Pediatric Compounding: Challenges and Updates

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Learning Objectives

- Describe the rationale for compounding medications for pediatric patients.
- Identify patient safety issues in pediatric compounding.
- List benefits of using standard concentrations when compounding.
- Access and apply literature and regulatory guidelines for safe pediatric compounding.

Rationale for Pediatric Compounding

Pediatric Drug Development and Labeling

Best Pharmaceuticals for Children Act (BPCA)

Incentivizes pharmaceutical companies to voluntarily conduct pediatric studies

6-month extension of marketing exclusivity

Pediatric Research Equity Act (PREA)

Gives the FDA the authority to require pediatric studies when the drug is expected to be used in a substantial number of children

https://www.fda.gov/drugs/development-resources/reviews-pediatric-studies-conducted-under-bpca-and-pediatric-assessments-conducted-under-prea-2012

Why Compound for Pediatric Patients?

- Lack of age-appropriate commercial formulations
- Need for individualized dosing
- Palatability and administration route considerations
- Excipient allergies or intolerances
- Dietary considerations

Limitations of Commercial Products

- Inappropriate
  - Dose
  - Concentration
  - Excipients

Common Indications

- Chronic conditions
- Rare diseases
- Oncology
- NICU-specific needs: lower concentrations, parenteral nutrition

To Compound or Not to Compound

- Alter a tablet or dispense a compounded liquid?
- Dispense a vial or dispense a patient-specific dose in a syringe?
- Dispense a vial nursing will dilute vs. dilute and dispense from pharmacy?

Patient Safety Issues

Safety Concerns in Pediatric Compounding

- Stability issues
- Impact of contamination risks
- Limitations of automated compounding software and other dispensing technologies
- Excipient toxicities
- Variability in compounding formulations/concentrations

USP <795> and <797> Updates

- Revised chapters apply to compounding for all age groups
- Some changes may be more impactful to pediatric compounding

USP <795> Updates

- More stringent requirements for personnel training/competency, facility design and compounding areas, cleaning and sanitizing, equipment and components, and documentation
  - Fewer pharmacies are engaged in nonsterile compounding, harder for outpatients to access compounded medications?
- Nonaqueous oral liquid dosage form BUD limited to 90 days
- Aqueous CNSP: antimicrobial testing required for extended BUD

USP <797> Updates

- In-use limit for single dose vials extended from 6 to 12 hours
- In-use limit for stock solutions

12 Hour In-Use Limit for CSPs

- Not addressed in 2008 version
- When CSPs are used as a component to compound addition CSPs (stock solutions):
  - Must be entered/punctured in ISO Class 5 air
  - Must be stored in conditions the BUD is based on
  - May be used for sterile compounding for up to **12 hours after first dose is drawn** or assigned BUD, whichever is shorter
- Can consider:
    - Smaller stock solutions
    - Less frequent batching-more waste?

Limits to Technology/Automation

- TPN Compounding
  - Limits to volume additives
  - Problematic for NICU patients
  - Consider additional standard dilutions
- Workflow Management Systems
  - Dose calculation issues
  - Education and policies for “workarounds”
- Infusion Pumps
  - Guardrails for pediatric/neonatal dosing and infusion rates

Excipient Toxicity in Pediatrics

- There is no complete list of drugs containing potentially toxic excipients
- Pharmacists must be diligent in identifying and evaluating the presence of excipients when dispensing medications to pediatric patients
- Consider cumulative dose, age, organ function
- KIDs List

