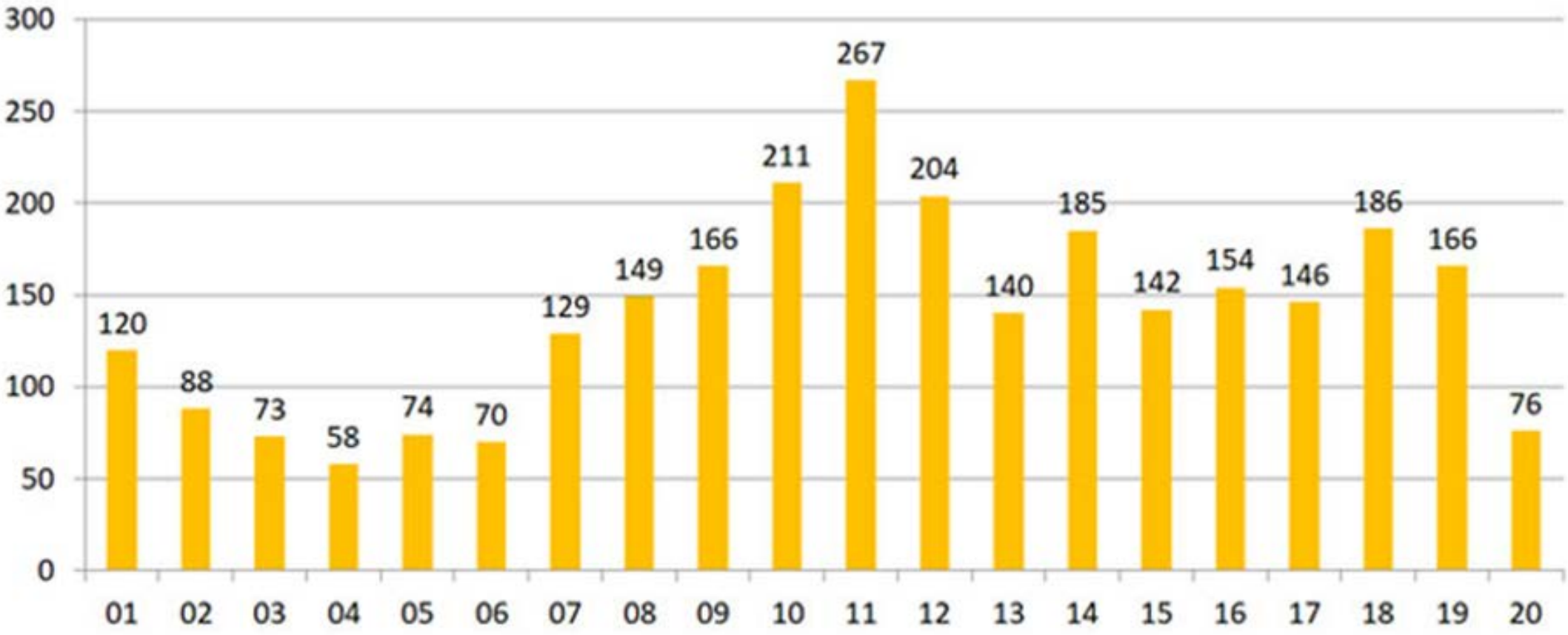
- Drug Shortages are not new
  - 1st reported in the 1920's - Insulin
- Major global public health concern
- Number of shortages are skyrocketing
- Critical drugs, longer shortages
- CNS agents are the longest-lasting shortages
- Chemotherapy consistently among the top 5 drug classes in short supply



