

Welcome to the Jungle: Real World Challenges with Pediatric Dosage Forms

Rachel Meyers, PharmD, BCPS, BCPPS, FPPA
Clinical Professor
Rutgers, The State University of NJ

Pediatric Clinical Pharmacist
Cooperman Barnabas Medical Center
Livingston, NJ

Objectives

- Describe dosage form problems with currently approved medications for children
- List some newer dosage forms which may offer innovative solutions
- Discuss possible solutions and ongoing efforts to improve dosage forms for children

What's Not Working

Liquid Medicines, still the answer?



Taste/Smell/Volume: Clindamycin

- Commonly used antibiotic for skin infections, pneumonia
- Administration issues
 - Taste – very bitter
 - Smell – unpleasant
 - Concentration – very dilute
 - 75 mg / 5 mL
 - A 12-month-old, 10 kg patient would receive 100 mg PO TID, which is 6.7 mL PO TID
 - A 5-year-old, 20 kg patient would receive 200 mg PO TID, which is 13.3 mL PO TID
- Dose – Frequent dosing, long course
 - TID x 10 days

Other problems with liquids

- Concentrations listed per 5 mL
- Too much math, adds an unnecessary calculation step
- Can lead to mix-ups in concentrations
- We aren't supposed to be dosing in teaspoons anyway!





Spoons are for Soup

- Do not use household spoons to give medicines.
- Spoons come in all shapes and sizes. Using a tablespoon instead of a teaspoon can mean 3 times too much medicine for your child.



To learn more, visit [cdc.gov/medication-safety](https://www.cdc.gov/medication-safety)



Milliliters (mL) are for Medicine

- Use the oral syringe or dosing cup that comes with your liquid medicine to make sure your child gets the right amount.
- Ask your pharmacist if you don't have one.

Still more problems with liquids

- Shelf life – especially after reconstitution
- Oral syringes and the need for adapters
- Osmolarity of oral liquids for premature infants
- Ketogenic diet patients – carbohydrate content is often high due to flavoring and other agents in oral liquids



Image 1. Without adapter



Image 2. With adapter

Nifedipine Immediate Release Capsules



Qvar RediHaler® (beclomethasone)



Table 2. Medications With Potentially Significant Effect on BAC (Ethanol Exposure ≥ 15 mg/kg/dose)

Product	Manufacturer(s)	Ethanol Content, % w/v	Alcohol-Free Alt.	10-kg Patient			20-kg Patient			40-kg Patient		
				Single Dose	Ethanol Exposure, mg/kg	Rise in BAC, mg/dL [‡]	Single Dose	Ethanol Exposure, mg/kg	Rise in BAC, mg/dL [‡]	Single Dose	Ethanol Exposure, mg/kg	Rise in BAC, mg/dL [‡]
Acetaminophen-codeine 120 mg–12 mg/5 mL oral solution	Hi-Tech Pharmacal Co, Inc; Pharmaceutical Associates, Inc	7%	No	50/5 mg–100/10 mg	15–29	2.4–4.9	100/10 mg–200/20 mg	15–29	2.4–4.9	200/20 mg–400/40 mg	15–29	2.4–4.9
Citric Acid-Sodium Citrate (ORACIT) oral solution 1 mEq/mL	CMP Pharma, Inc	0.25%	Yes	6.7 mEq–66.7 mEq	1.7–16.7	0.28–2.8	13 mEq–133 mEq	1.7–16.7	0.28–2.8	27 mEq–267 mEq	1.7–16.7	0.28–2.8
Cyproheptadine 2 mg/5 mL oral solution	Lannett Company, Inc; Patrin Pharma; Rising Pharmaceuticals, Inc; VistaPharm, Inc.	5%	No	N/A	N/A	N/A	2.5 mg–6 mg	16–38	2.6 – 6.25	5 mg–8 mg	16–25	2.6–4.2
Diphenhydramine 12.5 mg/5 mL oral solution	Pharmaceutical Associates, Inc	14%	Yes	12.5 mg	70	11.7	25 mg	70	11.7	50 mg	70	11.7
Phenobarbital 20 mg/5 mL oral solution	Pharmaceutical Associates, Inc; Quagen Pharmaceuticals LLC; Rising Pharmaceuticals, Inc	13.5%	No	30 mg–50 mg	101–169	16.9–28.1	60 mg–100 mg	101–169	16.9–28.1	120 mg–200 mg	101–169	16.9–28.1
	Pharmaceutical Associates, Inc	14.25%			107–178	17.8–29.7		107–169	17.8–29.7		107–178	17.88–29.7
	BioRamo, LLC; e5 Pharma, LLC; Par Pharmaceutical Inc; Westminster Pharmaceuticals	15%			112.5–188	18.8–31.3		112.5–188	18.8–31.3		112.5–188	18.8–31.3
Phenobarbital 65 mg/1 mL IV solution*	Cameron Pharmaceuticals; West-Ward Pharmaceuticals Corp	8%	No	15 mg–200 mg	1.8–24.6	0.31–4.1	30 mg–400 mg	1.8–24.6	0.31–4.1	60 mg–800 mg	1.8–24.6	0.31–4.1
Sirolimus 1 mg/1 mL oral solution [†]	Amneal Pharmaceuticals LLC; Apotex Corp; Greenstone LLC; VistaPharm, Inc	1.5%–2.5%	No	0.7 mg–40 mg	1.1–100	0.175 – 16.7	1.2 mg–40 mg	0.9–50	0.146–8.3	2 mg–40 mg	0.75–25	0.125–4.2

