Pharmacy & Therapeutics Committee Meeting
Private Dining Room
April 13, 2017 7:00 a.m.

Agenda Items	Individual Responsible	
1. Call to Order	Richard Pesce, MD	
2. Approval of February, 2017 Minutes	Richard Pesce, MD	
3. CHI MUE Committee – Meeting decision briefs		Page
A. March MUE decision brief	Patrick Ellis	6-10
• Sotalol injection		
• Dantrolene formulations		
• Inpatient iron formulary		
• SGLT2 inhibitors		
• Long acting bronchodilators		
4. Therapeutic Interchanges and Formulary Decisions		
A. Latuda® (lurasidone)	Patrick Ellis	11-12
B. Invega® (paliperidone)		13-14
C. Relistor® (methylnaltrexone) Therapeutic Interchange	Justin Reinert	15-16
D. Reopro® (abciximab)	Patrick Ellis	
5. Medication Safety & Policy		
A. Hypertonic saline (3% NS)	Patrick Ellis	17-19
B. Perioperative Medication Management		20-22
C. Standard PCA settings (smart pump limits)		23
D. Nicardipine IV infusions		
6. MUE		
A. PPI Stress Ulcer Prophylaxis	Jenny Gibson	24-27
B. Glycemic Control	Shane Church	28-29
7. Protocols		
A. IV Iron Replacement Protocol – max dose consideration	Patrick Ellis	30
B. Nicotine Replacement Protocol	Justin Reinert	31-32
8. Nutrition Support		
A. Diet manual	Susan Fuchs	

Next Meeting will be June 8, 2017 at 7:00 AM in the Private Dining Room

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: February 9, 2017 CALLED TO ORDER: 7:00 A.M.
LOCATION: Private Dining Room ADJOURNED: 8:00 A.M.

Members Present:		**Members Absent**:	**Guests**:
Richard Pesce, M.D. David Dodson, M.D. Mark Anderson, MD Allen Atchley, M.D. Richard Yap, M.D. Helen Kuroki, MD Nathan Schatzman, M.D. Lee Hamilton, M.D.	Sandy Vredeveld, DPh Patrick Ellis, PharmD Lila Heet, PharmD Susan Fuchs, RD Karen Babb, PharmD	Nan Payne, RN Melissa Roden, RN Shannon Harris, RN Michael Stipanov, M.D. Nathan Chamberlain, M.D. Scott Harbaugh, Finance Avni Kapadia, M.D. Jeffrey Mullins, M.D Jamie Barrie, PharmD Patty Hicks, RN	Shane Church, PharmD Meredith Tate, PharmD Justin Reinert, PharmD Jenny Gibson, PharmD Jonathan Cobb, Student

This meeting will be convened under the protection of the Tennessee Statute 63-6-219 and the Health Care Quality Improvement Act of 1986, Public Law 99-660. All information, case reviews, meeting minutes, statistics and correspondence are confidential and protected. Included in that protection are those that are involved in the review of the information. Any discussion of this information outside the realm of Peer Review constitutes a breach and violates the protection of the persons involved in the breach.

