In This Issue

Duloxetine Feeding Tube Administration

Formulary Update

From the Department of Pharmacy
Drug Information Service
(216) 444-6456, option #1

Cleveland Clinic
Clinical Rx Forum

Comprehensive information about medications, biologics, nutrients, and drug therapy

Cleveland Clinic
Clinical Rx Forum
From the Department of Pharmacy

March/April Issue **2025 Volume 13 Issue 2**

Can the Contents of Duloxetine Capsules Be Administered via a Feeding Tube?

By: Yasmeen Hamza, Pharm.D.

Introduction: Duloxetine (Cymbalta®), delayed-release capsules, contain enteric-coated pellets. The package insert for duloxetine states that the capsules should be swallowed whole and not chewed, crushed, or opened and that their contents should not be sprinkled on food or mixed with liquids because these actions might affect the enteric coating. Duloxetine is on the "Do Not Crush List" in UpToDate® Lexidrug™ and the Cleveland Clinic Health-System's (CCHS) "Do Not Crush List".

In-Vitro Study: A 2008 in-vitro study determined that a 20-mg duloxetine capsule maintained its potency, purity, and dissolution when mixed with applesauce and apple juice (pH ~ 3.5). The efficacy and safety of oral administration were not tested. If this method is to be used, it is important that the pellets maintain their integrity and not be crushed, chewed, or broken. This study found that the duloxetine pellets did not preserve their potency, purity, and dissolution when mixed with chocolate pudding (pH ~ 5.5-6).

Feeding Tube Request: An internal request to evaluate adding percutaneous endoscopic gastrostomy (PEG) and PEG/jejunostomy (JET) tube routes of administration to the duloxetine Epic drug record was submitted. Due to the data provided in the in-vitro study and anecdotal reports of the successful administration of duloxetine capsules through large-bore tubes in patients coming in from long-term care facilities, the request was approved.

Changes in Epic: The Cleveland Clinic Epic record for duloxetine contains options for PEG and JET tube routes of administration. The administration instructions for duloxetine were changed from "Swallow whole; Do not crush, chew, or open" to "Capsules can be opened, but contents should be swallowed whole; Do not crush or chew". The contents of duloxetine capsules can potentially clog fine-bore feeding tubes. Therefore, Psychiatry recommends that patients taking duloxetine with fine-bore tubes switch to venlafaxine or fluoxetine to prevent withdrawal. A decision was made to maintain duloxetine on the CCHS "Do Not Crush List".

Rising Pharma Information: A 2024 document from Rising Pharma, a manufacturer of delayed-release duloxetine capsule, supported the decision to add feeding tube routes of administration to the Epic duloxetine drug file. The document stated the following regarding duloxetine capsule administration:

- You may open the capsule and sprinkle the contents over one tablespoon (15 mL) of applesauce. Swallow the mixture right away and do not save any of the mixture to use later.
- You may open the capsule and pour the contents into an all-plastic catheter tip syringe and add 50 mL of water. Do not use other liquids. Gently shake it for 10 seconds, and then administer it through a nasogastric tube. Rinse with additional water (about 15 mL) if needed.

References:

1. Package Insert. Cymbalta® (Duloxetine) delayed-release capsules for oral use. Indianapolis, IN: Lily USA, LLC, August 2023.
2. Lexicomp Online™, Lexi-Drugs Online™, Hudson, Ohio: Lexicomp, Inc; September 2024. Search "crush"
3. Wells KA, Losin WG. In vitro stability, potency, and dissolution of duloxetine enteric-coated pellets after exposure to applesauce, apple juice, and chocolate pudding. Clin Ther. 2008;30(7):1300-8.
4. White R, Bradman, V. The handbook of drug administration via enteral feeding tubes Third Edition. Pharmaceutical Press. 2015 p. 272.
5. Product Information. Rising Health, LLC. Saddle Brooke, NJ. September 2024.

Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Axatilimab-csfr (Niktimvo®) Intermittent Infusion	CSF-1R Inhibitor	cGVHD	Restricted to the Department of Hematology and Oncology in patients with cGVHD after failure of at least two lines of systemic therapy in patients ≥ 40 kg
Carbidopa/levodopa (Crexont®) Extended-Release Capsule	Anti-Parkinson Agent	Parkinson's Disease	Restricted to continuation of home therapy
Clevidipine (Cleviprex®) Intravenous Infusion	Calcium Channel Blocker	Hypertension	Restricted to use for blood pressure management in acute stroke patients Note: Administration of clevidipine will be limited to ICUs (including EDs) to mirror guidance for nicardipine
Datopotamab deruxtecan-dlnk (Datroway®) Intermittent Infusion	Monoclonal Antibody	Breast Cancer	Restricted to the Department of Hematology and Oncology for outpatient use only
Glecaprevir-pibrentasvir (Mavyret®) Oral Tablet	Antihepaciviral	Hepatitis C Prevention	Restricted to Transplant for the **prevention** of hepatitis C transmission in HCV Donor+/Recipient– patients Initiation or continuation of glecaprevir-pibrentasvir for the **treatment** of HCV will require the use of patient's own medication. Note: This is the same formulary restriction as sofosbuvir-velpatasivir (Epclusa®)
Glofitamab-gxbm (Columvi®) Intermittent Infusion	Monoclonal Antibody	Relapsed or Refractory Diffuse large B-cell Lymphoma	Restricted to the Department of Hematology and Oncology for outpatient use only with certain specifications for use listed in UptoDate® LexiDrug™.

Colony stimulating factor-1 receptor (CSF-1R) cGVHD=Chronic graft-versus-host disease ICU=Intensive care unit
ED=Emergency department HCV=Hepatitis C Virus

Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Isatuximab-irfc (Sarclisa®) Intermittent Infusion	Monoclonal Antibody	Multiple Myeloma	Restricted to the Department of Hematology and Oncology. Inpatient use is restricted to those patients who cannot be discharged due to disease burden. It is the preferred option for inpatients starting on anti-CD38 treatment. Doses will be rounded as follows: round dose down to the nearest vial if within 10%.
Ponatinib (Iclusig®) Oral Tablet	Tyrosine Kinase Inhibitor	Ph+B-ALL	Restricted to the Department of Hematology and Oncology for initiation of therapy for Ph+B-ALL Continuation of therapy should follow Medications from Home Policy. With the addition of ponatinib, nilotinib was removed from the CCHS Formulary.
Zanidatamab-hrii (Ziihera®) Intermittent Infusion	Monoclonal Antibody	Unresectable/ Metastatic HER2 Positive Biliary Tract Cancer	Restricted to the Department of Hematology and Oncology for outpatient use only
Zenocutuzumab-zbco (Bizengri®) Intermittent Infusion	Monoclonal Antibody	NSCLC Pancreatic Adenocarcinoma	Restricted to the Department of Hematology and Oncology for outpatient use only

ALL=Acute lymphoblastic leukemia Ph+B-ALL=Philadelphia positive b cell acute lymphoblastic leukemia
HER2=Human epidermal growth factor receptor 2 NSCLC=Non-small cell lung cancer

Denial to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Lubiprostone (Amitiza®) Oral Capsule	Gastrointestinal Agent	CIC OIC IBD-C	Addition to CCHS Formulary was denied due to cost and the use of high-dose osmotic laxatives, lactulose, and senna rescues as the standard of care. Patients can use their home supply via the Medication from Home Policy.

CIC=Chronic idiopathic constipation OIC=Opioid induced constipation IBD-C=Inflammatory bowel disease with constipation

Changes to Restrictions of Medications on the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes to Restrictions/ Comments**
Buprenorphine (Sublocade®, Brixadi®) Extended-Release Subcutaneous Injection	Opioid Partial Agonist	Opioid Use Disorder	Modified restriction criteria to include Palliative Medicine for the treatment of OUD in adult patients and limited to outpatient use only Note: Compliance with all REMS Program requirements for Sublocade® and Brixadi® must be ensured prior to dispensing the corresponding extended-release buprenorphine injection.
Daratumumab (Darzalex®) Intravenous Infusion Daratumumab-Hyaluronidase (Darzalex Faspro®) Subcutaneous Injection	Monoclonal Antibody	AL Amyloidosis	Modified restriction criteria to only allow for inpatient use only in patients who cannot be discharged due to disease burden for AL amyloidosis* Note: Inpatient use should continue to default to the least expensive formulation based on patient weight.
Dostarlimab-gxly (Jemperli®) Intermittent Infusion	Monoclonal Antibody	Endometrial Cancer	Modified restriction criteria to include neoadjuvant treatment of dMMR/MSI_H locally advanced rectal cancer restricted to the Departments of Hematology/Oncology for outpatient use only
Fosaprepitant (Emend®) Intermittent Infusion	Antiemetic	PONV	Modified restriction criteria to include use by the Department of Anesthesiology in bariatric surgery patients for prevention of PONV
Methylnaltrexone (Relistor®) Subcutaneous Injection	Opioid Antagonist	Opioid-Induced Constipation	Modified restriction criteria to include use in radical cystectomy patients if NPO, unable to tolerate oral medications, or receipt of opioids for more than 7 consecutive days prior to surgery

