HOUSTON Methodist LEADING MEDICINE

HOUSTON METHODIST
PHARMACY & THERAPEUTICS NEWS
February 2024

FORMULARY UPDATES

Laura M. Blackburn, PharmD

The following medications were ADDED to formulary

Medication	Formulary Updates
Venetoclax (Venclexta®)	• B-cell lymphoma 2 (BCL-2) inhibitor • FDA label for adult patients with chronic lymphocytic leukemia, small lymphocytic lymphoma, or in combination with azacytidine, decitabine, or low-dose cytarabine for newly diagnosed acute myeloid leukemia in adults ≥ 75 years old, or who have comorbidities that preclude use of intensive induction chemotherapy • Restricted for new start acute myeloid leukemia only • Restricted to hematology/oncology services via order set
Tremelimumab-actl (Imjudo®),	• Anti-CTLA-4 monoclonal antibody • FDA label for unresectable hepatocellular carcinoma and metastatic non-small cell lung cancer with no sensitizing epidermal growth factor receptor mutation or anaplastic lymphoma kinase genomic tumor aberrations • Restricted to use for FDA approved indications for outpatient use with prior financial approval • Restricted to hematology/oncology services
Epcoritamab-bysp (Epkinly™)	• Bispecific CD20-directed CD3 T-cell engager • FDA label for relapsed or refractory diffuse large B cell lymphoma, not otherwise specified, and high-grade B-cell lymphoma after 2 or more lines of systemic therapy • Restricted to outpatient use with prior financial approval • Restricted to hematology/oncology services
von Willebrand Factor, recombinant (Vonvendi®)	• Recombinant von Willebrand factor (rVWF) • FDA label for adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 von Willebrand disease receiving on-demand therapy • Restricted to hematology for FDA-approved indications via order set/panel

To request a medication for formulary review, **click here**

The *Pharmacy & Therapeutics News* is dedicated to providing the most current information regarding medication-use policy and formulary issues. Each issue details recently approved actions from the system P&T committee as well as relevant patient safety, pharmacotherapy and drug distribution updates. Entity representatives to the system P&T committee structure can be found here.

Med Safety Update

Amaris Fuentes, PharmD

Lithium Monitoring

Opportunities were noted for optimizing entry of lithium orders into PTA medication list and upon Epic ordering as well as optimization to medication history policy & lithium monitoring procedures. The following will be implemented:

- Remove default frequencies for lithium products
- Add extended release after lithium CR to reduce confusion between immediate release and longer acting formulations
- Standardize the frequency radio buttons across lithium orders to BID, TID, QHS
- Add a 450mg & 600mg dose button to lithium CR
- Include double check for narrow therapeutic index drugs in System _RXCLIN 170 Pharmacy Procedure for Obtaining and Reviewing Medication History

Update pharmacy monitoring note templates to prompt for comparison of home vs. ordered lithium doses and provide real time information on monitoring guidance

Formulary Management (continued)

Laura M. Blackburn, PharmD

The following medications were ADDED to formulary

Medication	Formulary Updates
Nirsevimab-alip (Beyfortus™)	• Human immunoglobulin G1 kappa monoclonal antibody • FDA label for patients <8 months born during or entering first respiratory syncytial virus (RSV) season and children up to 19 months who remain vulnerable to severe RSV disease • Restricted to neonatology for infants admitted to the neonatal intensive care unit
Abrysvo™	• Respiratory Syncytial Virus Vaccine (Recombinant) • Restricted for outpatient use in pregnant patients 32 through 36 weeks gestation not anticipating discharge or delivery within 2 weeks