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
Minutes	The October 13, 2016 minutes were approved as submitted.	Approved	Complete
CHI MUE Committee	The following medications were reviewed: 1. **CHI MUE Committee Decision Brief**: The medications that were reviewed at the October & November national MUE committee meeting were reviewed with the committee. The only two items that required local P&T review are the following: **A.** **Calcitonin injection restrictions:** Memorial has previously reviewed calcitonin utilization (April 2015 P&T) and educated prescribers on appropriate use and pharmacists screen all orders for appropriateness and communicate with prescribers regarding questionable orders. Memorial's current criteria for use are consistent with the national MUE criteria and no changes were recommended to the current process. Patrick will provide repeat education for the hospitalists at their next scheduled meeting. **B.** **Levalbuterol:** The national MUE has designated this medication as a formulary restricted medication that allows use in certain clinical scenarios although this has been non-formulary at Memorial for many years. Dr. Pesce recommended that this remain as a non-formulary medication at Memorial.	 No change recommended Affirmed non-formulary status	Complete Complete Complete
Therapeutic Interchanges and Formulary Decisions	**1.** **Tecentriq® (atezolizumab) –** A new PDL-1 directed monoclonal antibody indicated for the treatment of urothelial carcinoma & NSCLC. Although this agent is similar to other formulary agents (Opdivo, Keytruda) it is the first of these agents to be approved for treatment of advanced/refractory urothelial cancer. It was recommended by Dr. Stipanov to approve this for outpatient infusion use only for the labeled indication or other insurance approved off label indications. **2.** **Cetylev® (N-acetyleysteine) –** New effervescent tablet formulation of NAC for acute APAP overdose. Pharmacokinetic (PK) data comparing this to traditional liquid/oral formulations of NAC has shown no clinically meaningful differences in any PK parameter. Patrick recommended that	Approved Non-formulary, therapeutic interchange approved	Complete Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	this be designated non-formulary and the oral/liquid formulation of NAC be substituted for any Cetylev orders due to a higher cost and lack of data demonstrating superiority for this new formulation.		
	3. Relistor® (methylnaltrexone) oral formulation – New oral formation of existing sub-cutaneous formulary version of Relistor (peripheral acting mu-opioid receptor antagonist - PAMORA). Movantik® (naloxegol) is currently the only oral PAMORA on formulary. Although no head to head studies exist comparing oral Relistor to Movantik, the available data does suggest that the time of onset and efficacy of these two medications is very comparable and based on this information it was recommended to utilize and automatic therapeutic interchange in which all Relistor (oral) orders will be substituted to a therapeutically equivalent dose of Movantik.	Non-formulary, therapeutic interchange approved	Complete
	4. Opthalmic Glaucoma Agents Class Review – A formulary interchange for the following classes of ophthalmic agents has been suggested by the national MUE committee: alpha agonists, beta blockers, carbonic anhydrase inhibitors. The clinical efficacy among these various agents are all similar in regard to their ability to lower IOP with the only difference being some minor differences in adverse effect profiles between products. Patrick stated that most of the patients on these medications are continuation of home therapies and a therapeutic interchange could be utilized and patients intolerable to the formulary agent(s) or who wish to stay on their home therapies could utilize their home supply per the formulary policy. It was recommended to designate the following products as the formulary agents for these classes with all other orders to be substituted to a therapeutically equivalent do se of the formulary agent: brimonidine 0.2%, timolol 0.25 & 0.5%, dorzolamide 2%. All other formulary medications would be designated as "non-formulary". Patrick will work with our ophthalmologists that utilize apraclonidine for certain eye surgeries to ensure that this substitution will be appropriate for these indications before removing this agent from formulary.	Therapeutic interchange approved	Complete
	5. Blood factor products for inherited bleeding disorders – A review of the available clotting factors for both hemophilia and VWD were reviewed. Patrick discussed this review with Dr. Stipanov and he approved designating specific products as the formulary agents of choice for each clotting disorder. If a specific brand of clotting factor is requested the pharmacy will discuss with the provider the potential substitution to ensure this is appropriate for the ordered indication. The below process was discussed and approved by Dr. Stipanov. <u>Hemophilia A (Factor VIII)*</u> • No specific product requested – Alphanate (human derived factor VIII) will be utilized • Recombinant product requested – Xyntha (recombinant factor VIII) will be utilized • Anti-inhibitor coagulant complex – FEIBA (human factors II, VII, IX, and X) *FEIBA will be ordered on an as needed basis for patients with hemophilia with inhibitors or in patients with acquired inhibitors to other clotting factors* <u>Hemophilia B (Factor IX)*</u> • No specific product requested – Bebulin (human derived factor IX) will be utilized • Recombinant product requested – Benefix (recombinant factor IX) will be utilized • Anti-inhibitor coagulant complex – FEIBA (factors II, VII, IX, and X) *FEIBA will be ordered on an as needed basis for patients with hemophilia with inhibitors or in patients with acquired inhibitors to other clotting factors* <u>Von Willebrand Disease (vWF)*</u>	Approved	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	• No specific product requested – Humate-P (human derived vWF) will be utilized **If a specific product is requested by name the prescriber will be contacted and the above product offered as a potential alternative* **6. Specialty Pharmacy Medications –** Specialty pharmaceuticals are generally high cost maintenance medications for patients with rare and/or chronic diseases. The distribution system for these medications are typically dispensed as patient specific prescriptions direct to the patient from specialty pharmacy distributers. During a recent formulary review it was discovered that several "specialty" medications are currently on formulary without any restrictions for their use. It was recommended to designate these as "non-formulary, specialty" medications and for patients to utilize their own medications if these are home, maintenance medications. When these are ordered as new therapies it was recommended that the inpatient pharmacy along with case management and the medication patient assistance coordinator to navigate through the appropriate contracted specialty pharmacies to arrange for new medication orders to be filled as a direct to patient order when possible rather than these being ordered and dispensed directly from the inpatient pharmacy. This would help to ensure that the patient's ongoing therapy is insurance approved and can be continued once discharged and eliminates the need for the hospital to assume the total cost of therapy for their brief inpatient stay. The following drugs were recommended for this new "non-formulary, specialty" designation: sorafenib, erlotinib, dasatinib, imatinib, sunitinib, thalidomide, temozolomide, etoposide oral, cyclophosphamide oral, capecitabine, macitenan, ambrisentan, bosentan.	Approved	Complete
Medication Safety	**1. Hypoglycemia Management –** The hypoglycemia protocol has been updated to more accurately reflect current evidence based recommendations for treatment of hypoglycemia. The protocol was shared for informational purposes. Patrick also asked the committee if the protocol should automatically be available for ALL patients on oral or injectable hypoglycemic agents so the pharmacologic treatment options would be available on the EMAR if/when needed. Currently the hypoglycemia protocol is only attached to hospital protocols such as SQ correctional insulin protocols, insulin drip protocols, etc. The committee recommended that this would be a best practice and suggested that this recommendation be forwarded on to MEC for approval as a standing order for any applicable patient.	Information only – Recommendation to be forward to MEC for approval	Pending
	2. Hypertonic Saline – Dr. Hamilton shared with the committee a recent event in which a patient was incorrectly started on 3% NS based on an erroneous lab value. He questioned the committee regarding if this therapy should somehow be restricted in order to prevent future patient safety issues due to inappropriate utilization or lack of follow up laboratory values. The committee was unable to reach consensus on specific restriction criteria and it was recommended for pharmacy to develop (in collaboration with nephrology and Dr. Hamilton) appropriate use criteria that pharmacists can use to evaluate appropriateness when this therapy is ordered. Additionally, hospitalist education will be developed based on the use criteria that are to be developed. The appropriate use criteria will be reviewed at the April 2017 P&T meeting. In the interim Patrick agreed to prepare preliminary education on appropriate use to the pharmacy staff to utilize until the final use criteria is developed and approved.	Usage criteria to be developed and reviewed at April meeting	Pending
	3. Perioperative Medication Management – Dr. Schatzman discussed some recent literature that suggests that continuation of ACE/ARBs during the preoperative period can be correlated with both	Approved – education document to be developed	Pending

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	procedural hypotension and an increased risk of myocardial injury. After discussion, the committee supported Dr. Schatzman's recommendation and approved the proposal to modify the existing *Pre-Anesthesia Orders* to include holding ACE/ARBs for 24 hours prior to surgery. Dr. Kuroki recommended that an educational document be prepared and distributed to the medical staff prior to roll out. Drs. Atchley and Schatzman agreed to work with Patrick on the development of this document for distribution to the full medical staff prior to roll out of this new process. 4. **ADRs May to August 2016 –** Karen reviewed the ADRs and noted that no ADRs for this time period would need to be reported to the FDA's Medwatch program. No other significant trends were noted.	Information only	Complete
Medication Use Evaluation	**Pharmacy Discharge Service – Program Update:** Patrick shared with the committee a recent change to the pharmacy process in an effort to increase the scope and the number of patients seen by pharmacists prior to discharge. The pharmacists will be collaborating with the discharge LPNs to review the final discharge medication orders for accuracy and counsel the patients prior to their discharge. Instead of focusing on only high LACE score patients the pharmacists will focus on ANY patients whose discharge is being prepared by the discharge LPNs. Preliminary findings have demonstrated higher productivity for the pharmacists involved in this work and an ability to screen more patients prior to discharge. Patrick asked the committee for feedback as this work progresses so these efforts can best be utilized to have the greatest impact (high risk disease states, bundle patients, etc.).	Information only	Complete
Policy & Proceedure	**Look-Alike, Sound-Alike Policy –** Modifications to this policy were approved.	Approved	Complete
Protocols	**IV Iron Replacement – max dose consideration** **Nicotine Replacement Protocol**	Tabled to next meeting Tabled to next meeting	Pending Pending