*Isatuximab-irfc will be the preferred option for patients starting on anti-CD38 treatment inpatient.
OUD=Opioid use disorder REMS=Risk evaluation mitigation strategy
dMMR/MSI_H= Mismatch repair deficient/High microsatellite instability PONV=Post-operative nausea and vomiting
NPO=Nothing by mouth

Changes to Restrictions of Medications on the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes to Restrictions/ Comments**
Tolvaptan (Samsca®) Oral Tablet	Vasopressin Antagonist	Hyponatremia	Modified restriction criteria to include use by the Department of Nephrology in patients on regular nursing units (i.e., outside of the ICU) with a serum sodium ≤ 125 mmol/L, who have been unresponsive to fluid restriction and are without acute symptoms related to hyponatremia
Treprostinil (Tyvaso® DPI™) Dry Powder Inhaler	Prostaglandin	PAH	Modified restrictions as follows: Restricted to providers within the Respiratory Institute for initiation of therapy in adult patients (Respiratory Institute Providers- includes fellow and staff physicians within the Cleveland Clinic Respiratory Institute. This does not include medical residents rotating on Respiratory Institute services or nurse practitioners) Any prescriber may continue Tyvaso® DPI™ from home for adult patients. Note: Tyvaso® DPI™ should not be initiated in patients who are unable to procure their home treprostinil nebulizer device for inpatient use (i.e., efforts should be made to obtain the home nebulizer device rather than converting patients to dry powder inhaler as a bridge to nebulizer therapy).

ICU=Intensive care unit DPI=Dry powder inhaler PAH=Pulmonary arterial hypertension

Process Changes for the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Bevacizumab-maly (Alymsys®) Intermittent Infusion	Monoclonal Antibody	Various Oncology Indications	Alymsys® is the preferred biosimilar in Florida and bevacizumab-bvz (Zirabev®) is the preferred biosimilar for Ohio based on differences in payer contracts in these regions.*
Eculizumab (Soliris®) Intermittent Infusion	Monoclonal Antibody	Various Indications	New start eculizumab orders are limited at Main Campus to Drug Information business hours (Mon-Fri 8 am to 4:30 pm; Sat-Sun 7 am to 3:00 pm; Holidays: 7 am to 3:00 pm). Any orders for initiation of therapy received outside of these hours will be addressed first thing the following day.**
Levetiracetam (Keppra®) Intravenous Injection	Antiseizure Agent	Various Seizures	All levetiracetam IV infusion doses (maintenance and loading doses) up to 4.5 grams will be converted to IV push doses and these IV push doses will be administered as a bolus over 2 to 5 minutes in multiple syringes (for doses great than 1.5 grams).
Pharmacogenomics SOP for Pharmacy Consult Agreement	Various Medications	Various Indications	The consult agreement is between Pharmacy and the Center for Geriatric Medicine. The agreement originated from patients who were diagnosed with a disease state related to an area of behavioral health, such as anxiety and depression. The agreement now lists other diagnoses including hyperlipidemia. Per this agreement, the pharmacist will be able to order pharmacogenomic testing and make a therapeutic recommendation based on the results of those tests to the geriatrician.
Solid Organ Transplant SOP for Pharmacy Consult Agreement	Transplant Medications	Various Indications	Updates to the SOP included: 1) Criteria for managing pharmacists was added 2) Purpose was updated to include patients being evaluated for or are actively listed for transplant 3) Individual medications to be managed were updated to list drug classes 4) Vaccinations were updated to include additional vaccinations 5) Nivestym®, a filgrastim biosimilar, was added 6) Lab values were expanded 7) New hires language was clarified

*All restriction criteria approved for Zirabev® will apply to Alymsys® in adult patients.