The following are additional formulary decisions

Medication	Formulary Updates
Sodium polystyrene sulfonate (Kayexalate, Kionex, Kalexate)	• Removed from formulary, therapeutic interchange to sodium zirconium cyclosilicate • Based on assessment of current therapeutic interchange policy for potassium binders and usage, adverse effects, and cost considerations • Supported by Sullivan E, et al. Comparison of effectiveness and safety of sodium polystyrene sulfonate and sodium zirconium cyclosilicate for treatment of hyperkalemia in hospitalized patients. *Am J Health Syst Pharm* 2023;80 (18):1238-46.
Amisulpride (Barhemsys®)	• Not added to formulary • Review of post-operative nausea vomiting prophylaxis revealed inconsistency with 2020 guideline recommendations; education developed and Epic updated with risk factors assessments and formulary medication recommendations
Palivizumab (Synagis®)	• Added with restrictions as a last line treatment option for RSV prevention in neonates but made available to eligible patients if nirsevimab-alip (Beyfortus™) is in short supply or unavailable
Arexvy™	• Respiratory Syncytial Virus Vaccine (Recombinant [Adjuvanted]) • Not added to formulary in favor of Abrysvo™ based on better adverse effect profile and indications
Letermovir (Prevymis®)	• Updated restrictions to include solid organ transplant providers • In June 2023, the FDA updated the prescribing information for letermovir to include prophylaxis of cytomegalovirus (CMV) disease in adult kidney transplant recipients at high risk (donor CMV seropositive/Recipient CMV seronegative patients)
Posaconazole oral suspension	• Removed from formulary • Posaconazole suspension has erratic absorption, significantly impacted by pH and food intake, must be given multiple times per day, and is associated with a significant risk of underdosing patients. Posaconazole delayed release (DR) tablet has a more consistent bioavailability, can be crushed and put down feeding tubes, and is given once daily which significantly impacts efficacy and compliance.
Pneumococcal vaccine	• PCV 13 and 23 removed from formulary; PCV20 criteria revised to be used in patients >2 months • The approval and adoption of the PCV20 vaccine resulted in ACIP updating the adult and pediatric vaccination recommendations in Fall 2023 to include PCV20 as the primary recommended agent.

MEDSAFETY MATTERS!

Amaris Fuentes, PharmD

ISMP Medication Safety Newsletter Links: Acute Care & NurseERR & Community/Ambulatory

Updated IV Promethazine Labeling

Severe chemical irritations and tissue injuries have been described with administration of IV promethazine. The US Food and Drug Administration recently updated labeling requirements for IV promethazine to note the following to prevent this complication with IV promethazine. The preference for IM administration remains, but if IV is required the following should be completed:

1. Dilution with 0.9% sodium chloride
2. Avoidance of mixing with other medications
3. Use of a maximum concentration of 1mg/mL
4. Infuse over 20-40 minutes with a maximum infusion rate of 2.5mL/min when diluted in 50mL
5. Administration in a large vein, preferably a central venous catheter with avoidance of IV access in the hand or wrist.

Relevant ordering and dispensing updates are in progress to support these administration safe practices.

MEDICATION SAFETY ENHANCEMENTS

Clozapine REMS Compliance

An assessment was conducted of clozapine REMS compliance noting opportunities to update guidance documents, relevant policy & procedures, and EHR documentation to align with updated REMS requirements. Additionally, optimization of EHR ordering to include expanded laxative options, laboratory testing, and opportunities for improved pharmacy consult ordering will be completed.

Olanzapine IV

Off-label use of IV olanzapine was reviewed. Similar to IV haloperidol, IV olanzapine is not an FDA approved route of administration. However, studies have demonstrated adequate efficacy with IV olanzapine with less QTc prolongation than IV haloperidol. Ordering options for IV olanzapine will be updated to include a restriction to ED, ICU, and psychiatry services with additional guidance on avoidance of administration with parenteral benzodiazepines.

Tolvaptan Continuous Quality Improvement

An assessment was conducted of tolvaptan use noting a high incidence of policy compliant sodium monitoring with limited overcorrection episodes managed with appropriate therapies. Given the high right of compliance with structured ordering and monitoring of therapy, the required pharmacy consult will be retired with adoption of pharmacovigilance alerts to provide a safety net for monitoring and change in status.

Neostigmine for Constipation

To support clear orders for neostigmine for constipation, a neostigmine fo acute colonic pseudo-obstruction / refractory constipation was created. The panel additional supports ordering of PRN agents for potential bradycardia after neostigmine administration.

ANTICOAGULATION USE SAFETY

Michael Sirimaturos, PharmD

Assessing lab parameters upon ordering, verifying, and administering anticoagulation medications is essential to ensure patient safety. A review of common anticoagulation medications revealed that clinically relevant labs were not appearing consistently across various anticoagulation therapies at the point of provider ordering, nursing administration, or pharmacist order review. Effective December 22, 2023, the following labs were made visible within the order for each of the medications below:

	Hgb	Platelets	PT/INR	PTT	SCr	CrCl	PF4 Ab OD reading	Medication-specific Anti Xa	ALT/AST
Apixaban	x	x	x		x	x		x	
Rivaroxaban	x	x	x		x	x		x	
Fondaparinux	x	x	x		x	x		x	
Dabigatran	x	x	x	x	x	x			
Warfarin	x	x	x						
Argatroban	x	x	x	x					x
Bivalirudin	x	x	x	x	x	x			
Enoxaparin	x	x	x	x	x	x	x	x	
Heparin	x	x	x	x			x	x	