There being no further business, the meeting was adjourned at 8:00 A.M. The next P&T meeting is **April 13, 2017 at 7:00 a.m.**

Respectfully submitted,
Sandy Vredeveld, D.Ph. Director of Pharmacy
Patrick Ellis, Pharm.D Pharmacy Clinical Coordinator

Approved by,
Richard Pesce, M.D. Chairman

MEDICATION USE AND EVALUATION COMMITTEE DECISION BRIEF: March 2017

Executive Summary

March MUE Decision(s)

NOTE: Per MUE normal process, markets may implement or retain more restrictive formulary status.

Medication Name	*Medication Used for*	Formulary Status Decision				Comments/Restrictions/Therapeutic Interchange	Timeline to Implement
		Formulary, Unrestricted	Formulary, Restricted	Non-Formulary	Do Not Stock		
sotalol injection (intravenous)	*certain types of life threatening or abnormal heart beats*	**sotalol oral** **amiodarone injection**			**sotalol injection**		immediately
dantrolene sodium injection (Ryanodex™)	*health issue called malignant hyperthermia*	**dantrolene sodium** (Dantrium® or Revonto®)			**dantrolene sodium** (Ryanodex™)	Select most cost effective formulary, unrestricted agent	immediately
Inpatient Use: sodium ferric complex in sucrose (Ferrlecit®)	*anemia*	**sodium ferric gluconate in sucrose** (Ferrlecit®)	**iron dextran** (Infed®)	**iron sucrose** (Venofer®) **ferric carboxy-maltose** (Injectafer®) **ferumoxyytol** (Feraheme®)		Iron dextran (Infed®) is restricted to single dose. **Therapeutic Interchange for Inpatient Use** **Ordered for Inpatient (>single dose)** / **Provided for Inpatient** iron sucrose (Venofer®) 100mg → sodium ferric gluconate (Ferrlecit®) 125mg over 1 hour in 100mL NS intravenously Q 24 hours iron sucrose (Venofer®) 200mg – 300mg → sodium ferric gluconate (Ferrlecit®) 250 mg over 2 hours in 100mL NS intravenously Q 24 hours iron sucrose (Venofer®) > 300mg → Call provider and recommend sodium ferric gluconate (Ferrlecit®) 250 mg IV over 2 hours Q 24 hrs x 2 doses OR sodium ferric gluconate (Ferrlecit®) 250 mg IV over 2 hours Q 12 hrs x 2 doses	60 days from 3/21/17

Note: The Decision Brief summarizes the decisions of the national CHI Medication Use and Evaluation (MUE) Committee. Local P&Ts may act on MUE Decisions in one of three ways: 1) approve with no changes 2) approve with more restrictions 3) request an extension, exception or appeal per the MUE process. 1

Medication Name	*Medication Used for*	Formulary Status Decision				Comments/Restrictions/Therapeutic Interchange	Timeline to Implement
		Formulary, Unrestricted	Formulary, Restricted	Non-Formulary	Do Not Stock		
Outpatient Use: sodium ferric complex in sucrose (Ferrlecit®)	*anemia*	**Preferred: ferumoxytol** (Feraheme™) or **sodium ferric gluconate in sucrose** (Ferrlecit®)				For outpatient therapy, entity can determine the most cost effective and reimbursable agent. **Suggested Therapeutic Interchange for Outpatient Use** Ordered for Outpatient: Iron sucrose (Venofer®) Provided for Outpatient: Preferred outpatient iron: Ferumoxytol (Feraheme™) 510mg IV infusion over 15 minutes x 2 doses (separate doses 3 to 8 days apart) **OR** Outpatient dialysis patients if insurance does not cover Ferumoxytol (Feraheme™): Use Sodium ferric gluconate (Ferrlecit®)	60 days from 3/21/17
paliperidone (Invega®)	*schizophrenia and schizo-affective disorder*		**paliperidone** (Invega®) oral formulation **paliperidone palmitate injectable** (Invega Sustenna® and Invega Trinza®)			**Restrictions for paliperidone palmitate (Invega Sustenna® and Invega Trinza®) injectable formulations** • Outpatient use • Inpatients unable to provide home supply where scheduled injection cannot be postponed until discharge (See FULL Monograph) **Restrictions and Suggested Therapeutic Interchange for paliperidone (Invega®) oral formulation** • Acute psychiatric treatment centers or inpatient psychiatric units Note: Markets may choose to make this agent non-formulary and use a Therapeutic Interchange **Suggested Oral Formulation Therapeutic Interchange** Ordered: Paliperidone (Invega®) ER PO 1.5 mg daily; 3 mg daily; 6 mg daily; 9 mg daily Provided: Risperidone (Risperdal®) PO 0.5 mg bid; 1 mg bid; 3 mg bid; 4 mg bid	60 days from 3/21/17