Alt, alternative; BAC, blood alcohol concentration; IV, intravenous; N/A, not applicable

Ethanol

- Dexamethasone
 - Usual dose for respiratory distress/asthma/croup = 0.6 mg/kg/dose
 - 10 kg patient, dose = 6 mg
 - Dexamethasone elixir = 0.1 mg/mL, 5% ethanol
 - Dose of 6 mg = 60 mL

$$BAC(mg/dL) = \frac{Ethanol(g)}{Vd(L/kg) * BW(kg)} * 100$$

- VD = 0.6 L/kg
 - BAC = 50 mg/dL (0.5%)
- Parenteral product is 10 mg/mL with no ethanol.
Problem solved.

Protecting Parents: Hazardous Drugs

Table 2 (Continued). Drugs that meet the NIOSH definition of a hazardous drug and do not have MSHI, are not classified by NTP as “known to be a human carcinogen,” and are not classified by IARC as Group 1, “carcinogenic to humans,” or Group 2A, “probably carcinogenic to humans.” (Some may also have adverse developmental and/or reproductive effects.)

Drug	AHFS Classification	Biologics License Application	Only Developmental and/or Reproductive Hazard [†]
tacrolimus	84:92 skin and mucous membrane agents, miscellaneous; 92:44 immunosuppressive agents	No	No

Protecting Parents: Hazardous Drugs

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Formulation	Control Approaches						
		Engineering Controls			Personal Protective Equipment			
		Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impermeable, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
	Oral liquid drug: PO*/feeding tube/NG* tube	NA*	NA*	NA*	Yes	Yes	Eye and face protection if liquid likely to splash**	Yes, if inhalation potential

Tacrolimus Oral Granules



Some Wins

Neffy® (epinephrine)



Orkambi® (lumacaftor/ivacaftor) oral granules



STEP 1: Preparation



- Hold the packet with the cut line on top, shake it gently to settle the ORKAMBI granules, and either tear or cut the packet open along the cut line



- Carefully pour all of the ORKAMBI granules in the packet into **1 teaspoon (5 mL)** of soft food such as flavored pudding or yogurt, or liquid such as juice, in a small container. Food or liquid should be at or below room temperature. Then mix the granules with the food or liquid

Mavyret® (Glecaprevir; Pibrentasvir)

 **MAVYRET**
 (glecaprevir/pibrentasvir) Oral Pellets



1

Find the
number of
packets

↓

2

Choose
the right food

⋮

READ STEPS 1 - 5 before you get started!



The number of packets you need is on the pharmacy label.

Mix the day's packets together with food.



About 1-2 teaspoons of an acceptable food like the ones below



Remember, if you need help, you can always call!