Historical Perspective

National Drug Shortages: New Shortages by Year

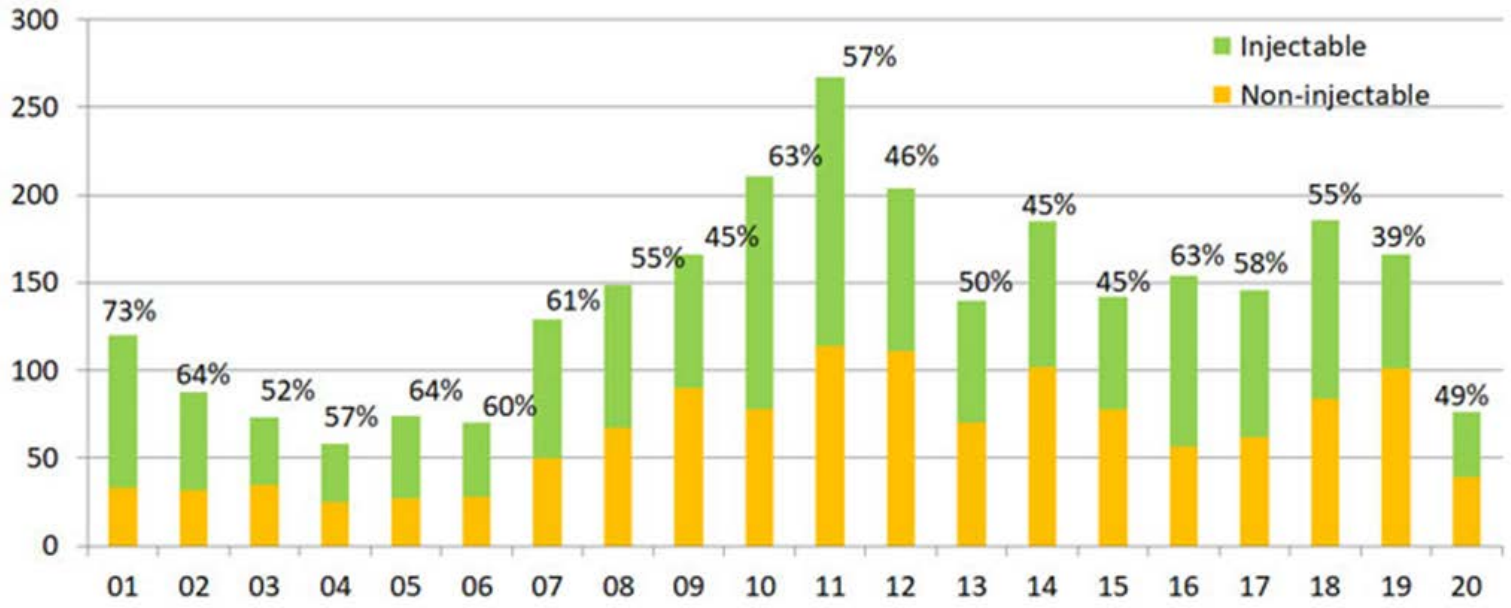
January 2001 to June 30, 2020



Note: Each column represents the number of new shortages identified during that year.

University of Utah Drug Information Service
Contact: Erin.Fox@hsc.utah.edu, @foxerinr for more information.

National Drug Shortages: New Shortages by Year - Percent Injectable



January 2001 to June 30, 2020,

% Injectable

Note: Each column represents the number of new shortages identified during that year.