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Medication Name	*Medication Used for*	Formulary Status Decision				Comments/Restrictions/Therapeutic Interchange	Timeline to Implement
		Formulary, Unrestricted	Formulary, Restricted	Non-Formulary	Do Not Stock		
lurasidone (Latuda®)	*schizophrenia and for depression in people with bipolar disorder*		**lurasidone** (Latuda®)			Restricted to acute psychiatric care facilities only Non-formulary for traditional acute inpatient facilities Note: Markets with acute psychiatric care facilities may choose to make this agent non-formulary	30 days from 3/21/17
Sodium-glucose co-transporter (SGLT2) Inhibitor Class Review	*type 2 diabetes*			**All SGLT2 inhibitors: Empagliflozin** (Jardiance®) **Canagliflozin** (Invokana®) **Dapagliflozin** (Farxiga®)		SGLT2 Inhibitors should be held during hospitalization	90 days from 3/21/17
long-acting beta agonists (LABA), inhaled broncho-dilators	*chronic lung conditions like emphysema, chronic bronchitis and chronic obstructive asthma*	**If LABA used, nebulized preferred: aformoterol** (Brovana®) **If LABA inhaler required: Salmeterol** (Serevent Diskus® institutional size)		**All Other LABA products** **Nebulized: Formoterol** (Perforomist®) **Inhaler: olodaterol** (Striverdi Respimat®) **indacaterol** (Arcapta Neohaler®)		For markets choosing to use long-acting, nebulized beta agonists (LABA), the most cost-effective agent (Brovana) should be used: LABA Therapeutic Interchange Ordered: Perforomist® (formoterol) INH BID → Provided: Brovana® (aformoterol) INH BID Ordered: Arcapta Neohaler® (indacaterol) INH BID → Provided: Brovana® (aformoterol) INH BID Ordered: Striverdi Respimat® (olodaterol) Daily → Provided: Brovana®(aformoterol) INH BID Ordered: Serevent Diskus® (salmeterol) INH BID → Provided: Brovana®(aformoterol) INH BID If sites not utilizing nebulized LABAs wish to have a formulary LABA, Serevent Diskus® (institutional size) is the agent of choice as the only institutional size inhaler product available. **ONLY sites that are unable to utilize Brovana® due to respiratory therapist availability should select this option.** Note: Markets may choose to make **all LABA agents non-formulary** with a Therapeutic Interchange to albuterol (nebulized) Q6 hour.	60 days from 3/21/17

Note: The Decision Brief summarizes the decisions of the national CHI Medication Use and Evaluation (MUE) Committee. Local P&Ts may act on MUE Decisions in one of three ways: 1) approve with no changes 2) approve with more restrictions 3) request an extension, exception or appeal per the MUE process. 3

<table>
<tr><th rowspan="2">Medication Name</th><th rowspan="2">Medication Used for</th><th colspan="4">Formulary Status Decision</th><th rowspan="2">Comments/Restrictions/Therapeutic Interchange</th><th rowspan="2">Timeline to Implement</th></tr>
<tr><th>Formulary, Unrestricted</th><th>Formulary, Restricted</th><th>Non-Formulary</th><th>Do Not Stock</th></tr>
<tr><td>inhaled long-acting anti-muscarinics (LAMA)</td><td>chronic lung conditions like emphysema, chronic bronchitis and chronic obstructive asthma</td><td>tiotropium (Spiriva HandiHaler® institutional size)</td><td></td><td>aclidinium (Tudorza®)

glycopyrrolate (Seebri Neohaler®)

tiotropium (Spiriva Respimat®)

umeclidinium (Incruse Ellipta®)</td><td></td><td><table><tr><th>Ordered</th><th>Provided</th></tr><tr><td>Tudorza® (aclidinium) INH BID</td><td>Spiriva HandiHaler® (tiotropium) 1 cap INH daily</td></tr><tr><td>Seebri Neohaler® (glycopyrrolate) INH BID</td><td>Spiriva HandiHaler ® (tiotropium) 1 cap INH daily</td></tr><tr><td>Spiriva Respimat® (tiotropium) INH daily</td><td>Spiriva HandiHaler ® (tiotropium) 1 cap INH daily</td></tr><tr><td>Incruse Ellipta® (umeclidinium) INH daily</td><td>Spiriva HandiHaler ® (tiotropium) 1 cap INH daily</td></tr></table>Note: Markets may choose to make all LAMA agents non-formulary with a Therapeutic Interchange to ipratropium (nebulized) Q6 hour.</td><td>60 days from 3/21/17</td></tr>
<tr><td>combination LAMA/LABA (long-acting anti-muscarinic and long-acting beta agonist) inhalation products</td><td>chronic lung conditions like emphysema, chronic bronchitis and chronic obstructive asthma</td><td>umeclidinium /vilanterol (Anoro Ellipta® institutional size)</td><td></td><td>glycopyrrolate /formoterol (Bevespi Aerosphere®)

glycopyrrolate /indacaterol (Utibron Neohaler®)

tiotropium/ olodaterol (Stiolto Respimat®)</td><td></td><td><table><tr><th>Ordered</th><th>Provided</th></tr><tr><td>Bevespi Aerosphere® (glycopyrrolate/formoterol) INH BID</td><td>Anoro Ellipta® (umeclidinium/vilanterol) INH daily</td></tr><tr><td>Utibron Neohaler® (glycopyrrolate/indacaterol) INH BID</td><td>Anoro Ellipta® (umeclidinium/vilanterol) INH daily</td></tr><tr><td>Stiolto Respimat®(tiotropium/ olodaterol) INH daily</td><td>Anoro Ellipta® (umeclidinium/vilanterol) INH daily</td></tr></table>Note: Sites may elect to use Spiriva HandiHaler® PLUS Brovana® instead of the formulary combination product (Anoro Ellipta®).

Note: Markets may choose to make all LAMA/LABA agents non-formulary with a Therapeutic Interchange to albuterol (nebulized) PLUS ipratropium (nebulized) Q6 hour.</td><td>60 days from 3/21/17</td></tr>
</table>

Note: The Decision Brief summarizes the decisions of the national CHI Medication Use and Evaluation (MUE) Committee. Local P&Ts may act on MUE Decisions in one of three ways: 1) approve with no changes 2) approve with more restrictions 3) request an extension, exception or appeal per the MUE process. 4

