Medication Route Interchange – Pediatric – Inpatient Clinical Practice Guideline

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Executive Summary

Guideline Overview

This purpose of this guideline is to identify medications clinically appropriate to automatically change the route of administration based on bioavailability, safety, and efficacy data. This document provides criteria for safe and effective change in route of medication administration for inpatients (between parenteral and enteral and within the enteral route including administration via various feeding tubes).

Key Practice Recommendations

See Appendix A: Summary of Clinical Recommendations

Companion Documents

- Pharmacist Medication Route Interchange – Adult/Pediatric – Inpatient [14]
- UW Health Intravenous Administration of Formulary Medications – Pediatric/Neonatal – Inpatient/Ambulatory Clinical Practice Guideline

Scope

Intended Users:

Pharmacists, nurses, advanced practice providers, physicians

Objective: The objective of this guideline is to identify criteria for safe, effective, and clinically appropriate interchange of medication routes based on bioavailability, pharmacokinetic, and safety and efficacy data.

Target Population:

Pediatric inpatients older than 48 weeks post menstrual age, defined as gestational age plus postnatal age.

Interventions and Practices Considered:

Providing the safest and most appropriate route of administration for medications included in this guideline.

Major Outcomes Considered:

Medication orders with the appropriate route of administration

Methodology

Methods Used to Collect/Select the Evidence:

Electronic database searches (e.g., PUBMED) were conducted by the guideline authors and workgroup members to collect evidence for review. Data and recommendations from existing institutional guidelines within and external to UW Health were evaluated. Workgroup expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:

The workgroup members arrived at consensus recommendations through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees.

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:

Internally developed recommendations were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see Appendix B: Evidence Grading Scheme).

Rating Scheme for the Strength of the Evidence/Recommendations:

See Appendix B for the rating scheme used within this document.

Recognition of Potential Health Care Disparities:
No healthcare disparities identified in literature search

Introduction

The enteral route of medication administration is preferred over the intravenous route for improved safety, increased patient comfort, and decreased cost.[1] The intravenous route of medication administration is classified as an independent risk factor for having an adverse drug event (ADE) and is considered a high-risk activity due to the potential for error resulting from the multiple necessary complex steps.[2,3,4] Studies demonstrate that intravenous medication administration is associated with a 3% higher risk for ADE per each medication administered and represents the highest risk for ADE over all other routes of administration.[3,5] The magnitude of harm resulting from these errors has also contributed to its high-risk classification.[3,4] Furthermore, enteral administration may reduce the risk of intravenous catheter related infections, medication incompatibilities, medication errors, and thrombophlebitis.[1,5-7] Increased costs, increased length of stay, and significantly higher mortality (versus other medication errors) have all been linked to intravenous administration of medications.[8,9] Intravenous administration of medications should be minimized whenever possible by encouraging conversions to oral route whenever possible.[3] Enteral medication is associated with decreased cost in comparison to intravenous medications and associated lines, sets, and infusion pumps necessary for administration. Early interchange to oral medications has been linked to shorter lengths of stay without clinical outcome compromise, independent of ADEs.[10-13]

Criteria for inclusion of medications in the guideline were high oral bioavailability and good enteral tolerance.[14] Medications were included in this guideline based upon clinical data confirming tolerability and high oral bioavailability.

Recommendations

1. Parenteral to enteral

1.1. To initiate the parenteral to enteral interchange, which includes medications administered orally or via feeding tubes, the medication must be listed in Table 1. In addition, the patient must meet all inclusion criteria and have none of the exclusion criteria. Enteral doses shall be rounded to standardized doses as clinically appropriate.

1.2. Inclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)

1.2.1. Patient must have a diet order and be tolerating either a clear liquid or more advanced diet or must be tolerating enteral tube feedings.[10]

1.2.2. For antibiotic route interchange, patient must be showing clinical improvement in symptoms as well as exhibiting downtrends in fever height, fever spike occurrence, and previously elevated white blood cell count. [14,15]

1.2.3. For antibiotic route interchange, the availability of a palatable pediatric formulation[13]

1.3. Exclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)

1.3.1. For antibiotic route interchange, patient has been receiving intravenous antibiotics for a duration fewer then 48 hours.

1.3.2. Patient is strict NPO, unable to swallow and without feeding tube, refuses oral medications, or requires continuous gastric suctioning.[10]

1.3.3. Severe vomiting or diarrhea has been documented within the past 24 hours or patient has an acute condition that affects gastrointestinal absorption (e.g. gastrointestinal obstruction or bleed, ileus, grade III or IV mucositis, gastrointestinal transit time too short for absorption, malabsorption syndromes, partial/total removal of the stomach, or short bowel syndrome).