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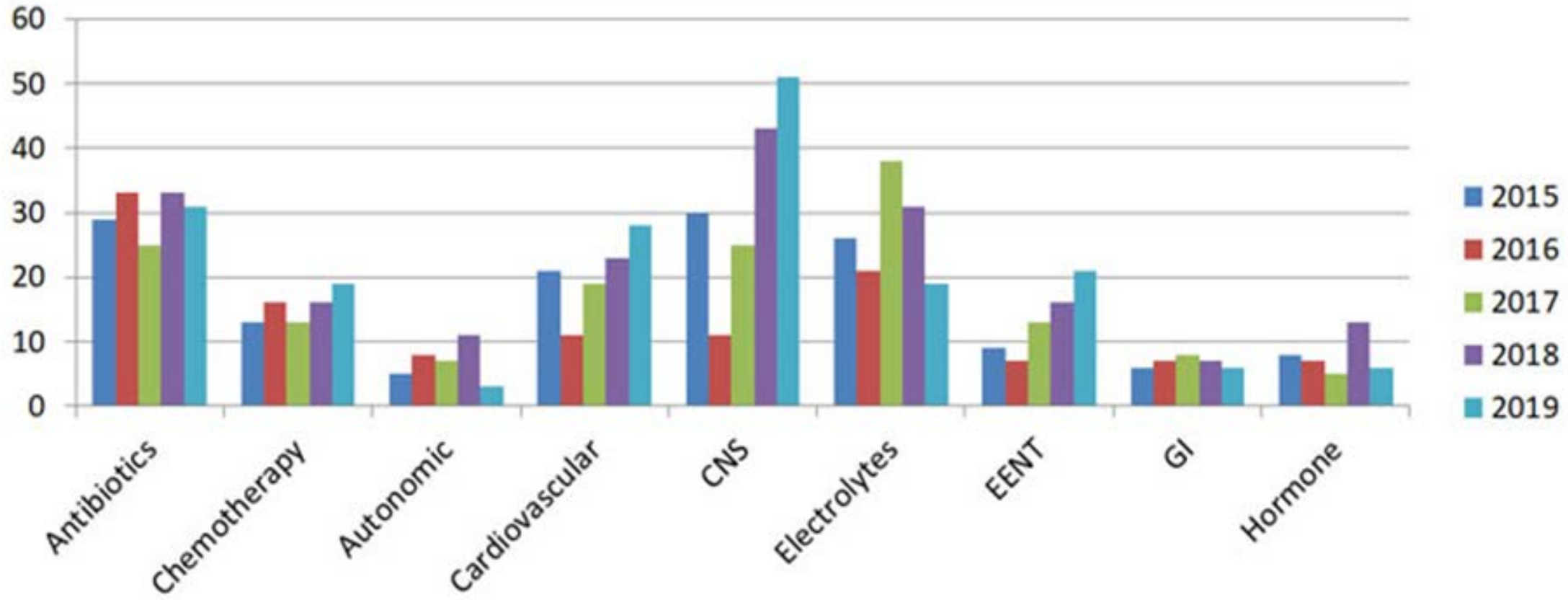
National Drug Shortages: Common Drug Classes in Short Supply