**This applies to Main Campus only. Regional sites may follow their own new start processes related to eculizumab.

IV=Intravenous SOP=Standard of practice

Process Changes for the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Teplizumab (Tzield®) Intermittent Infusion	Monoclonal Antibody	Delay Onset of DM type 1	Dose rounding down to the nearest teplizumab 2 mg vial if the dose is within 10%. Example: teplizumab 2180 mcg rounds down to 2000 mcg (2 mg/2 mL vial)
Tocilizumab-aazg (Tyenne®) Tocilizumab-bavi (Tofidence®) Intermittent Infusion	Monoclonal Antibody	CRS	Biosimilar adoption was approved by various specialty areas that utilize tocilizumab (Rheumatology, Hematology/Oncology, Bone Marrow Transplant, Infectious Diseases). Biosimilar tocilizumab products may vary by Ohio and Florida markets. All restriction criteria and dose rounding protocols approved for tocilizumab (Actemra®) will apply to the biosimilar agents.
Updated Infectious Disease SOP for Pharmacy Consult Agreement	Various Antimicrobial Agents	Various Indications	The consult agreement was updated to add STD testing, treatment, and vaccinations to the injectable antiretroviral for treatment of HIV infection portion of the consult agreement and to update the required quality assurance evaluation to every 2 years.
Updated Restricted Drug Policy for Antimicrobials	Antimicrobials	Various Infections	In order to clarify and prevent delayed initiation of ID-restricted antimicrobials the following verbiage have been added to the restriction criteria: An ID-restricted antimicrobial may be prescribed by an LIP, however continued use must be authorized by a physician/LIP from the Department of Infectious Diseases within 24 hours of the initial order. Note: **An active ID consult is NOT required for pharmacist verification of an ID-restricted antimicrobial.** The pharmacist should communicate to the ordering provider to place an ID consult order and leave an open I-Vent for follow-up. **Exception: One-time, long-acting antimicrobial doses (e.g., dalbavancin), ID authorization is required prior to administration.**

DM=Diabetes mellitus CRS=Cytokine release syndrome STD=Sexually transmitted disease HIV=Human immunodeficiency virus
ID=Infectious disease LIP=Licensed Independent Practitioner

Product Standardization to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Cefotetan (Cefotan®) Intravenous Injection	Antibiotic	Various Infections	Cefotetan therapeutic interchange was removed from all CCHS sites

Removals from the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Epoprostenol (Flolan®) Inhalation	Prostaglandin	PAH	Veletri® replaces Flolan® as the sole epoprostenol product on Formulary due to its more favorable stability.
Ethanolamine (Ethamolin®) Intravenous Injection	Sclerosing Agent	Esophageal Varices	Ethanolamine has been largely been replaced by more effective treatments, including endoscopic band ligation. Removing ethanolamine from formulary would prevent waste and reduce costs.
Insulin Detemir (Levemir®)	Insulin	Diabetes	All presentations of insulin detemir have been discontinued by the manufacturer. Insulin glargine and NPH insulin are suitable alternatives.
Nilotinib (Tasigna®) Oral Capsule	Tyrosine Kinase Inhibitor	Various Oncology Indications	Ponatinib (Iclusig®) is a more cost effective agent than nilotinib (Taigna®).
Quinupristin/ Dalfopristin (Synercid®) Intermittent Infusion	Antibiotic	Various Infections	Medication was discontinued by the manufacturer.
Sarilumab (Kevzara®) Intermittent Infusion	Interleuikin-6 Receptor Antagonist	COVID-19 Pneumonia	Sarilumab is no longer needed on the formulary since the tocilizumab shortage has resolved. Tocilizumab is a first-line option for COVD-19 pneumonia

PAH=Pulmonary arterial hypertension COVID-19=Corona virus disease 2019

Additions to the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Axatilimab-csfr (Niktimvo™) Intermittent Infusion	CSF-1R Inhibitor	cGVHD	Restricted to the Department of Pediatric BMT in patients with cGVHD after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg.
Riociguat (Adempas®) Oral Tablet	Soluble Guanylate Cylase Stimulator	Pulmonary Arterial Hypertension	Restricted as follows: 1) For initiation of therapy in pediatric patients, riociguat is restricted to patients with a recommendation from the Pediatric Pulmonary Hypertension Team. The prescriber must be registered with the REMS program. 2) For continuation of therapy in pediatric patients receiving medication supplied by a CCHS inpatient pharmacy, the prescriber must be registered with the REMS Program. Note: If a patient brings in their home supply of medication (i.e., the medication is not supplied by a CCHS inpatient pharmacy), then the inpatient order may be written by any prescriber, including those not registered with the REMS program. This is permitted by the REMS program.
Sodium Phenylacetate and Sodium Benzoate 10%/10% (Ammonul®) Intravenous Infusion	UCD Agent	Acute Hyperammonemia	Restricted to Staff Physicians from the Pediatric ICU

