CEDARS-SINAI MEDICAL CENTER

Product Information Update

June 2019

Pharmacy & Therapeutics Committee Updates	
Drugs for Formulary Consideration	**Angiotensin II (Giapreza®) for Vasoplegic Shock** – Non-formulary, case-by-case as last line therapy **DRUG CRITERIA** 1. Diagnosis of refractory vasoplegia resistant to methylene blue 2. Hemodynamic instability defined as at least 2 moderate-dose vasopressors infusing for at least 2 hours and failure to achieve goal MAP: a. Norepinephrine ≥ 20 mcg/min b. Vasopressin 0.04 units/min c. Epinephrine ≥ 8 mcg/min 3. On DVT prophylaxis or therapeutic anticoagulation 4. Orders written by attending physician and dose adjustments by MD only Assess and wean every 12 hours: progress towards at least ↓20% in combined vasopressor usage. Taper angiotensin II if no response at 12 hours (maximum duration 48h) ▪ Mechanism of action: Synthetic human peptide of the renin-angiotensin-aldosterone system, resulting in vasoconstriction, ↑aldosterone release and BP ▪ Dosing: 0-80 ng/kg/min (initial dose 20ng/kg/min, titrate down from 80 ng/kg/min after no more than 3h), maximum dose 40 ng/kg/min. ▪ Adverse effects: Thrombosis, tachycardia, peripheral ischemia, acidosis, delirium, thrombocytopenia, fungal infection ▪ Warnings: Thromboembolic events have been reported; use concurrent VTE prophylaxis ▪ Drug-drug interactions: Angiotensin receptor blockers (ARBs) may diminish the therapeutic effect of angiotensin II and Angiotensin-Converting Enzyme Inhibitors (ACEI) may enhance therapeutic effect of angiotensin II ▪ Monitoring: BP response, MAP, thrombosis **IVIG for Idiopathic Thrombocytopenic Purpura (ITP)** –revised dosing based on American Society of Hematology Guideline ▪ ITP with platelet count ≤20,000 remains a primary indication – Pediatrics: 0.8-1 g/kg x 1 – Adults: 1 g/kg x 1 (repeat x 1, ≥ 48 hours following initial dose) ▪ Expected time to response: *Initial:* 1-3; *Peak* 2-7 days **Erythropoetin α-epbx (Retacrit®)** – Add to formulary; remove Epogen® and Procrit® from formulary ▪ Mechanism of action: Stimulates erythropoiesis by the same mechanism as endogenous erythropoietin ▪ Dosing: Dependent on indication and initiate only if Hb < 10g/dL ▪ Indications: ***(similar indications between all products)*** Anemia induced by chemotherapy and anemia associated with chronic renal disease, HIV infection (zidovudine associated), and surgery (elective noncardiac, nonvascular surgery) ▪ Adverse Reactions: ***(similar between all products)*** Arthralgias/myalgias, cough, dizziness, fever, headache, hypertension, nausea/vomiting, injection site pain, pruritis, skin rash, stomatitis ▪ Warnings: ***(same black box for all products)*** Increased risk of death, MI, stroke, thrombosis, and tumor progression or recurrence – Retacrit® contains a small amount of phenylalanine (phe) (0.5 mg/vial) and carries a warning/precaution in phenylketonurics (note: a "low phenylalanine diet" = <500 mg phe/day) ▪ Monitoring: Iron panel, hemoglobin, blood pressure, signs of seizures **Vortioxetine (Trintellix®)** – Add to formulary; restrict to prior to admission therapy ▪ Indication: Major depressive disorder (MDD) ▪ Mechanism of Action: Enhances CNS serotonergic activity through inhibition of reuptake serotonin (5-HT) ▪ Dosing: Initial 10mg once daily, increase to 20 mg once daily as tolerated. ▪ Adverse effects: Nausea, sexual dysfunction, dizziness, abnormal dreams ▪ Warnings: (Black Box) Suicidal thoughts and behaviors ▪ Monitoring: Suicidal ideation, anxiety, mania, panic attacks, hyponatremia, hepatic function, serotonin syndrome **Other formulary updates** ▪ **Mesalamine Delayed Release (DR) (Lialda®)** – Mesalamine DR 1200 mg tablets (generic): Add to formulary – Pentasa® 250 mg ER cap, Delzicol® 400 mg DR cap, Canasa® 1000mg rectal supp, and mesalamine rectal enema 4 g/60mL: maintain on formulary ▪ **Rasagiline (Azilect®) 1 mg**: Add to formulary, for prior to admission therapy and for renal dysfunction (CrCl < 30mL/min) when selegiline is not an option ▪ **Long-acting beta-adrenoceptor agonist/Inhaled corticosteroid (LABA/ICS) combination inhalers** – Fluticasone/salmeterol (Advair®): maintain on formulary as preferred LABA/ICS combination inhaler – Fluticasone/vilanterol (Breo Ellipta®): do not add to formulary