New Shortages Reported: 2015–2019



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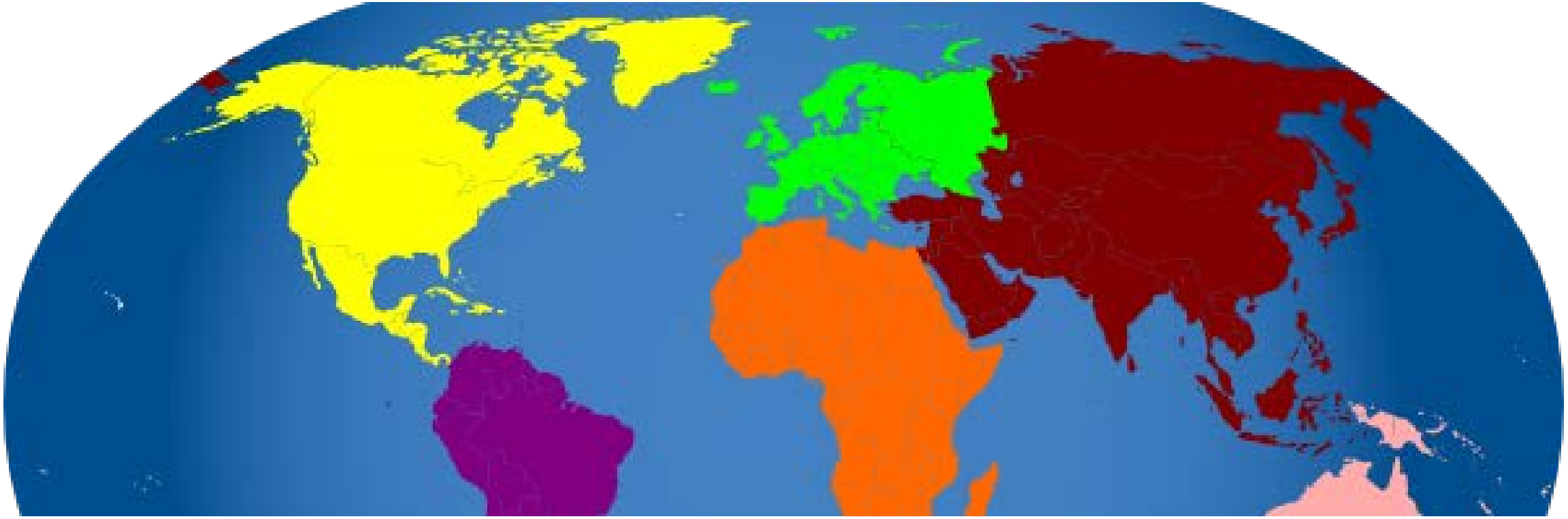
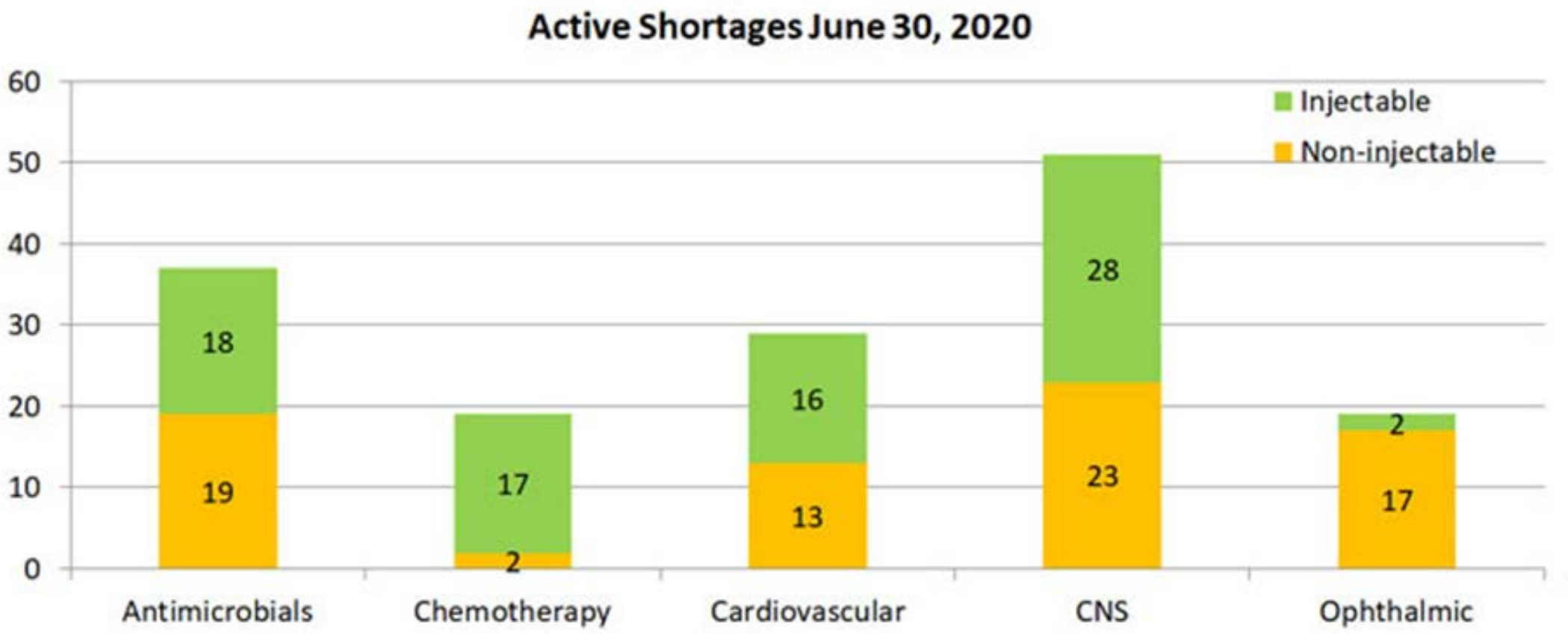


Current State

National Drug Shortages: Active Shortages Top 5 Drug Classes

Active Shortages June 30, 2020



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Examples of Drug Shortages: July 24th, 2020

CURRENT

- Asparaginase Erwinia
- Leucovorin Calcium injection
- Ondansetron injection
- Cefepime
- Propofol
- Tacrolimus capsules
- Sodium Chloride 0.9% vials & syringes
- Hydromorphone injection
- Morphine injection