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<tr><th>Formulary, Unrestricted</th><th>Formulary, Restricted</th><th>Non-Formulary</th><th>Do Not Stock</th></tr>
<tr><td>Update: Ophthalmic Antihistamine Class Review</td><td></td><td>ketotifen (Zaditor®)</td><td></td><td>Three agents added: alcaftadine (Lastacaft®), bepotastine (Bepreve®), lodoxamide (Alomide®)</td><td></td><td>Updated Therapeutic Interchange
<table>
<tr><th colspan="2">THERAPEUTIC INTERCHANGE</th></tr>
<tr><th>Ordered</th><th>Provided</th></tr>
<tr><td>azelastine -1 drop in each eye twice daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>epinastine -1 drop in each eye twice daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>olopatadine 0.1% -1 drop in each eye twice daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>olopatadine 0.2% -1 drop in each eye once daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>emedastine -1 drop in each eye four times daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>alcaftadine - 1 drop in each eye once daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>bepotastine - 1 drop into affected eye twice daily</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
<tr><td>lodoxamide – 1-2 drops into eye four times/day</td><td>ketotifen 1 drop in each eye twice daily</td></tr>
</table></td><td>30 days from 3/21/17</td></tr>
</table>

Attendance Roster: 2017 MUE Attendance Roster Cumulative 03 21 2017
Voting Roster: MUE Voting Record March 2017
Items above are listed in same order as they appear in the Committee Meeting Packet: CHI MUE Committee Compiled Packet 03-21-2017

FORMULARY REVIEW

GENERIC NAME: LUPRASIDONE

PROPRIETARY NAME: *Latuda*

INDICATIONS:

FDA Approved
Bipolar Depression
Schizophrenia
Non-FDA Approved
Psychosis/agitation associated with dementia

THERAPEUTIC CATEGORY:
Second generation atypical antipsychotic

PHARMACOKINETICS:

Absorption	Lurasidone peak concentrations (Cmax) are reached within 1 to 3 hours following oral administration. Systemic bioavailability is 9% to 19% of the dose. When administered with food, the mean Cmax was increased about 3-fold and the mean area under the curve (AUC) was increased about 2-fold compared with administration under fasting conditions. The increase in absorption was not influenced by meal fat and was not altered by increasing the meal size from 350 to 1,000 calories.
Distribution	Steady-state concentrations are reached within 7 days of initiating therapy. Dose-proportional pharmacokinetics have been observed over a range of doses from 20 to 160 mg. Lurasidone is 99% plasma protein–bound with a volume of distribution of 6,173 L.
Metabolism	Lurasidone is primarily metabolized by CYP3A4 to two active metabolites and two major nonactive metabolites.
Elimination	The mean elimination half-life is 18 hours.

CLINICAL STUDIES:
Although there are limited data comparing the efficacy of Latuda to other antipsychotics, the literature does seem to suggest comparable safety and efficacy to quetiapine, ziprasidone, and olanzapine. This is based on both placebo controlled and active controlled, non-inferiority designed trials.

DRUG INTERACTIONS:
Lurasidone is contraindicated in combination with strong CYP3A4 inducers and inhibitors. Dose adjustments are recommended for moderate CYP3A4 inhibitors, such as diltiazem). Lurasidone in combination with centrally acting drugs or alcohol may cause additive CNS effects.

DOSING AND ADMINISTRATION

Adult Dosing/Indication	The starting dose is 40 mg once daily. The maximum dose is 80 mg once daily, although doses ranging from 40 to 120 mg were effective in clinical trials. No additional benefit was seen and an increase in adverse effects are observed with doses > 80 mg daily.
Pediatric Dosing/Indication	Lurasidone is not approved for use in the pediatric population.
Administration	Lurasidone should be administered with a meal containing at least 350 calories for optimal absorption.

DOSING ADJUSTMENTS:

Hepatic Impairment	Moderate Impairment: 80 mg/day maximum Severe Impairment: 40 mg/day maximum
Renal Impairment	Reduce dose to a maximum of 80 mg/day for CrCl <50 ml/min.
Moderate CYP inhibitors or inducers	The starting dose for lurasidone is 20 mg per day with a maximum recommended dose of 80 mg per day. Reduce dose by 50% already taking lurasidone.

RECOMMENDED MONITORING:
Patients should be monitored for weight gain and hyperglycemia. Obtain complete blood cell counts frequently during initiation and in patients with a history of leukopenia or neutropenia.

PHARMACOECONOMICS/COST:

Product (Name, Strength, Form)	Cost per Dose Contract/GPO
Latuda 20 mg tablet (#30)	$30.60
Latuda 40 mg tablet (30	$30.60
Latuda 60 mg tablet	$30.60
Latuda 80 mg tablet	$30.60
Latuda 120 mg tablet	$45.67

CONCLUSION & RECOMMENDATION:

Latuda® (lurasidone) is a novel benzoisothiazol-derivative atypical antipsychotic agent that was FDA approved in 2010 for the treatment of schizophrenia in adults and adolescents (aged 13-17 years) and for depressive episodes associated with Bipolar I Disorder as monotherapy or in adjunct with lithium or valproate. It has a similar side effect profile compared to the other atypical antipsychotic agents. Although there are no head-to-head trials comparing the efficacy of Latuda to other antipsychotics, the literature does seem to suggest comparable safety and efficacy to quetiapine, ziprasidone, and olanzapine.

The CHI MUE committee recommendation is to classify this agent as non-formulary for traditional acute care inpatient facilities and restrict formulary use to acute psychiatric care facilities only. Non-psychiatric inpatient facilities in CHI will address patients who are admitted with this as a maintenance home medication through their non-formulary medication procedures (e.g. seeking to have the patient use their home supply, or only obtaining this product when necessary for an individual patient on a case by case basis).

FORMULARY REVIEW

GENERIC NAME: PALIPERIDONE

PROPRIETARY NAME: *Invega*

INDICATIONS:

FDA Approved
Schizophrenia
Schizoaffective disorder
Non-FDA Approved
Delusional parasitosis
Psychosis/agitation associated with dementia

THERAPEUTIC CATEGORY:
Second generation atypical antipsychotic. Paliperidone (Invega®) is a psychotropic agent that belongs to the chemical class of benzisoxazole derivatives. It is the major active metabolite of risperidone (Risperdal®).