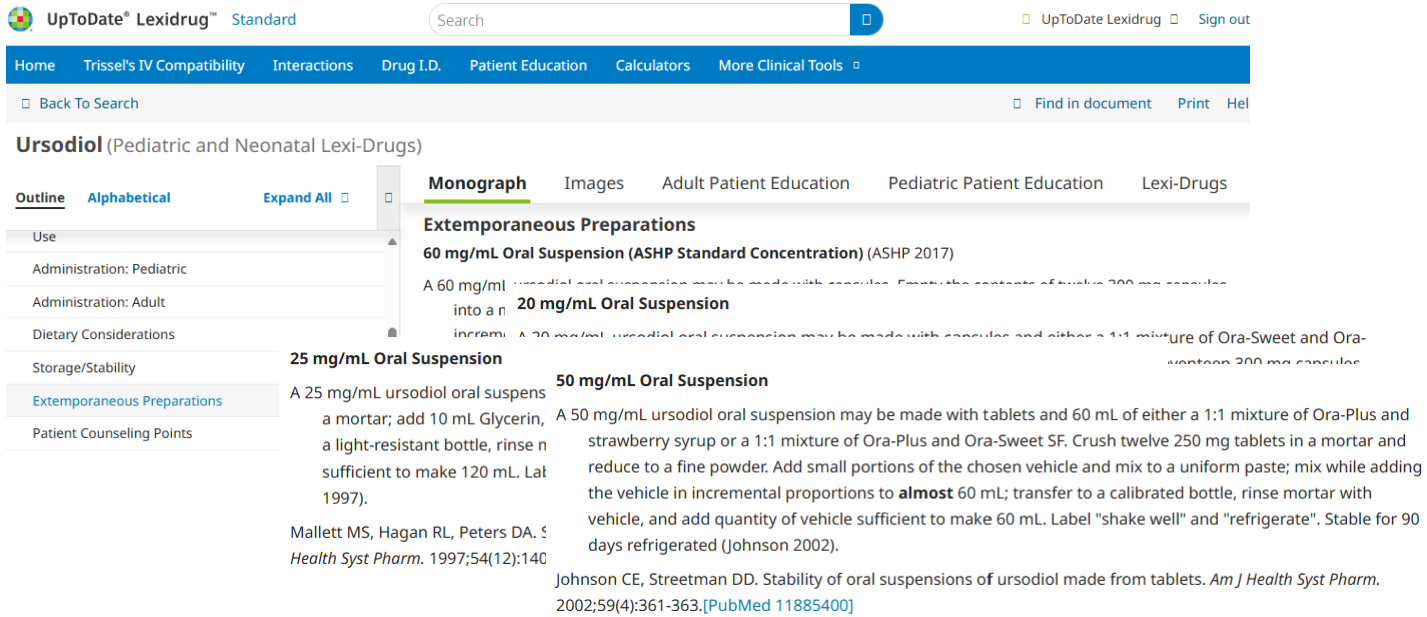
KIDs List

- Pediatric Pharmacy Association 2025 KIDs List of Key Potentially Inappropriate Drugs in Pediatrics
- Summary of potentially toxic excipients paired with recommendation strategies
- Benzyl alcohol/sodium benzoate/benzoic acid, ethanol/ethyl alcohol, isopropyl alcohol, methyl and propylparabens, phenylalanine, Polysorbate 80, propylene glycol

McPherson C et al. J Pediatr Pharmacol Ther 2025; 30(4): 422-439.

Variability in Concentrations

- Medications commonly compounded for pediatric patients have multiple compounding formulations at different concentrations.
- Confusion surrounding what concentration to compound-most during transitions of care (TOC)-can lead to medication errors.



Ursodiol. *Pediatric and Neonatal Lexi-Drugs*. UpToDate Lexidrug. UpToDate Inc. https://online-lexi-com.gate.lib.buffalo.edu. Accessed August 12, 2025.

Standard Concentrations

Case Example 1

- Infant discharged on sildenafil for pulmonary arterial hypertension. Hospital compounding oral suspension (concentration: 2.5 mg/mL). Outpatient pharmacy dispensed commercial oral suspension (concentration: 10 mg/mL). Prescription contained dose only in mL; patient received four-fold overdose.

Case Example 2

- Child receiving clonidine for iatrogenic withdrawal. Hospital compounding oral suspension (concentration: 0.1 mg/mL). Patient transferred to different hospital for escalation of care and continued clonidine (concentration: 0.01 mg/mL). Change in concentration not noted during transfer; patient received 10-fold underdose and experienced withdrawal symptoms.

Case Example 3

- An oncology patient is discharged on Enoxaparin 10 mg subQ daily. Inpatient pharmacy prepared patient-specific doses during admission. Outpatient pharmacy dispensed 30 mg/0.3 mL syringe; caregiver administered full syringe.