RESOLVED

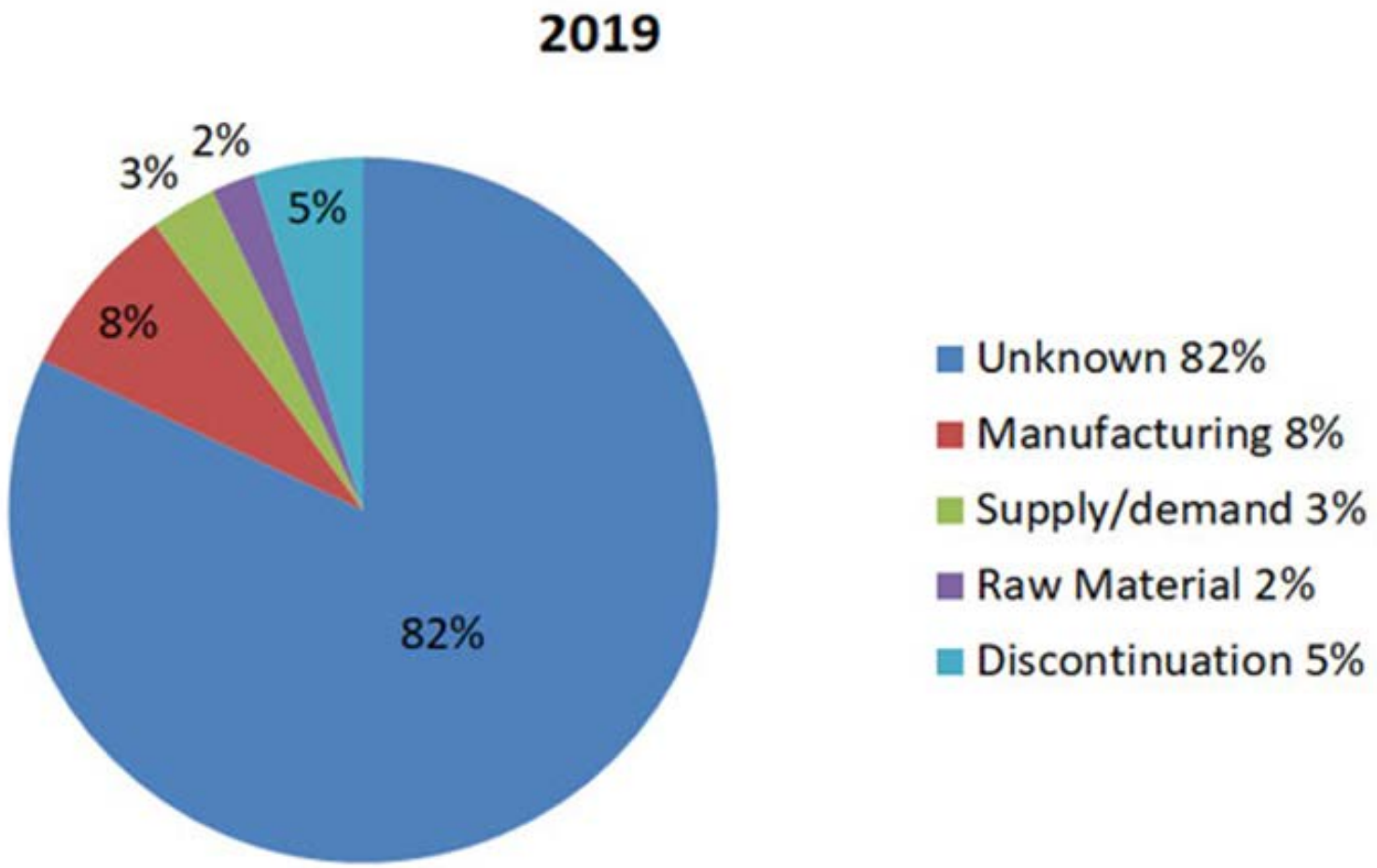
- Nelarabine
- Pentamadine for inhalation
- Zosyn
- Sodium Chloride 0.8% injection bags
- Vinblastine Vincristine

Information obtained from:
FDA Drug Shortage Database

Causes of Drug Shortages

- Limited financial gain
- Manufacturing/quality issues
- Limited raw materials
- Production delays
- Discontinuation of drug
- Supply & demand

Reasons for Shortages as Determined by UUDIS During Investigation - 2019



University of Utah Drug Information Service

Drug Shortages: Root Causes

Inter-agency Drug Shortage Task Force , led by the FDA, identified 3 root causes for drug shortages:

- Lack of incentives for manufacturers to produce less profitable drugs
- Market does not recognize & reward manufacturers for “mature quality systems” that focus on continuous improvement and early detection of supply chain issues
- Logistical & regulatory challenges make it difficult for the market to recover from a disruption