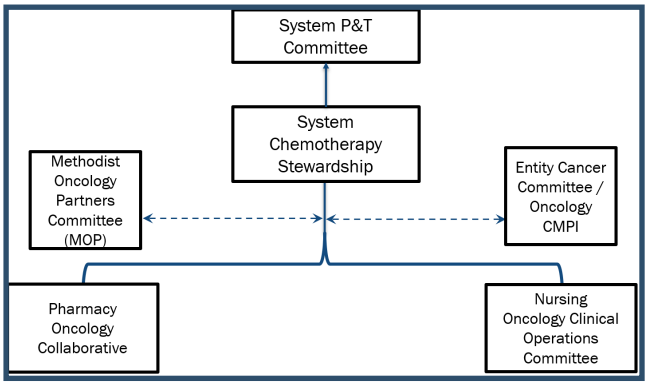
CHEMOTHERAPY STEWARDSHIP COMMITTEE

Adam Smith, PharmD

To better address the expanding, unique needs of the hematology, oncology patient population and the regular introduction of new medications for this population, Houston Methodist formed the System Chemotherapy Stewardship Subcommittee to the System P&T Committee. The subcommittee will have oversight to management and communication of drug shortages relevant to this population and managed formulary and quality assurance reporting for this therapeutics area.

Chemotherapy Stewardship P&T Subcommittee (SCSC) Objectives

- Hematology/oncology quality and safety related measures and initiatives
- Review hematology/oncology policies and procedures and formulary evaluations and additions
- Hematology/oncology drug shortage mitigation
- Anti-cancer therapy stewardship and formulary exception panel oversight



Hematology/Oncology Drug Shortage Patient Prioritization

Hematology/Oncology patients will be prioritized in the following manner during a drug shortage:

1. Active patients with curative intent
2. Active patients on palliative/life extension therapy
3. New start requests driven through exception review panel

ANTIMICROBIAL STEWARDSHIP

Clostridium Difficile: Two-Step Testing, Isolation, and Treatment

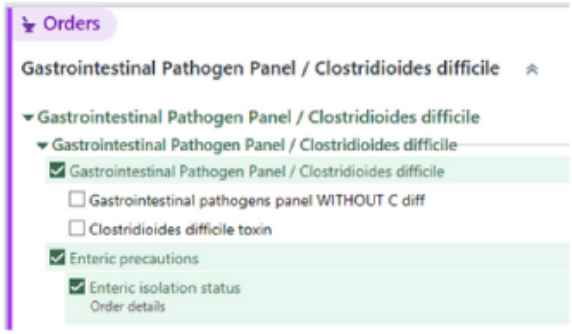
A Joint Management Guidance Document from Infection Prevention and Control, Clinical Microbiology, & Antimicrobial Stewardship

Clostridium difficile infection (CDI) is the leading cause of nosocomial diarrhea in the United States. Accurate and timely diagnosis of CDI is crucial for effective patient management and infection control. Currently, Houston Methodist utilizes the C. difficile PCR result through the stand-alone test or the Gastrointestinal panel. The implementation of the two-step testing process is recommended by the most recent IDSA/SHEA and ACG guidelines as a method to aid clinicians in distinguishing colonization from active infection. The two-step testing approach consists of initial screening with a sensitive assay (C. difficile PCR) followed by confirmatory testing using a specific assay (C. difficile Toxin).

The new two-step testing process will go-live on December 13, 2023.

C. difficile and Gastrointestinal Panel Testing

- C. difficile testing should be ordered using the "C. difficile/ Gastrointestinal Panel Order Set" in Epic.
  - The Gastrointestinal panel **will no longer include** C. difficile PCR.
  - **If both tests are desired,** both tests will have to be ordered within the order set - See image below.
  - A single specimen is sufficient for both tests.
  - Initial isolation orders are included within the order set



Infection Prevention Isolation Measures

Isolation of patients with positive *C. difficile* PCR Test

- Out of abundance of caution, patients with positive *C. difficile* PCR will be placed on enteric isolation regardless of the EIA test results.
- Please follow the criteria below for discontinuation of enteric isolation related to *C. difficile*:
  - At least 10 days have passed since the date of the patient's first positive *C. difficile* PCR (Step 1) test (with the day of test being day zero) **AND**
  - No diarrhea for >48 hours **AND**
  - Antimicrobial Therapy completed (if initiated)