1.3.4. Patient is hemodynamically unstable according to Table 4 or on high-doses of vasopressors in presence of shock.[13]
1.3.5. Patient requires continuous tube feedings that cannot be interrupted and patient requires a medication known to bind to enteral nutrition formulas (e.g. ciprofloxacin).[16]
1.3.6. Patient with endocarditis, meningitis, brain abscess, orbital cellulitis, CNS infection, osteomyelitis, endophthalmitis, bacteremia, ventriculoperitoneal shunt infection, fever with neutropenia, or necrotizing enterocolitis that should be treated with intravenous antibiotic therapy.[15,16]
1.3.6.1. Patient may initially require prolonged IV therapy, however, conversion to oral therapy may be considered after discussion with attending team.

2. Enteral to parenteral

2.1. For a patient to be eligible for the enteral to parenteral interchange the medication must be listed in Table 1 and the patient must meet all inclusion criteria and have none of the exclusion criteria.
2.2. Inclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)
2.2.1. Patient is unable to tolerate oral medications or has failed a swallow study and does not have a feeding tube in place.[10]
2.2.2. Patient has an acute condition that affects gastrointestinal absorption (e.g. gastrointestinal obstruction or bleed, ileus, grade III or IV mucositis, gastrointestinal transit time too short for absorption, malabsorption syndromes, partial/total removal of the stomach, or short bowel syndrome).[16]
2.2.3. Patient is nutritionally compromised and parenteral administration of medication is clinically warranted to minimize the amount of time the enteral nutrition is interrupted (e.g. phenytoin, fluoroquinolones, etc.).[16]
2.2.4. Patient has had an NPO order for greater than two days.[10]
2.2.5. Patient requires continuous gastric suctioning.[16]
2.3. Exclusion Criteria (*UW Health low quality evidence*, *strong recommendation)*
2.3.1. Acetaminophen, isavuconazole, posaconazole, and voriconazole cannot be converted from enteral to parenteral formulation without a prescribing provider order.

3. Transdermal to Enteral

3.1. For a patient to be eligible for the transdermal to enteral interchange the medication must be listed in Table 3 (transdermal) and the patients must meet all inclusion criteria and have none of the exclusion criteria.
3.2. Inclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)
3.2.1. Patient must have a diet order and be tolerating either a clear liquid or more advanced diet or must be tolerating enteral tube feedings.[10]
3.2.2. An active medication order for the patient's home transdermal dose must exist in Health Link.
3.2.3. The transdermal form of the medication is a non-formulary item and the oral analogue exists on the UW Health formulary.
3.3. Exclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)
3.3.1. Patient is strict NPO, unable to swallow and without feeding tube, or refuses oral medications.[10]
3.3.2. Severe vomiting or diarrhea has been documented within the past 24 hours or patient has an acute condition that affects gastrointestinal absorption (e.g. gastrointestinal obstruction or bleed, ileus, grade III or IV mucositis, gastrointestinal transit time too short

for absorption, malabsorption syndromes, partial/total removal of the stomach, or short bowel syndrome).[16]

3.3.3. Patient requires continuous tube feedings that cannot be interrupted and patient requires a medication known to bind to enteral nutrition formulas[16]

4. Rectal to enteral

4.1. For a patient to be eligible for the rectal to enteral interchange the medication must be listed in Table 2 and the patients must meet all inclusion criteria and have none of the exclusion criteria.

4.2. Inclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)

4.2.1. Patient must have a diet order and be tolerating either a clear liquid or more advanced diet or must be tolerating enteral tube feedings.[10]

4.3. Exclusion Criteria (*UW Health low quality evidence*, *strong recommendation*)

4.3.1. Patient is strict NPO, unable to swallow and without feeding tube, or refuses oral medications.[10]

4.3.2. Severe vomiting has been documented within the past 24 hours or patient has an acute condition that affects gastrointestinal absorption (i.e., gastrointestinal obstruction or bleed, ileus, grade III or IV mucositis, gastrointestinal transit time too short for absorption, malabsorption syndromes, partial/total removal of the stomach, or short bowel syndrome).[16]

4.3.3. Patient requires continuous tube feedings that cannot be interrupted and patient requires a medication known to bind to enteral nutrition formulas[16]

5. Documentation

5.1. Medication orders meeting the above criteria for the change in the route of administration are subject to interchange as soon as the patient meets the established criteria.