PHARMACOKINETICS & DOSING ADJUSTMENTS:

	Product Name		
	Invega	**Invega Sustenna**	**Invega Trinza**
Metabolism	Major: Dealkylation, hydroxylation, dehydrogenation, benzisoxazole scission, minor: CYP2D6 and CYP3A4		
Bioavailability (%)	28%	-	-
t ½ (hr)	23 hr	25-49 days	84-95 days following deltoid injection; 118-139 days following gluteal injection
Vd (L/kg)	487 L	391 L	1960 L
Excretion	Urine (80%); feces (11%)		
Protein binding (%)	74%		
Fraction excreted unchanged in urine (%)	59%		
Dose adjustment in renal insufficiency	CrCL 50 to < 80 ml/min: Initial 3 mg once daily; max 6 mg once daily CrCL 10 to < 50 ml/min: Initial 1.5 mg once daily; max 3 mg once daily CrCL < 10 ml/min: Use not recommended		
Dose adjustment in geriatric patients	Adjustment not necessary with normal renal function		
Dose adjustment in hepatic insufficiency	Child Pugh A and B adjustment not necessary		

CLINICAL STUDIES:
Nineteen studies were identified irrespective of the study design and duration of the follow-up period. Randomized, double-blind, placebo-controlled trials found that schizophrenia patients receiving paliperidone (PP) showed a significant improvement in psychotic symptoms and similar adverse events compared to placebo and suggested that all doses of PP were efficacious and well tolerated. Other studies demonstrated noninferiority of PP compared to risperidone long-acting injectable in recently diagnosed schizophrenia patients, chronically ill patients, as well as in acute and nonacute symptomatic schizophrenia patients, and a similar proportion of treatment-emergent adverse events between both groups were also noted.

DRUG INTERACTIONS
INVEGA® should be used with caution in combination with other centrally acting drugs and alcohol. Paliperidone may antagonize the effect of levodopa and other dopamine agonists. Because of its potential for inducing orthostatic hypotension, an additive effect may be observed when INVEGA® is administered with other therapeutic agents that have this. Paliperidone is not expected to cause clinically important pharmacokinetic interactions with drugs that are metabolized by cytochrome P450 isozymes. Paliperidone is a weak inhibitor of P-glycoprotein (P-gp) at high concentrations.

Co-administration of a single dose of INVEGA® 12 mg with divalproex sodium extended-release tablets (two 500 mg tablets once daily) resulted in an increase of approximately 50% in the Cmax and AUC of paliperidone. Dosage reduction for INVEGA® should be considered when INVEGA® is co-administered with valproate after clinical assessment.

DOSING:

Adult Dosing/Indication	Schizoaffective disorder: **Oral:** Usual: 6 mg once daily (administered in the morning in clinical trials); titration not required, though some may benefit from lower or higher doses (range: 3 to 12 mg daily). If exceeding 6 mg daily, increases of 3 mg daily are recommended at intervals of more than 4 days, up to a maximum of 12 mg daily.

RECOMMENDED MONITORING:

- CBC with differential; frequently during the first few months of therapy in patients with a history of low WBC or drug-induced leukopenia or neutropenia
- Fasting blood glucose test; prior to treatment, at week 12, and annually in all patients; more frequently for patients with risk factors for diabetes mellitus; worsening of glucose control in patients with known diabetes mellitus
- Fasting lipid profile; prior to treatment, at week 12, and every 5 years thereafter
- Blood pressure; prior to treatment, at week 12, and annually thereafter throughout duration of treatment; more frequently in patients with risk factors for hypertension
- Waist circumference; prior to treatment and annually thereafter

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Contract/GPO Price
PALIPERIDONE 1.5MG ER TAB 30	$ 404.84
PALIPERIDONE 3MG ER TAB 30	$ 678.34
PALIPERIDONE 6MG ER TAB 30	$ 401.44
PALIPERIDONE 9MG ER TAB 30	$ 603.28

Note: Paliperidone is also available as an injectable formulation although this is not to be considered for inpatient formulary addition.

CONCLUSION & RECOMMENDATION:

Paliperidone is the major active metabolite of risperidone (Risperdal®). Based on this receptor activity, paliperidone has been found effective in decreasing both positive and negative symptoms of schizophrenia. Oral paliperidone is dosed once daily with similar efficacy as compared to twice a day oral risperidone. Because the threshold at which extrapyramidal symptoms (EPS) started was similar between the agents it is inferred that dosing is similar for these oral agents. Due to high cost and the fact that paliperidone is the active metabolite of risperidone, it is recommended that oral paliperidone not be added to the formulary.

The CHI MUE committee recommendation is to designate this as non-formulary for all non-acute psychiatric treatment centers or facilities with inpatient psychiatric units. Non-psychiatric inpatient facilities in CHI will address patients who are admitted with this as a maintenance home medication through their non-formulary medication procedures (e.g. seeking to have the patient use their home supply, or only obtaining this product when necessary for an individual patient on a case by case basis). Alternatively, the below therapeutic interchange may be used if deemed appropriate by local P&T committees.

SUGGESTED THERAPEUTIC INTERCHANGE			
Ordered		**Provided**	
Paliperidone (Invega®) ER PO	1.5mg daily	Risperidone (Risperdal®) PO	0.5mg bid
	3mg daily		1mg bid
	6mg daily		3mg bid
	9mg daily		4mg bid

Therapeutic Interchange

Relistor® (methylnaltrexone) and Movantik® (naloxegol)

Relistor® and Movantik® are FDA-approved for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, while Relistor® has the additional indication for OIC that is not responsive to laxative therapy. These medications antagonize peripheral Mu-opioid receptors with minimal central mu-opioid mediating effect, making them efficacious in treating opioid-induced constipation without affecting the analgesic effect of opioid medications. Relistor® is available as a subcutaneous injection and oral tablets, while Movantik® is only available as an oral tablet. CHI Memorial currently stocks both subcutaneous Relistor® and oral Movantik®.