<table>
<tr><th colspan="2">Pharmacy & Therapeutics Committee Updates</th></tr>
<tr><td></td><td>

Breo® 100/25 daily: auto-substitute to Advair® 250/50 BID
Breo® 200/25 daily: auto-substitute to Advair® 500/50 BID

– Budesonide/formoterol (Symbicort®): do not add to formulary, continue with current auto-substitutions
– Umeclidinium/ vilanterol (Anoro Ellipta®): add to formulary for patients on therapy prior to admission
▪ Silodosin (Rapaflo®) 4mg and 8mg tablets: Add to formulary for treatment of signs/symptoms of BPH for patients on therapy prior to admission, history of tamsulosin treatment failure, and orthostasis or labile blood pressures
▪ Automatic Substitutions:
– Mesalamine DR (Delzicol®) 400mg (2) capsules interchangeable with Asacol HD® 800mg tablet
– Blephamide® (sulfacetamide sodium 10% / prednisolone acetate 0.2%) ophthalmic suspension: auto-substitute to sulfacetamide 10% / prednisolone sodium phosphate 0.25%, at same dose and frequency
▪ Remove from formulary: Due to low usage and/or manufacturer discontinuation
– Acetaminophen 80mg chewable tablet → replace with acetaminophen 80mg rapid tablet
– Amyl nitrate inhalant
– Pseudoephedrine nasal decongestant oral solution 30mg/5ml
– Mi-Acid DS chewable tablets (calcium carbonate 700mg + magnesium hydroxide 300mg)
– Dimenhydrinate 50mg chewable tablets
– Quinidine gluconate inj
– Procaine penicillin-G inj
– Ampicillin 250mg inj
– Gentamicin 0.3% ophthalmic 3.5g ointment
</td></tr>
<tr><td>Pediatric Intranasal Midazolam Guideline for Anxiolysis or Seizure in ED</td><td>
A guideline was developed to allow safe and effective intranasal administration of midazolam in pediatric patients for anxiolysis or active seizure treatment in the ED.
Indications for use: This is a minimally invasive option when alternative routes are not available (e.g. lack of IV access) or practical (e.g. non-cooperative pediatric patients).
<table>
<tr><th><u>Seizure</u></th><th><u>Anxiolysis</u></th></tr>
<tr><td>Age > 1 months and less than 12 years of age</td><td>Age ≥ 6 months and less than 12 years of age</td></tr>
</table>
The guideline further details administration techniques, monitoring, and reversal.
</td></tr>
<tr><td>Pediatric Intranasal Fentanyl Guideline for Pain Management in ED – Revision</td><td>The guideline revisions standardize the process for intranasal fentanyl as an analgesic for moderate to severe pain in children 1 year of age and older. The first dose, 2mcg/kg/dose (max: 100mcg), and the second dose, 0.5mcg/kg/dose (max: 100mcg) must be ordered by ED MD for up to two doses. The guideline outlines administration techniques, monitoring, and reversal.</td></tr>
<tr><td>Gluten Allergy and Intolerance: Medication Review</td><td>
There have been increasing requests for gluten-free medications for patients with either gluten allergy, intolerance, or sensitivity. To accommodate the volume of requests and to improve patient care, a pharmacy process was developed for patients with true gluten (wheat) allergy with clinically significant intolerance (anaphylaxis, celiac disease, non-celiac gluten sensitivity).
1. <u>Continuation of Therapy (preferred)</u>: Check patient's home medications (or list of specific known tolerated, gluten-free medications) that are denoted 'safe' in patient's medical record for current and future admissions
