Table S1. Definitions for Drug Therapy Problems (DTPs)

Drug Therapy Problem (DTP)	Definition	Example
ADR occurred	ADR affecting the patient identified through chart review based on side effect profile and drug references. Discussed ADR with medical and nursing staff and the collective team decided on the likelihood of a direct causal/contributory effect. The ADR was managed by decreasing/discontinuing the medication or, if necessary, adding on another medication to treat the reaction. Appropriate monitoring parameters were also identified and implemented.	Frequent hospital readmissions, imaging visits and daily medications due to recurrent kidney stones. Patient on high-dose topiramate (25% above maximum daily dose). Seizures controlled on topiramate, phenobarbital and levetiracetam. Potential topiramate causality of kidney stones discussed with pLTCF team and consultant neurologist. Agreed to taper off topiramate. Seizures were controlled and kidney stones resolved with no recurrence.
ADR monitored/prevented	Identified that monitoring for a potential common and/or serious ADRs had been omitted. Recommended instituting monitoring parameters to prevent ADR.	Ordering sodium and bicarbonate levels via basic metabolic panel in patients on carbonic anhydrase inhibitors
Alternative therapy	Substituting one medication for another more appropriate medication which could be due to availability, side effect profile, etc.	Selection of glycopyrrolate for secretion management in place of scopolamine given the side effect profile of tertiary amines (scopolamine) is much more severe than quaternary amines (glycopyrrolate). This is especially important in children with agitation issues (scopolamine crosses blood brain barrier and more likely to cause agitation) and also on a medication that affects the heart rate (scopolamine is more likely to cause rate and rhythm disturbances).
Drug acquisition	Identified urgent need for medication. Acquired product by calling pharmacies to inquire about drug availability and facilitated delivery of product to pLTCF	Oseltamivir in setting of drug shortage and pLTCF influenza outbreak
Drug-drug interaction prevented/managed	Identified (via Lexicomp interaction software) and prevented/managed a class D or class X drug-drug interaction (e.g., discontinued a medication or retimed medications to avoid interaction).	Identified phosphate supplement administered at same exact time as calcium carbonate in patient with low calcium levels. Recommended alternative dosing schedule.
Dosage too high	Supratherapeutic dose, defined as exceeding upper end of dosing range for condition/age in Lexicomp or primary literature by ≥ 20%, which could result in adverse effect	Clonidine patch ordered for behavioral issues at dose twice the highest end of recommended dosing range. Recommended transition to enteral tablet to avoid adverse event and enable titration.
Dosage too low	Subtherapeutic dose, defined as ≥ 20% below the lowest end of the dosage range for condition/age in Lexicomp or primary literature, which could result in lack of efficacy or unnecessary exposure to a medication at a dose not high enough to elicit a therapeutic response	Metoclopramide dosed at 0.04 mg/kg/dose every 8 hr in 2 yr old for an indication of reflux (typical dose 0.1–0.2 mg/kg/dose every 6–8 hr).
Frequency decrease interval	Identify the clinical need for a more frequent administration of a medication based on clinical condition, dosing references and/or primary literature.	Patient with frequent painful muscle spasms and receiving twice daily baclofen. Recommend increasing to three times daily.

Table S1. Continued.