Significance of Drug Shortages

Results in:

- Treatment delays
- Inability to provide standard of care
- Inferior outcomes
- Increased patient deaths
- Increased costs
- Medication errors
- Interference with clinical research
- Significant emotional distress for patients/families
- Ethical dilemmas for health care professionals

Vincristine Shortage

Managing Drug Shortages

PREVENTION AND MANAGEMENT OF DRUG SHORTAGES

ETHICAL DECISION MAKING IN DRUG ALLOCATION

Prevention of Drug Shortages

“A Call to Arms”

FDA Executive Order (2011)

- Require manufacturers to report planned discontinuation of production
- Expedite review of new drug suppliers
- Work with Department of Justice to report hoarding and exorbitant pricing

FDA Safety and Innovation Act (2012)

- Require an annual report to Congress on drug shortages and amelioration efforts

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Prevention of Drug Shortages

Working Group on Chemotherapy Drug Shortages in Pediatric Oncology (2013)

At the national level:

- Create a critical drug and critical drug shortage list for pediatric oncology
- Incentivize and reward high-quality manufacturing processes
- Amend the Medicare and Prescription Drug and Modernization Act to allow greater price increases for generic oncology drugs on the critical drug list
- Examine feasibility of a national stockpile of critical drugs
- Explore voluntary sharing of drugs at the state, regional, or national level
- Explore international agreements to allow rapid access to international suppliers of ingredients or drugs during a shortage

DeCamp, M.,et. al. (2014). Chemotherapy drug shortages in pediatric oncology: a consensus statement. *Pediatrics, 133(3),* e716-724.

Management of Drug Shortages

Operational

Drug Shortage Team

- Data gathering and monitoring
- Purchasing alternatives
- Storage, preparation, and dispensing procedures
- Conservation or rationing strategies
- Technology changes
- Communication

Therapeutic

Resource Allocation Committee

- Identifying patient population
- Identifying therapeutic alternatives
- Oversight of allocation

Minimizing the Impact of Drug Shortages

Maximizing Efficiency and Eliminating Waste

- Review evidence-based indications of drugs and eliminate use of drugs that lack proven efficacy
- Cohort patients receiving the same therapy to share vials during drug preparation
- Reduce advanced preparation of drugs that may lead to waste
- Use safe dose rounding practices to eliminate waste
- Evaluate expiration times and shelf life to extend safe drug use

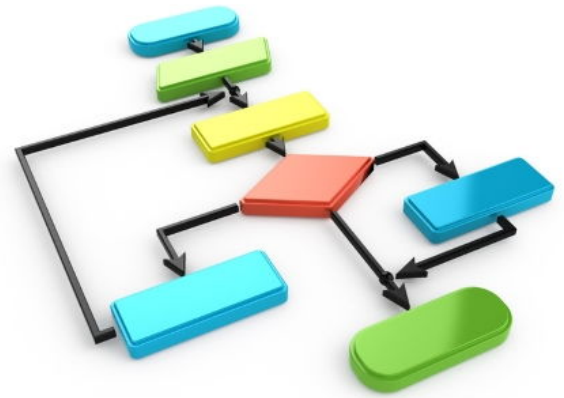
Avoiding Unsafe and Unethical Practices

- Drug hoarding
- Re-using drug
- Administering expired drug
- Discrimination based on patient age, development, ability to pay, race, ethnicity, disability, or immigration status

Strategies for Drug Allocation

Allocation Committee

- Interprofessional (pharmacy, nursing, social work, physician, ethics committee member)
- Standardize allocation protocol
- Ethical principles
- Apply ethical decision-making principles
- Explore reasonable therapeutic drug alternatives
- Make prioritization decisions that are applied equitably to patients impacted by drug shortages
- Provide an appeal process for patients and families who have been affected by drug allocation decisions



Ethical Approaches to Allocation

Social or Instrumental Value Criteria

- *Patient is given priority due to their social standing or value in society*

Fair Innings Approach

- *Each person should have an equal opportunity to live a normal life*
- *Prioritizing a child over an aging adult to increase years of life preserved*

Sickest First, or "Rule of Rescue"

- *Prioritize patients based on degree of illness*

First Come, First Served

- *Prioritize those diagnosed first*

Beck, J. C., et. al. (2015). An ethical framework for responding to drug shortages in pediatric oncology. *Pediatric Blood and Cancer, 62,* 931-934.