Efforts to Standardize

- ASHP Standardize 4 Safety Initiative
- Neonates: Vermont Oxford Network (VON)/ISMP
- Institution-specific SOP and protocols

ASHP Standardize 4 Safety

- National, interprofessional effort to standardize medication concentrations to reduce errors, especially during transitions of care.
- Includes standard concentrations for:
  - Compounded oral liquid medications
  - IV continuous infusions (adult, pediatric)
  - PCAs (patient-controlled analgesia) and epidurals

American Society of Health-System Pharmacists (ASHP). Standardize 4 safety initiative. ASHP, 2025.

Compounded Oral Liquids

- One standard concentration for each included medication
  - Exception: Amiodarone
- Use commercial product if available
- Limit to one concentration if possible
- Must have primary literature support/stability studies
  - And antimicrobial studies if extending beyond USP <795>!
- Consider taste and palatability
- Reimbursement considerations

American Society of Health-System Pharmacists (ASHP). Standardize 4 safety initiative. ASHP, 2025.

Pediatric Continuous Infusions

- Multiple standard concentrations for each included medication
- Use commercially available products when possible
- Limit to one concentration when possible
- Consider fluid status when selecting concentration to dispense
- Operational considerations, including waste

American Society of Health-System Pharmacists (ASHP). Standardize 4 safety initiative. ASHP, 2025

Neonatal Drug Concentrations

- Joint effort by the Institute for Safe Medication Practices (ISMP) and Vermon Oxford Network (VON) to standardize neonatal drug concentrations.
- Recommendations based on birth weight
  - NICU patients weighing ≥500 g
  - NICU patients weighing <500 g

Neonatal Drug Concentrations. VON, 2023. Available at https://public.vtoxford.org/neonatal-drug-concentrations/

Standard Concentrations: Institutional SOPs

- Must have institution-specific standard concentrations for IV and oral liquid medications and process by which these are selected/approved
- ALSO, must consider: what is the procedure for when these standards don't work?
  - Lowest IV standard concentration can't be run on IV pump
  - Highest IV standard concentration causing fluid overload
  - Standard oral liquid concentration too small to be measured OR too large to be tolerated

Safe Practices at Transitions of Care

- Despite standardization, inconsistencies in concentrations can still occur:
  - Patient discharged from the hospital
  - Patient transferred to another institution
  - Patient admitted to the hospital

Safe Practices at Transitions of Care

At the Hospital

- Conduct thorough medication reconciliation; ALWAYS verify dosage units (mg, mcg, mEq, etc.) and do not rely on transcribing mL, tsp, tbsp.
- Conduct thorough discharge counseling/medication teaching; review outpatient bottles whenever possible.
- Assist prescribers when writing prescriptions for compounded medications so that dose and directions are clearly stated.

In the Community

- When interpreting prescriptions for compounded medications, ALWAYS verify dosage units (mg, mcg, mEq, etc.) and do not rely on transcribing mL, tsp, tbsp.
- Do not make assumptions about what concentration an institution was compounding; standard concentrations not always used.
- Clear labels including medication concentration.

Safe Practices at Transitions of Care

- Heightened awareness of
  - New liquid formulations available on the market that were previously compounded
    - Careful transition from compounded formulation to commercially available formulation with careful consideration of dose and excipients.
    - Prioritize patient/caregiver education
  - Drug shortages that may have necessitated compounding

Pediatric Compounding Resources

Compounding Resources

- Not necessarily different than adult compounding resources
- Tertiary references can be a great place to start
  - Lexi-Drugs, Micromedex, Clinical Pharmacology
  - Website may have additional information
    - Nationwide Children's Compounding Formulas
    - UNC Pharmlabs Formulation Records
- Key point: Caution with extending beyond-use dating past USP <795> recommendations. Most references still contain formulations with stability data only, not the antimicrobial data stipulated by the revised chapter.

Compounding Resources

- If new or unsure in pediatric compounding, phone a friend!
- Collaboration needed for safe and successful patient care.

Summary

- **Pediatric compounding is essential** due to the lack of age-appropriate commercial formulations, individualized dosing needs, and excipient concerns.
- **Patient safety risks** include variability in concentrations, excipient toxicity, and challenges during transitions of care, emphasizing the need for vigilance and standardization.
- **Standardization efforts** like ASHP's Standardize 4 Safety and VON/ISMP neonatal initiatives aim to reduce medication errors and improve consistency across care settings.
- **Safe transitions of care** require thorough medication reconciliation, clear labeling, and caregiver education to prevent dosing errors and ensure continuity.

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Questions?

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