5.2. Once a patient meets the criteria, the pharmacist discontinues the current medication order and converts the medication to the appropriate corresponding dosage form by placing an order in the EMR.

5.3. The pharmacist will communicate the route interchange by page to the patient's primary service provider on-call (e.g. intern physician, resident physician, advanced practice prescriber, attending physician).

UW Health Implementation

Potential Benefits:

- Decreased length of stay
- Decreased cost of medication therapy
- Increased patient comfort
- Decreased risk associated with intravenous administration of medications (e.g. extravastation, ADE associated with IV administration)

Potential Harms:

- No potential harms identified

Qualifying Statements: As new data becomes available for safety and efficacy of route administration of medications recommendations may change.

Guideline Metrics

1. Guideline adherence

Implementation Plan/Clinical Tools

1. Guideline will be posted on uConnect in a dedicated location for Clinical Practice Guidelines.
2. Release of the guideline will be advertised in the Physician/APP Briefing newsletter.
3. Content and hyperlinks within clinical tools, documents, or Health Link related to the guideline recommendations (such as the following) will be reviewed for consistency and modified as appropriate.

Delegation Protocols

- Pharmacist Medication Route Interchange – Adult/Pediatric – Inpatient [14]

Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Appendix A. Summary of Clinical Recommendations

Table 1. Medications Approved for Parenteral and Enteral Route Interchange
*****See Lexi-Comp or Micromedex "Do not crush" list for applicability of crushing tablets

Parenteral regimen	Parenteral dose/frequency	Enteral dose/frequency	Bioavailability	Comments
Acetaminophen[17,18]	10 to 15 mg/kg/dose	10 to 15 mg/kg/dose	85-98%	1 to 1 dosing
	500 mg	500 mg		
	1000 mg	1000 mg		
Azithromycin[17,18]	10 mg/kg every 24 h	10 mg/kg every 24 h	37% to 38%	1 to 1 dosing Extended release suspension (Zmax) is not interchangeable with immediate-release formulations
	5 mg/kg every 24 h	5 mg/kg every 24 h		
	250 mg every 24 h	250 mg every 24 h		
	500 mg every 24 h	500 mg every 24 h		
Ciprofloxacin[1,14,19,20]	10 mg/kg/dose every 12 h	15 mg/kg/dose every 12 h	60% to 80%	Extended release tablets and immediate release formulations are not interchangeable. Absorption decreased if given thru a jejunostomy tube as opposed to a gastrostomy tube due to the site of drug absorption. When using feeding tubes, use crushed tablets as the suspension form cannot be used with any feeding tube. (*UW Health moderate quality evidence, weak/conditional recommendation*)
	10 mg/kg/dose every 8 h	20 mg/kg/dose every 12 h		
	15 mg/kg/dose every 12 h	20 mg/kg/dose every 12 h		
	200 mg every 24 h	250 mg every 24 h		
	200 mg every 12 h	250 mg every 12 h		
	400 mg every 24 h	500 mg every 24 h		
	400 mg every 12 h	500 mg every 12 h		
	400 mg every 8 h	750 mg every 12 h		
Clindamycin[17,18]	20 mg/kg/day divided every 6-8 h	20 mg/kg/day divided every 6-8 h	90%	Maximum oral dose is 450 mg due to tolerability
	30 mg/kg/day divided every 6-8 h	30 mg/kg/day divided every 6-8 h		
	40 mg/kg/day divided every 6-8 h	40 mg/kg/day divided every 6-8 h		
	300 mg every 6-8 h	300 mg every 6-8 h		
	600 mg every 6-8 h	450 mg every 6-8 h		
Diphenhydramine[17,18]	0.25-1 mg/kg/dose	0.25-1 mg/kg/dose	65% to 100%	1 to 1 dosing Maximum single dose: 50 mg Oral solution has a higher bioavailability than capsules
	6.25 mg	6.25 mg		
	12.5 mg	12.5 mg		
	25 mg	25 mg		
Doxycycline[2,17,18]	2-4 mg/kg/day divided every 12-24 h	2-4 mg/kg/day divided every 12-24 h	Virtually completely absorbed	1 to 1 dosing No enteral solution available, only interchange to available enteral doses within 10% of intravenous dose
	100 mg every 12 h	100 mg every 12h		
Fluconazole[14,17,18]	3-12 mg/kg/dose	3-12 mg/kg/dose	>90%	1 to 1 dosing
	100 mg every 12 h	100 mg every 12h		