Call your healthcare provider, your pharmacist, or us:
877-MAVYRET
(877-628-9738)

USE THESE



YES

Choose soft foods that stick to the spoon

! IMPORTANT:

If the pellets are chewed, or dissolve in the food, the medicine tastes bad and might not work.



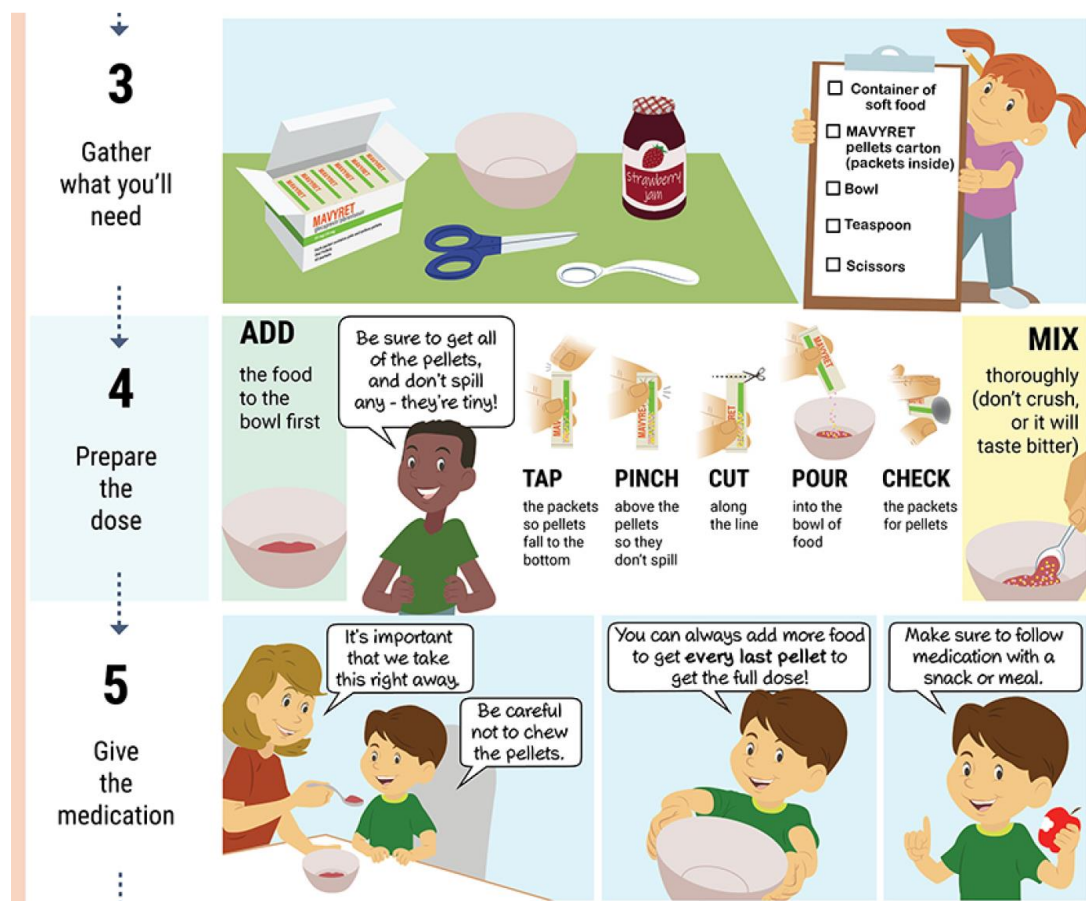
NOT THESE



NO

Watery, heated, frozen, or solid foods

Mavyret® (Glecaprevir; Pibrentasvir)



Summary

- Liquids are sometimes good, but have lots of problems (taste, excipients, measuring issues)
- Issues with devices too!
- We have to remember safety of caregivers administering hazardous drugs
- Solid oral dosage forms won't solve all problems, rather they will have their own challenges (i.e., tubes)
 - Lack of acceptability data on mini tablets in the U.S.

Welcome to the Jungle: Real World Challenges with Pediatric Dosage Forms

Rachel Meyers, PharmD, BCPS, BCPPS, FPPA
Clinical Professor
Rutgers, The State University of NJ

Pediatric Clinical Pharmacist
Cooperman Barnabas Medical Center
Livingston, NJ