Ethical Approaches to Allocation

Ethical Principle	Application
Justice	• Proactively develop a standard policy of allocation for drug shortages • Clinically similar patients are treated the same, regardless of age, race, social standing, or immigration status
Benefiiciene	• Rely on evidence-based indication for drug • Prioritize evidence-based indications over off-label use • Prioritize curative intent over palliation
Non-maleficence	• Begin new therapy only when there will be sufficient drug to complete the course of treatment

Beck, J. C., et. al. (2015). An ethical framework for responding to drug shortages in pediatric oncology. *Pediatric Blood and Cancer, 62,* 931-934.

What About Children?

Off-label Use of Drugs in Pediatrics

- Greater available data in adults than children, but both populations stand to benefit
- Decreased investment in obtaining FDA approval in pediatrics

Efficacy in Adults vs Children

- No data demonstrating greater efficacy in children compared to adults
- Age alone may not be a determinant of outcome

Quantity of Drug

- Dosing based on weight or size
- One adult dose may use the same amount of drug needed to treat several children

What About Research?

Childhood cancer research has led to improving survival to over 84%

- Drug shortages threaten the pace and discovery of successful treatment strategies

Consider two scenarios:

- Scarce drug is the investigational agent in a clinical trial (efficacy not proven)
- Scarce drug is part of a proven backbone within a clinical trial (patients would receive drug regardless of participation in the trial

COG WG on Chemotherapy Drug Shortages

- Prioritize accepted and evidence-based drugs over experimental uses of drugs during a shortage

- Give equal priority to patients receiving standard, evidence-based treatment with a drug, regardless of whether the patient is receiving the drug as part of a clinical trial or not

A Case Study in Decision Making

Your oncology center sees 150 new childhood cancer diagnosis per year. Your pediatric oncology clinic has 50,000 mg of methotrexate for the foreseeable future. There are 21 patients who are expected to receive MTX within the next 2 months.

- 9 patients with ALL (IT-MTX)
- 7 patients with SR-ALL (Capizzi-dosed MTX)
- 2 patients with HR-ALL (Interim maintenance with HD-MTX and IT-MTX)
- 1 patient with OS (HD-MTX)
- 1 patient with ATRT
- 1 patient on Phase I study (MTX with investigational agent)

Total MTX needed: 108,791 mg

Russell, H. V., Bernhardt, M. B., & Berg, S. (2016). Using decision modeling to guide drug allocation during a shortage. *Pediatric Blood and Cancer,* 00, 1-7.

A Case Study in Decision Making

First Come, First Served Decision

- First 7 patients would receive intended therapy
- Eighth patient with OS would receive a partial dose
- 13 remaining patients would receive no MTX

First Come, First Served Decision, eliminating the partial dose patient

- First 7 would receive intended therapy
- 8th patient would receive no MTX
- 9th through 20th patients would receive intended therapy
- 21st patient would receive no MTX

A Case Study in Decision Making

Effectiveness of Regimen Decision (mg of MTX per life years saved)

- 11 patients would receive IT-MTX for CNS prophylaxis
- 7 children would receive HD-MTX for SR-ALL
- 1 child with ATRT would receive MTX
- 1 of 2 children with HR-ALL would receive MTX
- 1 Phase I study patient would receive ALL
- 1 patient with OS and 1 patient with HR-ALL would receive no MTX

A Case Study in Decision Making

With a first-come, first served approach:

Only seven patients would receive intended MTX therapy

With an allocation decision-making model:

There is no way to treat both children with HR-ALL and the child with OS

Without an allocation decision-making model (i.e., first come, first served)

The first HR-ALL patient and the OS patient would exhaust the supply for all other patients

No allocation scenario exists that does not result in a worse outcome for some patients…

Ethical Approaches to Allocation

Utilitarian Approach: Benefitting the Most

- *Balancing the good of an individual patient with the good of a group of patients or society at large*