Parenteral regimen	Parenteral dose/frequency	Enteral dose/frequency	Bioavailability	Comments
	100 mg	100 mg		
	200 mg	200 mg		
	400 mg	400 mg		
Folic acid[17,18]	100 mcg/day	100 mcg/day	76% to 93%	1 to 1 dosing
	200 mcg/day	200 mcg/day		
	300 mcg/day	300 mcg/day		
	400 mcg/day	400 mcg/day		
Lacosamide[17,18]	1-15 mg/kg/day divided twice daily	1-15 mg/kg/day divided twice daily	100%	1 to 1 dosing
	50-200 mg	50-200 mg		
Levocarnitine[17,18]	20-100 mg/kg/day IV	*See comments	15-16%**	*When appropriate, patient may be converted to prior enteral home regimen **mucosal absorption may be saturated at doses >2 grams
Levothyroxine[14,20-22]	15 mcg/day	25 mcg/day	capsule: 40-80% tablet: 48-80%	Parenteral dose should be approximately 80% of enteral dose. The relative bioavailability of the oral capsule is approximately 103% compared to the tablet. When appropriate, patient may be converted to prior enteral home regimen
	35 mcg/day	50 mcg/day		
	50 mcg/day	75 mcg/day		
	75 mcg/day	100 mcg/day		
	85 mcg/day	125 mcg/day		
	100 mcg/day	150 mcg/day		
	125 mcg/day	175 mcg/day		
	150 mcg/day	200 mcg/day		
Levetiracetam[14,17,18]	7-50 mg/kg/dose	7-50 mg/kg/dose	100%	1 to 1 dosing
	500 mg	500 mg		
	1000 mg	1000 mg		
Levofloxacin[17,18]	5 to 10 mg/kg/dose	5 to 10 mg/kg/dose	99%	1 to 1 dosing
	250 mg	250 mg		
	500 mg	500 mg		
	750 mg	750 mg		
Linezolid[14,17,18]	10 mg/kg/dose every 8 h	10 mg/kg/dose every 8 h	100%	1 to 1 dosing
	600 mg every 12 h	600 mg every 12 h		
Metronidazole[17,18]	30 to 40 mg/kg/day divided every 6-8 h	30 to 40 mg/kg/day divided every 6-8 h	100%	1 to 1 dosing
	100 mg	100 mg		
	500 mg	500 mg		
Moxifloxacin[2,17,18]	10 mg/kg/dose	10 mg/kg/dose	90%	1 to 1 dosing No enteral solution available, only interchange

Parenteral regimen	Parenteral dose/frequency	Enteral dose/frequency	Bioavailability	Comments
	400 mg	400 mg		to available enteral doses within 1% of intravenous dose
Pantoprazole[14,17,18]	< 5 yo: 0.5-1 mg/kg/dose every 12-24 h	< 5 yo: 0.5-1 mg/kg/dose every 12-24 h	77%	1 to 1 dosing
	> 5 yo: 20-40 mg once daily	> 5 yo: 20-40 mg once daily		
Ranitidine[17,18]	2 to 4 mg/kg/day IV divided every 6-8 h	4 to 8 mg/kg/day enterally divided twice daily	48%	
	50 mg IV every 8 h	150 mg enterally twice daily		
Rifampin[17,18]	10 to 20 mg/kg/day	10 to 20 mg/kg/day	90 to 95%	1 to 1 dosing
	600 mg	600 mg		
Sulfamethoxazole-Trimethoprim[17,18]	6-20 mg TMP/kg/day divided every 6-12 h	6-20 mg TMP/kg/day divided every 6-12 h	90 to 100%	1 to 1 dosing Dosed by trimethoprim component
	80 mg	80 mg		
	160 mg	160 mg		
Thiamine[17,18]	200 mcg/day	200 mcg/day	5.3%	1 to 1 dosing
	500 mcg/day	500 mcg/day		
	1000 mcg/day	1000 mcg/day		
Valproic Acid[17,18]	10-15mg/kg/day divided q6h	10-15mg/kg/day in divided doses*	90%	Total daily IV dose is equivalent to the total daily oral dose; however, IV dose should be divided with a frequency of every 6 hours. Conversion from oral Depakote IR to ER may require a total daily dose increase of 8-20%. *When appropriate, patient may be converted to prior enteral home regimen