Drug Therapy Problem (DTP)	Definition	Example
Frequency increase interval	Identify the clinical need for a less frequent administration of a medication based on clinical condition, dosing references and/or primary literature.	Patient receiving clonidine every 6 hours for agitation but has experienced multiple cases of bradycardia and hypotension over previous weeks necessitating holding of doses. Recommend taper to every 8 hour dosing, then reevaluate to determine if a less frequent interval is necessary all while monitoring for rebound hypertension/tachycardia.
Inappropriate dosage form	A medication dosage form that is not appropriate per the patient's age or enteral access	Calcitriol capsule prescribed to be administered via gastrostomy tube
Inappropriate Route	Route administered would result in decreased medication absorption, decreasing the effectiveness of the drug or rendering the drug inactive	Ciprofloxacin suspension binds extensively to enteral feed tubing. Patients requiring enteral feeding tube administration should be transitioned to the tablet formulation to be crushed and mixed with water.
Inappropriate/ unnecessary therapy with risk	Medication that is inappropriate, no longer warranted, and carries a potential risk to the patient due to the side effect profile or potential for drug-drug interactions	Sucralfate used every 6 hr for gastric bleeding that has not been present for weeks. Patient also receiving more than 30 doses of other medications throughout the day. Sucralfate is known to bind to many medications, rendering them ineffective.
Inappropriate/ unnecessary therapy without risk	PRN medications not being utilized or medication that is not indicated per the patient's current clinical picture, but not a potential risk to the patient.	PRN simethicone order that has not been utilized in 3 yr
Inappropriate/ inadequate administration instructions	Identify medication that requires specific administration instructions and recognize the current nursing order in the medication administration record does not contain this information. Nurse does not have adequate information on how to appropriately administer the medication.	Order missing tube flushing requirements after Epidiolex (cannabidiol) administration. Epidiolex (cannabidiol) requires avoiding administration via enteral feeding tubes made of polyvinyl chloride or silicone nasogastric tubes < 50 cm in length or < 5 French in diameter. If administered via larger silicone feeding tubes, the recommended volume for flushing (with room temperature drinking water) after each dose is approximately 5 times the priming volume of the tube.
Laboratory work or consultant medical appointments overdue	Overdue lab work or outside consultant prescriber appointments	Consultant neurologist recommends follow-up visits every 6 mo for epilepsy, including every 6 mo comprehensive metabolic panel, complete blood count and antiepileptic medication therapeutic monitoring levels. Last labs and visit were 9 mo ago. Pharmacist alerts team to lack of appointment and labs so they can be scheduled.
Needs additional drug therapy	Pharmacist chart assessment identifies additional therapy needed which is not on the medication profile.	Sterile water for irrigation is often utilized for all water intake in pLTCF patients (reconstituting feeds, tube flushes, etc.). This prevents adequate fluoride intake and dental caries is a problem in pLTCF patients. Recommendation to add daily fluoride.
Prior authorizations	Identified that a patient therapy is being delayed due to lack of prior authorization through the insurance company and primary provider lacks the time to complete the process	Prior authorization required for every dose of infliximab being administered every 6 wk. Any delay in prior authorization resulted in weeks long delay in therapy and previous hospital admissions from delay in therapy

ADR, adverse drug reaction; pLTCF, pediatric long-term care facility

* Drug information and drug-drug interaction information obtained via Lexicomp, Micromedex, Natural Medicines Comprehensive Database, medication package inserts, or primary literature.

Table S2. Example ADRs With Interventions and Outcomes

Medication	ADR	Intervention	Outcome
Albuterol	Tremor after doses	Reduced dose	Tremors resolved and patient maintained response to albuterol
Amantadine	Neuroexcitement on high dose	Decreased dose	Neuroexcitement resolved and enhancement of cognitive function still maintained
Baclofen	Not in ketosis on ketogenic diet	Changed from high-carbohydrate containing liquid to solid dosage form	Achieved ketosis
Bethanechol	Hyperhidrosis	Discontinue medication in consultation with Pulmonary	Hyperhidrosis resolved. No additional tracheal tone effects
Calcium carbonate	Hypophosphatemia/ bone health impact	Separate from administration of phosphate	Normal phosphate levels and a reduced calcium carbonate requirement (due to no binding)
Calcium carbonate	Hypophosphatemia/ bone health impact	Separate from administration of phosphate	Normal phosphate levels and a reduced calcium carbonate requirement (due to no binding)
Calcium carbonate	Hypophosphatemia/ bone health impact	Separate from administration of phosphate	Normal phosphate levels and a reduced calcium carbonate requirement (due to no binding)
Calcium carbonate	Hypophosphatemia/ bone health impact	Separate from administration of phosphate	Normal phosphate levels and a reduced calcium carbonate requirement (due to no binding)
Calcium carbonate	Decreased iron saturation	Separate from administration of iron supplement	Repeat iron studies normal. No need to increase iron dose
Calcium carbonate	Thyroid labs showing hypothyroidism	Spaced administration of calcium and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal
Calcium carbonate	Thyroid labs showing hypothyroidism	Spaced administration of calcium and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal
Calcium carbonate	Thyroid labs showing hypothyroidism	Spaced administration of calcium and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal
Clonidine	Recurrent hypotensive/ bradycardic events	Weaned off medication	Events resolved. No rebound hypertension or tachycardia. No additional agitation issues
Clonidine	Recurrent hypotensive/ bradycardic events	Weaned off medication	Events resolved. No rebound hypertension or tachycardia. No additional agitation issues
Clonidine	Recurrent hypotensive/ bradycardic events	Weaned daily dose and interval; eventually made PRN	Events resolved. No rebound hypertension or tachycardia. No additional agitation issues
Dexamethasone	Extreme agitation	Recommended more rapid taper in consultation with Neurology. Monitor HPA axis. Recommend ACTH stim test after	Neurological issues stable. Extreme agitation resolved. ACTH stimulation test normal