Comparison of Relistor® and Movantik®

	Relistor® (methylnaltrexone)	**Movantik® (naloxegol)**
Time to peak concentration	30 minutes	<2 hours with secondary plasma peak 0.4-3 hrs after initial peak
Efficacy Onset	**% of patients with SBM within 4 hrs of first dose:** Study 1: Methylnaltrexone 12 mg daily - 33% (~50% of patients had SBM within 24 hours) Study 3: Methylnaltrexone 0.15 mg/kg – 62% Methylnaltrexone 0.3 mg/kg – 58% Study 4: Methylnaltrexone 0.15 mg/kg – 48%	**Median time to first SBM:** KODIAC-04: 25mg – 5.9 hrs 12.5 mg – 20.4 hrs KODIAC-05: 25 mg – 12 hrs 12.5 mg – 19.3 hrs
Adverse Effects	Abdominal Pain: 21-29% Nausea: 9-12% Diarrhea: 6% Flatulence: 13% Hyperhidrosis: 6% Dizziness: 7%	Abdominal Pain: 12-21% Diarrhea: 6-9% Nausea: 7-8% flatulence 3-6% vomiting 3-5%
Cost/dose	$92.84	$9.19

The absence of clinical studies between the products make it difficult to determine comparative efficacy, however; a similar tolerability and onset profile between the products may warrant therapeutic interchange on the basis of acquisition cost.

Retrospective Medication Use Evaluation of Subcutaneous Relistor®

Characteristic	**Number (%)**	
Prescribing Service	ED: 18 (36%) Hospitalist: 17 (34%) Oncology: 6 (12%) GI: 5 (10%) Surgery: 4 (8%)	
Patient taking and tolerating PO medications at time of subcutaneous Relistor® use:	Yes: 19 (38%)	58 total doses given
	No: 31 (62%)	43 total doses given

The relatively high amount of use in the ED may warrant discussion about on how to best ensure that patients are receiving Relistor® appropriately, and to determine if Movantik® would be an appropriate alternative. Relistor® 12 mg subcutaneous injections are currently stocked in the ED Pyxis, while Movantik® is not. It may be reasonable to stock Movantik® in the ED Pyxis to encourage PO use when able, and to remove Relistor® subcutaneous injections and have them dispensed from the main pharmacy when required for patient treatment.

Proposed Therapeutic Interchange

When you order this	**You will receive**
Methylnaltrexone (Relistor) 12 mg subcutaneously	Naloxegol (Movantik) 25 mg po same frequency
Methylnaltrexone (Relistor) 8 mg subcutaneously	Naloxegol (Movantik) 12.5 mg po same frequency
Methylnaltrexone (Relistor) weight based dosing (0.15 mg/kg) Weight based dose < 12 mg Weight based dose ≥ 12 mg	Naloxegol (Movantik) 12.5 mg po same frequency Naloxegol (Movantik) 25 mg po same frequency

**discontinue all maintenance laxative therapy prior to initiation of naloxegol

**adjust initial naloxegol dose for CrCl ≤60 ml/min to 12.5 mg daily, may increase to 25 mg if ineffective

**for use with concomitant moderate CYP3A4 inhibitors reduce dose to 12.5 mg daily (use with strong CYP3A4 inhibitors is contraindicated

Hypertonic Saline (3% NS) for Adults Policy - *Draft*

PURPOSE:

To outline the necessary requirements for the safe ordering, dispensing and administration of hypertonic saline solution (HTS), which is a concentrated electrolyte solution and a high risk medication.

POLICY:

Ordering Requirements and Restrictions

1.) Hyponatremia Treatment
HTS may be ordered by any prescriber for the treatment of symptomatic hyponatremia although any orders from providers other than nephrology or critical care must use the hospital approved "Hypertonic Saline (3% NS) IV Infusion Order – Hyponatremia Treatment" orders. All orders must have total volume/dose and/or duration in the order. All orders must comply with minimum requirements for laboratory monitoring.

2.) Acute Neurologic Indications
HTS for acute neurological indications other than hyponatremia treatment (increased intracranial pressure or other acute neurological deficits, etc.) may be ordered by neurology and administered without requiring the use of a hospital approved order set. However, mandatory laboratory monitoring still required as indicated below.

3.) Maximum infusion rates:
   a. Peripheral line: $\leq$ 30 ml/hr
   b. Central line: $\leq$ 50 ml/hr

4.) Maximum order volume:
   a. No more than 500 ml of HTS may be ordered for treatment of hyponatremia. If the ordered volume exceeds 500 ml, prescriber will be contacted after initial infusion of 500 ml for continuation order.
   b. HTS for acute neurologic indications may be ordered as a continuous infusion exceeding 500 ml if ordered by neurology provider. Mandatory laboratory monitoring still required for duration of infusion.

Laboratory and Patient Assessment Monitoring

1.) Required labs*:
   a. Baseline serum sodium required prior to treatment initiation
   b. BMP at least every 4 hours for duration of HTS infusion (if not already ordered). May be ordered more frequently at discretion of provider.

   ** If labs are not ordered by provider these may be ordered by pharmacy or nursing.*

2.) The infusion must be held and provider notified for the following conditions:

   Hyponatremia Treatment:
   a. Serum sodium increases by more than 2 mEq/L in any 4 hour period
   b. Serum sodium increases by more than 8 mEq/L during 24 hour period.
   c. Serum sodium $\geq$ 130

   Neurologic Indications:
   a. Serum sodium $\geq$ 155 mEq/L
   b. Serum osmolality > 320

3.) Nursing - patient assessment:
    a. Strict input and output every 4 hours
    b. Neurological checks Q 4 hours for duration of infusion

Storage and Dispensing

1.) Only pharmacy will stock pre-mixed HTS for intravenous use. Pharmacy will dispense the exact volume to be administered (transferred to an empty IV bag) and no more than a 500 ml premix bag at one time.

2.) Specific for hyponatremia indication: Further doses will only be sent after pharmacist review of sodium levels to prevent overly rapid correction (as outlined above).

Administration

1.) Administration via central line is preferred. If central line is not available, infusion via the largest peripheral vein available is acceptable for durations < 24 hours. If prolonged infusion is required, central line administration is highly recommended.

2.) HTS is a High Alert medication. An independent double check (documentation of 2nd nurse verification) is required and will be performed/documented during initiation of the infusion, for any rate change, shift change (verification of pump setting), and when any new bag is programmed for infusion.