Table 2. Guidance for Rectal and Enteral Route Interchange

Rectal regimen	Rectal dose/frequency	Enteral regimen	Enteral dose/frequency	Bioavailability	Comments
Acetaminophen Suppository[17,23]	10 to 20 mg/kg/dose every 4 to 6 h	Acetaminophen	10 to 15 mg/kg/dose every 4 to 6 h	80%	Max: 75 mg/kg/day

Table 3. Guidance for Transdermal and Enteral Route Interchange

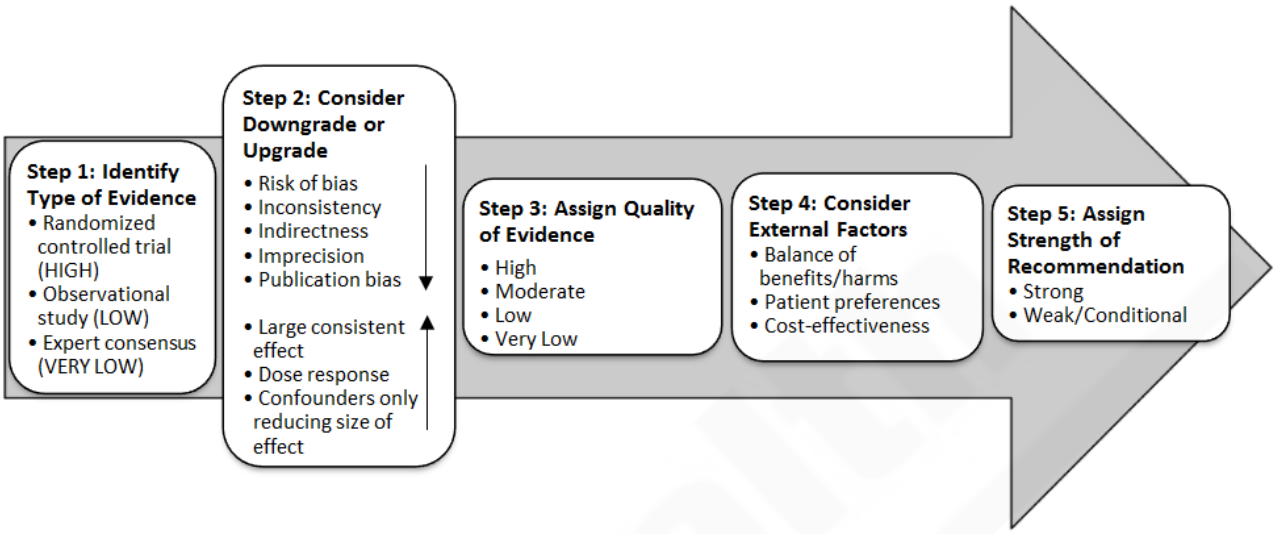
Transdermal regimen	Transdermal dose/frequency	Enteral regimen	Enteral dose/frequency	Bioavailability	Comments
Methylphenidate Patch (Daytrana)[17,18,24]	Patch Size(cm^2):	Methylphenidate IR		Oral: 22% (d-methylphenidate), 5% (l-methylphenidate)	The manufacturer recommends patients converting from another formulation of methylphenidate to the transdermal patch should be initiated at 10 mg regardless of their previous dose and titrated as needed due to the differences in bioavailability of the transdermal formulation
	12.5 (10 mg/9 h)		5 mg enterally 3 times daily		
	18.75 (15 mg/9 h)		7.5 mg enterally 3 times daily		
	25 (20 mg/9 h)		10 mg enterally 3 times daily		
	37.5 (30 mg/9 h)		15 mg enterally 3 times daily		
Oxybutynin Patch[17,18]	3.9 mg/day patch every 3-4 days	Oxybutynin IR	0.1 to 0.2 mg/kg/dose enterally up to 5 mg 2-3 times daily	Oral: 6%	

Table 4. Pediatric Unstable Vital Signs

Age	Respiratory Rate	Heart Rate	Systolic Blood Pressure
0-6 months	<40 or >60	>180	<70
6-24 months	<25 or >50	>160	<72
3-7 years	<20 or >30	>140	<76
7-10 years	<10 or >30	>120	<84
11-17 years	<10 or >30	>120	<90

Appendix B. Evidence Grading Scheme

Figure 1. GRADE Methodology adapted by UW Health



GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations For or Against Practice

Strong	The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.
Weak/conditional	Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.

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