Table S2. Continued.			
Medication	**ADR**	**Intervention**	**Outcome**
Diazepam	Hypotension with dual benzodiazepine therapy	Decreased dose. Monitored for withdrawal or issues with increased tone	Hypotension resolved. Hypertonicity management effective. No withdrawal issues
Fluticasone inhaler	Recurrent thrush episodes	Antifungal addition for acute treatment. Rinse mouth well after each administration	Thrush cleared and no additional episodes have occurred
Furosemide	Hypokalemia	Added potassium chloride	Normal potassium levels
Gabapentin	Not in Ketosis on Ketogenic Diet	Changed from high-carbohydrate containing liquid to capsule	Achieved ketosis
Glycopyrrolate	Not in ketosis on ketogenic diet	Changed from high-carbohydrate containing liquid to solid dosage form	Achieved ketosis
Glycopyrrolate	Constipation	Recommended decreasing dose and addition of onabotulinumtoxinA to manage secretions	Constipation resolved and secretion management improved
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Glycopyrrolate	Constipation	Recommended decreasing dose and addition of onabotulinumtoxinA to manage secretions	Constipation resolved and secretion management improved
Ferrous sulfate	Constipation/not warranted per CBC	Discontinued medication	Constipation resolved and CBC remained stable
Ferrous sulfate	Thyroid labs showing hypothyroidism	Spaced administration of iron and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal.
Ferrous sulfate	Thyroid labs showing hypothyroidism	Spaced administration of iron and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal.
Ferrous sulfate	Thyroid labs showing hypothyroidism	Spaced administration of iron and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal.
Ferrous sulfate	Thyroid labs showing hypothyroidism	Spaced administration of iron and levothyroxine	Avoided increasing dose of levothyroxine. Repeat thyroid panel normal.
Levetiracetam	Not in ketosis on ketogenic diet	Changed from high-carbohydrate containing liquid to solid dosage form	Achieved ketosis
Levetiracetam	Drowsiness due to high level	Decreased dose	Drowsiness resolved and seizures well controlled

Table S2. Continued.