Colony stimulating factor-1 receptor(CSF-1R) BMT=Bone marrow transplant cGVHD=Chronic graft versus host disease
REMS=Risk evaluation mitigation strategy UCD=Urea cycle disorder ICU=Intensive care unit

Changes to Restrictions of the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes to Restrictions/ Comments**
Intravenous Immune Globulin (Gammagard®) Intravenous Infusion	Monoclonal Antibody	Various Indications	Modified restrictions to include these indications: 1) MOGAD 2) Optic neuritis 3) Neuromyelitis optica 4) ADEM 5) Autoimmune encephalitis
Infliximab (Inflectra®) Intravenous Infusion	Monoclonal Antibody	Acute Rejection with Intestinal or Multi-visceral Transplant	Modified restriction criteria as follows: Restricted to Staff Physicians from Transplant or Gastroenterology or Transplant Surgeons for **acute rejection** in pediatric intestine or multi-visceral transplant patients who are refractory to high-dose steroids and anti-thymocyte globulin
Rituximab (Rituxan®) Intravenous Infusion	Monoclonal Antibody	Induction Therapy for Multi-visceral Transplant	Modified restriction criteria as follows: Restricted to Staff Physicians from Transplant or Gastroenterology or Transplant Surgeons for **induction therapy** in pediatric multi-visceral transplant patients
Vedolizumab (Entyvio®) Intermittent Infusion	Monoclonal Antibody	Induction, Rejection, and Post intestinal Transplant Ileitis	Modified restriction criteria as follows: Restricted to Staff Physicians from Transplant or Gastroenterology, or Transplant Surgeons for **induction, rejection, and post intestinal transplant ileitis therapy** in pediatric intestinal transplant or multi-visceral transplant patients

MOGAD=Myelin oligodendrocyte glycoprotein antibody-associated disease ADEM=Acute disseminated encephalomyelitis

Removals from the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Insulin Detemir (Levemir®)	Insulin	Diabetes	All presentations have been discontinued by the manufacturer.
Prednisolone Sodium Phosphate 1% Ophthalmic Drops	Corticosteroid	Various Indications	Prednisolone acetate 1% ophthalmic drops will remain on Formulary. It has better bioavailability and is more effective than prednisolone sodium phosphate 1% ophthalmic drops.
Quinupristin/ Dalfopristin (Synercid®) Intermittent Infusion	Antibiotic	Various Infections	Medication was discontinued by the manufacturer.

Process Changes to the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes**
Advanced Practice Provider SOP for Prescribing Antineoplastic Agents	Antineoplastic Agents	Various Indications	Restriction criteria were addended to allow APPs from pediatrics to order chemotherapy in inpatient and outpatient settings. Additionally, APPs will be permitted to modify doses (both increases/decreases), change dates, or continue therapy. The APP will be allowed to "Apply" a new antineoplastic regimen **but can't sign it.** In order to be eligible the APP must have the following: 1) One year of experience (in direct provider level of patient care) in the area of Hematology/Oncology managing patients on active antineoplastic treatment. 2) A signed agreement form from the disease program director/site physician or collaborating physician to be kept on file. 3) Successful completion of APSHO Cancer Therapy Prescribing Course. 4) A proctoring period demonstrating the safe ordering of antineoplastic drugs.
Eculizumab (Soliris®) Intermittent Infusion	Monoclonal Antibody	Various Indications	New start eculizumab orders are limited at Main Campus to Drug Information business hours (Mon-Fri 8 am to 4:30 pm; Sat-Sun 7 am to 3:00 pm; Holidays: 7 am to 3:00 pm). Any orders for initiation of therapy received outside of these hours will be addressed first thing the following day.*

*This applies to Main Campus only. Regional sites may follow their own new start processes related to eculizumab.
APP=Advance practice practitioner APSHO=Advanced Practitioner Society for Hematology and Oncology