2. <u>New medication orders</u>: Review gluten content using FDA product labeling
a. https://gluten.org/wp-content/uploads/2015/01/EDU_CD-Medications.pdf
b. www.fda.gov/drugs/ensuring-safe-use-medicine/medications-and-gluten
c. pillbox.nlm.nih.gov
d. glutenfreedrugs.com
3. <u>OTC medication orders</u>: Review gluten content listed in the "Drug Facts" labeling
For patients with other reasons to avoid gluten, follow the current dispensing process.
</td></tr>
<tr><td>Peri-Operative Lung Transplant Pain and Coagulopathy Management Protocol</td><td>Pain management strategies have been protocolized for lung transplant patients during the pre-operative and post-operative phase. In the post-operative phase, patients will receive neuraxial or regional anesthesia in addition to multi-modal therapies. Also, anticoagulation and management of coagulopathy have been standardized for these patients prior to placement/removal of the epidural catheter, based on INR, PTT, platelet counts, and fibrinogen levels. If neuraxial anesthesia is contraindicated, single block intercostal or erector spinae block will be administered at discretion of the regional pain MD.</td></tr>
<tr><td>Infliximab Accelerated Infusion
• Maintenance Therapy Plan for Accelerated Infusion</td><td>Infliximab is currently infused over 2 hours (per FDA-approved labeling) with vital signs monitored during and post-infusion. Studies have reported the safety of 1-hour infusions, and health systems/Inflammatory Bowel Disease centers have since adopted this rapid infusion. Given supporting literature and experience from other centers, 1-hour rapid infusions are recommended only for patients on scheduled maintenance therapy and have tolerated at least 3 maintenance infusions over two hours without any reactions. Patients with documented anti-infliximab antibodies will be excluded.</td></tr>
<tr><td>Medication Management Safety Committee</td><td>
▪ Riociguat (Adempas®) Risk Evaluation and Mitigation Strategies (REMS) Updates
Due to regulatory updates on Adempas® REMS Program, modifications to the CSMC REMS Procedure and CS Link order questions will be made:
1. <u>Remove</u> order question: "Is this continuation of therapy."
Rationale: Prescriber enrollment is now required for continuation of therapy. Previously, it was required for initiation.
2. <u>Add</u> order question: "I hereby attest that I have counseled the patient on the risk of embryo-fetal toxicity, the need for use of contraception, and to inform me of the pregnancy immediately"
</td></tr>
</table>

Pharmacy & Therapeutics Committee Updates

Rationale: The Adempas® medication guide for patients was removed as a requirement, and this order question will ensure education compliance for females of reproductive potential

3. Patients will be dispensed no more than a 15-day supply at/upon discharge.

- **Acetaminophen (APAP) 24-hour Total – CS-Link Alert Revision**
  The medical center established a 3 grams/24h limit to APAP to minimize risk of overdose/toxicity given the number of other APAP containing combination products. In an inpatient setting, physicians should be able to exercise their discretion and recommend up to 4 grams/24h limit. A new override option "MD notified, Approved x 1 Dose Only" will be incorporated to CS-link to prevent delays when an additional dose above 3 grams is warranted.