Medication	ADR	Intervention	Outcome
Losartan	Hyperkalemia	Added to hydrochlorothiazide due to persistent elevated BPs to avoid losartan dose increase and further hyperkalemia	Hyperkalemia resolved, no evidence of electrolyte disturbances and blood pressure managed
Metoclopramide	Serotonin syndrome in setting of venlafaxine therapy	Discontinued medication	Hypertension/hyperhidrosis resolved. No additional reflux/motility issues
Montelukast	Neuropsychiatric effects (irritability, agitation)	Discontinued medication	Irritability/agitation improved and no additional issues with allergies/asthma
Montelukast	Neuropsychiatric effects (irritability, agitation)	Discontinued medication	Irritability/agitation improved and no additional issues with allergies/asthma
Montelukast	Neuropsychiatric effects (irritability, aggressiveness)	Discontinued medication	Irritability/aggressiveness improved and no additional issues with allergies/asthma
Omeprazole	Recurrent small intestinal bacterial overgrowth	Recommend consultation with GI for discontinuation of omeprazole	Omeprazole discontinued. No recurrences of SIBO
Oxcarbazepine	Hyponatremia in patient with renal impairment	Decreased to appropriate dose for renal impairment and added low dose sodium chloride	Hyponatremia resolved and seizures controlled
Phenobarbital	Thrombocytopenia	Weaned phenobarbital and transitioned to zonisamide in consultation with Neurology	Thrombocytopenia resolved. Seizures controlled. Less somnolent
Potassium chloride	Nausea and vomiting surrounding high dose volume administration	Broke up dose more frequently allowing for smaller volumes	Nausea and vomiting resolved
Potassium chloride	Hyperkalemia	Discontinued medication	Normal potassium levels
Potassium chloride	Hyperkalemia	Decreased potassium	Hyperkalemia resolved and no hypokalemia occurred
Prednisone	Extreme agitation	Recommended more rapid taper	Respiratory flare managed and agitation resolved
Propranolol	Hypotension/bradycardia	Weaned daily dose and interval	Hypotension/bradycardia resolved. No rebound hypertension or tachycardia
Scopolamine	Xerostomia, constipation	Recommend addition of Botox in effort to remove scopolamine	Constipation/xerostomia resolved and secretion management improved. Scopolamine discontinued
Sirolimus	Severe hypertensive episodes	Obtain sirolimus level. Found to be very supratherapeutic. Recommended to obtain basic metabolic panel and to hold dose. Patient found to be in kidney failure. Worked with transplant team to develop monitoring plan, when to restart and new dose	Restarted at half the dose. Hypertension resolved and levels continue to be within range
Sirolimus	Elevated cholesterol and triglycerides	Add statin (discussed with transplant team)	Statin resulted in normalization of cholesterol and triglycerides

Table S2. Continued.

Medication	ADR	Intervention	Outcome
Sodium citrate	Diarrhea/nausea/ vomiting	Transitioned to sodium bicarbonate tablets	Diarrhea/nausea/vomiting resolved. Bicarbonate dose able to be decreased
Sodium citrate	Diarrhea/nausea/ vomiting	Transitioned to sodium bicarbonate tablets	Diarrhea/nausea/vomiting resolved. Bicarbonate dose able to be decreased
Sodium citrate	Diarrhea/nausea/ vomiting	Transitioned to sodium bicarbonate tablets	Diarrhea/nausea/vomiting resolved. Bicarbonate dose able to be decreased
Sodium citrate	Diarrhea/nausea/ vomiting	Transitioned to sodium bicarbonate tablets	Diarrhea/nausea/vomiting resolved. Bicarbonate dose able to be decreased
Sodium citrate	Diarrhea/nausea/ vomiting	Transitioned to sodium bicarbonate tablets	Diarrhea/nausea/vomiting resolved. Bicarbonate dose able to be decreased
Sucralfate	Elevated liver function tests and bilirubin	Discontinue drug as no longer indicated and likely binding ursodiol given concomitant administration	Liver function tests and bilirubin improved. No gastrointestinal bleeding issues
Topiramate	Recurrent kidney stones	Weaned off medication	Kidney stones resolved without recurrence and seizures controlled
Topiramate	Recurrent kidney stones	Weaned off medication	Kidney stones resolved without recurrence and seizures controlled
Topiramate	Metabolic acidosis	Added sodium bicarbonate and dose adjusted topiramate for renal impairment	Acidosis resolved and seizures controlled
Valproic acid	Hyperammonemia	Weaned off medication (used for behavior)	No additional issues with behavior and hyperammonemia resolved
Valproic acid	Not in ketosis on ketogenic diet	Changed from high-carbohydrate containing liquid to solid dosage form	
Zinc	Nausea, dizziness, headaches, upset stomach, vomiting due to high levels	Reduced zinc dose by 50%	Zinc levels within normal range. All side effects resolved

ADR, adverse drug reaction; BP, blood pressure; CBC, complete blood count; GI, gastrointestinal