Rationale for Two-Step Testing

Benefits of new testing pathway

1. **Sensitivity and Specificity:** The two-step testing approach capitalizes on the strengths of the different assays. The first step includes a highly sensitive assay, such as the C. difficile PCR, which can detect the presence of C. difficile DNA with high sensitivity. The second step utilizes a more specific assay, such as immunoassay for toxins, to confirm the presence of toxigenic strains and eliminate false positives.
2. **Reduction of False Positives:** CDI diagnosis based solely on sensitive assays, like PCR, may yield false positives due to the detection of non-toxigenic C. difficile or colonization without active infection. Confirmatory testing in the second step helps mitigate the risk of over diagnosis and unnecessary treatment.
3. **Infection Control Measures:** Accurate diagnosis is paramount for effective infection control measures. The two-step testing method aids in identifying true cases of CDI, allowing healthcare facilities to implement appropriate isolation precautions, and prevent the spread of the infection within the healthcare setting.

ANTIMICROBIAL STEWARDSHIP (Continued)

Interpretation of Results and Recommendations for Treatment

C. Difficile Toxin Gene (PCR) Result	C. Difficile Toxin Antigen Result	Interpretation	Result display in Epic
Not Detected	Not Detected	• Toxigenic C. Difficile is not detected • **Treatment is not recommended**	
Detected	Detected	• Toxigenic C. Difficile is detected • **Treatment recommended**	
Detected	Not Detected	• Positive C. Difficile PCR likely represents colonization • **Treatment is not recommended**	

Houston Methodist C. Difficile Treatment Guidelines Summary

Houston Methodist C. Difficile Treatment Guidelines Summary

Clinical Definition	Recommendations
1st Episode Non-Fulminant	• Vancomycin 125 mg PO QID x 10 days • High Risk of Recurrence (Immunocompromised or ≥65 yo): Fidaxomicin 200 mg PO BID x 10 days
1st Recurrence Non-Fulminant	• Fidaxomicin 200 mg PO BID x 5 days, then 200 mg PO once every other day x 20 days • Alternative: Vancomycin taper • Adjunctive Therapy for Prevention: Bezlotoxumab
2nd Recurrence/ Subsequent Recurrence Non-Fulminant	• Fidaxomicin 200 mg PO BID x 5 days, then 200 mg PO once every other day x 20 days • Alternative: Vancomycin taper • Adjunctive Therapy for Prevention: Fecal Microbiota Transplant or Live Biotherapeutic Products
Fulminant	• Vancomycin 500 mg PO QID + Metronidazole 500 mg IV Q8H • Consider adding vancomycin rectal enema if ileus present

*Recurrent C. diff infection (CDI) defined as new onset of CDI symptoms and positive testing with 2-8 weeks after a previously resolved episode
*Fulminant CDI defined as CDI with hypotension/shock, ileus, or megacolon
*Fidaxomicin is restricted to ID and GI
*Adjunctive therapies are for outpatient use only (ie., bezlotoxumab, microbiota transplant, live biotherapeutic products). Refer to additional patient inclusion/exclusion criteria.
*Vancomycin taper dosing: 125 mg PO QID x 14d, TID x 7d, BID x 7d, once daily x 7d, then every other day x 14d. Consider for patients with severe allergy to fidaxomicin or cost prohibits use of fidaxomicin.

Location of C. Difficile Results in Epic

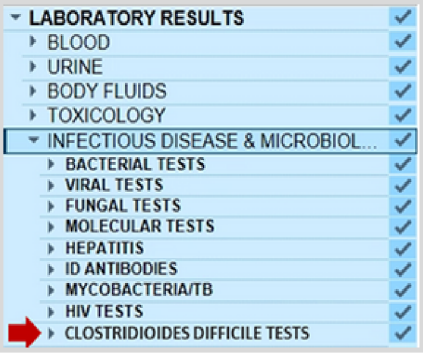
Finding your information

All positive C. difficile toxin PCR tests will **AUTOMATICALLY** be followed by a C. difficile toxin antigen test **if PCR is positive.**

These tests will be resulted along with an interpretation comment.

The test results will appear together in result review in EPIC

1. LABORATORY RESULTS →
2. INFECTIOUS DISEASE AND MICROBIOLOGY →
3. CLOSTRIDIOIDES DIFFICILE TESTS



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