Antimicrobial Stewardship Committee

- **Doravirine (Pifeltro®)** – add to formulary

DRUG CRITERIA

1. Patients unable to receive first-line/preferred antiretrovirals
2. NNRTI therapy required and unable to receive rilpivirine (e.g. HIV RNA > 100,000 copies/mL or CD4 <200)
3. Risk for adverse effects (neuropsychiatric and metabolic toxicities) associated with alternative NNRTIs
4. Significant drug interactions precluding use of alternative NNRTIs
5. Continuation of outpatient therapy

  - Mechanism of action: non-competitive inhibition of the HIV-1 reverse transcriptase
  - Dosing: 100 mg tablet PO daily; if co-administered with rifabutin, take 100 mg tablet twice daily
  - Adverse Reactions: nausea, dizziness, headache, fatigue, abdominal pain, and ↑ in bilirubin, AST/ALT, CPK, SCr
  - Contraindications: co-administration with strong CYP 3A enzyme inducers
  - Monitoring: Viral load, CD4 count

- **Polymixin B Review:**
  Based on new 2019 consensus guidelines and contemporary pharmacokinetic analysis for optimal polymyxin B use, polymyxin B kinetics are more predictable than colistin and associated with less nephrotoxicity. Therefore,
  - Polymyxin B will be the preferred systemic polymyxin for **non-urinary** infections
  - Colisitin will be reserved for **urinary** infections only
  - Microbiology reports will be updated to include colistin susceptibility predicts susceptibility to polymyxin B
- **Uncomplicated Skin Abscess Guideline for Emergency Department**
  A guideline for the ED was developed to (1) standardize management of health immune-competent patients presenting with uncomplicated skin abscesses and (2) to optimize patient satisfaction and resource utilization. Uncomplicated simple abscesses should be treated by incision and drainage and antibiotics, with trimethoprim-sulfamethoxazole (TMP-SMX; Bactrim®) being the preferred oral agent. IV vancomycin is recommended only for patients admitted for complicated soft tissue infections.
- **Fluoroquinolone Use Guideline Update:** Revised with new FDA warnings, 1st/2nd line therapies, and prophylaxis therapy
- **CLSI Daptomycin Breakpoint 2019 Update:**

***Enterococcus faecium*:**	**Other *Enterococcus* Species:**
▪ MIC ≤ 4 mg/L –Susceptibility based on 8-12 mg/kg/day ▪ MIC ≥ 8 mg/L – Report as resistant	▪ MIC ≤ 2 mg/L – Report as susceptible ▪ MIC ≥ 4 mg/L – Report as non-susceptible

- **Add to formulary, maintain current restrictions:** Liposomal amphotericin B (Ambisome®), atovaquone/proguanil, aztreonam, ceftazidime, ertapenem, imipenem-cilastatin

Other Updates (please refer to the intranet for the most updated version)

Policies, Procedures, and Guideline Updates

- Statin Drug Interactions Table (Updates)
- Nursing Intravenous Medication Guidelines for Adults – Summary of Changes
- 2018 Antibiograms (House-wide & ICU)
- 2019 Annual Look-Alike Sound-Alike (LASA) Analysis
- Dobutamine Stress Echocardiography: Clinical Manual/Cardiology: Echocardiology
- Pain Pumps (Implanted): Patients Admitted with Policy: Clinical Manual/ General Clinical
- Latent Tuberculosis Infection Post Exposure Nurse Practitioner Protocol /Employee Management: General Clinical
- Chest Tubes - Removal of for Pediatric and Neonate Protocol General Clinical/Nurse Practitioner Std Procedures & Protocols
- Outpatient Pharmacies: Patient Medication (Injectable) in Outpatient Setting Procedure: Pharmacy
- Outpatient Pharmacies: Prescription Processing Procedure: Pharmacy
- Medication Refrigerator & Freezer Temperature (MM.03.01.01.b) Procedure: Medication Management
- Arterial Line Insertion with and Without Ultrasound: Radial, Axillary, Femoral, and Brachial: Standardized Procedure and Protocol for Nurse Practitioners

Requests for full monographs or questions regarding this listing may be addressed to the Drug Information Center at **(310) 423-3784**

Chau Chu, PharmD, BCPS — *Pharmacist, Drug Use Policy*
Hai Tran, PharmD, BCPS — *Associate Director, Drug Use Policy*
Nari Kim, PharmD — *Pharmacy Resident, Drug Use Policy*