Guiding Factors

- *Focus on unique indications for a particular, specific drug **and** goals of care*
- *Emphasize curability and prognosis (30% vs 80% overall survival)*
- *Consider efficacy of drug in the regimen (MTX in ALL vs MTX in OS)*
- *Consider phase of therapy (VCR for ALL in induction vs VCR for MRD-neg ALL at end of maintenance)*
- *Consider amount of drug per regimen (curable disease requiring little of drug vs difficult to treat disease requiring more drug)*
- *Consider use of drug as standard of care vs investigational use*

Ethical Approaches to Allocation

Patients and Families

- Transparency regarding drug allocation decisions
- Involvement in allocation teams
- Process for appeals

Clinicians

- Involvement in allocation teams
- Disclosure to patients and families
- Support and guidance

Role of the Pediatric Hematology Oncology Nurse

APHON RESOURCES

ADVOCACY

Role of the Pediatric Hematology Oncology Nurse

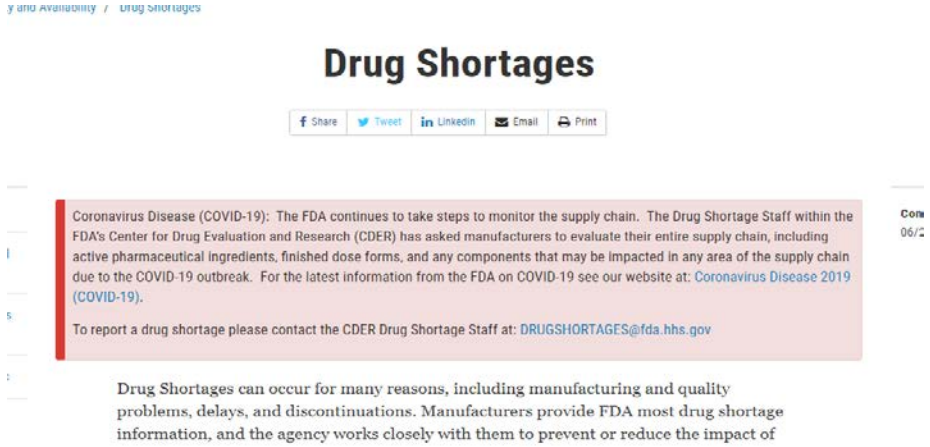
APHON Position Statement

Nursing Actions

APHON Position Statement: Awareness

APHON SUPPORTS

- Promoting awareness of drug shortages through reliable information sharing



RESOURCES

- FDA Drug Shortages
- ASHP Drug Shortages
- COG
- Erwinaze Supply

APHON Position Statement: Advocacy

APHON SUPPORTS

- Advocacy for strategies that minimize the impact of drug shortages on the quality of care
- Cooperation and collaboration that prioritize the prevention and management of drug shortages
- Advocacy for federal, local, and institutional policy changes that address drug shortages

RESOURCES

- APHON Advocacy Center

- APHON Position on Social Media in the Workplace

MEDS Act Introduced

Senate 2723: **Mitigating Emergency Drug Shortages Act** introduced in Oct. 2019

If passed, this legislation would:

- Require manufacturers to disclose causes & expected duration of medication shortages
- Require manufacturers to create detailed plans to maintain availability of medications
- Grant FDA expanded ability to expedite inspections/new drug applications to mitigate shortages
- Assign Dept. of Health and Human Services & Homeland Security to assess impact of critical product supplies
- Allow the Dept. of Health and Human Services to develop incentive programs for manufacturers to domestically produce active pharmaceutical ingredients and final dosage forms

APHON Position Statement: Allocation

APHON SUPPORTS

- Participating in developing institutional polices
- Ensuring explicit and transparent communication with patients & families
- Using evidence-based strategies to minimize the impact
- Developing institutional drug allocation committees

RESOURCES

- APHON Drug Shortages FAQ

APHON Position Statement

APHON DOES **NOT** SUPPORT

- Unethical Practices

  Examples: drug hoarding or discrimination based on patients' age, developmental level, ability to pay, race, ethnicity, disability, or immigration status

- Unsafe strategies of waste reduction

  Examples: strategies that violate infection prevention protocols (e.g., re-using drugs, administering expired drugs) or compromise quality of care.

Nursing Actions

01

Maintain Awareness

02

Communicate Effectively

03

Provide Support

Special Thanks…

- Jill Hartley, MSN RN CPHON®
- Yoram Unguru, MD, MS, MA
- Nicole Wallace

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