Hypertonic Saline (3% NS) IV Infusion Orders – Hyponatremia Treatment

Required Labs:

1.) BMP Q 4 hours for duration of 3% NS infusion – if not already ordered by physician. If more frequent monitoring has been ordered by provider defer to provider orders.

Assessments:

1.) Strict input and output every 4 hours
2.) Neurological checks Q 2 hours for duration of infusion

Hold infusion and notify physician at any point during infusion if:

1.) Rate of serum sodium change per hour exceeds 2 mEq/L in 4 hours
2.) Serum sodium increases by more than 8 mEq/L during 24 hours
3.) Serum sodium $\geq$ 130 mEq/L

Administration:

1.) Central line is preferred for administration but if not available, a large peripheral vein is needed for the administration of 3% NS.

□ **Slow, IV infusion:**
preferred for chronic (> 48 hr onset) severe hyponatremia with symptoms (Na+ < 120) or asymptomatic acute (onset w/i 24 hrs) hyponatremia (Na+ < 120); consider nephrology consult for acute hyponatremia or hyponatremia with severe neurological symptoms (onset w/i 24 hours)

3% NS to infuse IV at _____ ml/hr for _____ hours for a total volume of _____ ml.*
Discontinue infusion when Sodium reaches target of _____ mEq/L.

- *Maximum rate of administration:*
  - *Peripheral line: 30 ml/hr*
  - *Central line: 50 ml/hr*
- *Maximum volume:*
  - *May not exceed 500 ml unless indication is management of acute ICP secondary to acute neurological abnormality.*
  - *For treatment of hyponatremia: if ordered volume exceeds 500 ml, prescriber will be contacted after initial infusion of 500 ml for continuation order.*

DATE/TIME ORDERED

PRE-OPERATIVE ANESTHESIA ORDERS FOR ADULT PATIENTS

PRE-MEDICATION ORDERS:

1. The following medications should be held for the time period indicated:
    a. MAOI inhibitors
        i. **Selegiline, pargyline, phenelzine, procarbazine, rasagiline, tranylcypromine** - Anesthesia should be alerted to any patient taking these medications due to interactions with ephedrine and other sympathomimetic medications.

    b. Anti-hypertensives
        i. **ACE inhibitors/angiotensin receptor blockers** should be held for 24 hours prior to surgery.

    c. Antihyperlipidemics
        i. **Bile acid resins (cholestyramine, colestipol), gemfibrozil, fenofibrate, niacin, and ezetimibe** should be held the day of surgery.

    d. Antibiotics
        i. **Linezolid** - Anesthesia should be alerted to any patient taking these medications due to interactions with ephedrine and other sympathomimetic medications (MAOI inhibitor).

    e. Anti-coagulants
        i. **Coumadin, Lovenox, Pradaxa, Xarelto, Savaysa, and Eliquis** must be stopped by the ordering physician*.
        See *Antithrombotic Reversal & Surgical Management Recommendations* for specific guidance on these medications.

    f. Anti-platelets
        i. **Aspirin** should be stopped 5 days prior to procedure **unless** ordered by physician, then check with ordering physician. Aspirirn should not be stopped if ordered for patients at high risk of CV events (cardiac stents, cerebrovascular disease, etc.) without consent of ordering physician.
            1. Heart surgery/CABG: May continue Aspirin up to 162 mg until day of surgery.
        ii. **Effient, Plavix, and Brilinta** must be stopped by ordering physician
        iii. **Aggrenox (dipyridamonle/aspirin)** should be stopped 7 days prior to surgery if ok with prescribing physician
        iv. **Cilostazol** should be stopped 5 days prior to surgery

    g. Diabetic Agents - SEE BELOW "Diabetes Medications" section

    h. Diuretics
        i. **Diuretics (furosemide, bumetanide, torsemide, HCTZ, etc.)** should be held the day of surgery. Anti-hypertensive combinations containing HCTZ may be continued EXCEPT those combined with ACE/ARBs.

    i. Gout medications
        i. **Allopurinol, colchicine** - should be held the day of surgery

    j. Herbal supplements
        i. **Herbals** should be for 2 weeks prior to surgery

DATE/TIME ORDERED

PRE-OPERATIVE ANESTHESIA ORDERS FOR ADULT PATIENTS

k. Hormone replacement therapy (post-menopausal)
   i. Consult ordering physician

l. NSAIDS
   i. **NSAIDs** should all be held for 5 days prior to surgery

m. Respiratory medications
   i. **Theophylline** should be held the evening prior to and the morning of surgery.
   ii. All inhaled respiratory medications may be taken and patient should be instructed to bring inhalers to hospital on admission.

n. Rheumatoid arthritis medications
   i. **Methotrexate, infliximab, etanercept, adalimumab, certolizumab, rituximab, tocilizumab, etc.** - consult patient's rheumatologist

o. Weight-loss agents
   i. **Phentermine-containing drugs** should be held for 2 weeks prior to elective surgery. If unable to hold, consult Anesthesia.
   ii. **HCG** should be held 10 days prior to procedure.
   iii. Stop 500 calorie diet 48 hours prior to procedure.

2. Diabetes Medications

PATIENTS ON ORAL/NON-INSULIN INJECTABLE DIABETES MEDICATIONS

a. Hold all **Metformin/Metormin containing drugs** day of procedure; resume 48 hours following procedure

b. Hold **oral diabetes medications** the morning of surgery; these may be continued the day before surgery (except Metformin as noted above).

c. **Bydureon, Byetta, Tanzeum, Trulicity, Victoza** - continue usual oral/non-insulin injectable diabetes meds the day before surgery and hold the morning of surgery.

PATIENTS ON DAILY INSULIN INJECTIONS

Day Prior to Surgery

a. **Regular, Novolog, Humalog, Apidra** - meal doses and **pre-mixed insulin 70/30, 75/25** - administer as usual

b. **Basal insulin (Levemir, Lantus, Toujeo, Tresiba, Basaglar)** - administer AM and PM dose as usual

c. **NPH or U-500** - AM and meal doses as usual; bedtime administer 1/2 dose

Day of Surgery

a. **Regular, Novolog, Humalog, Apidra (meal doses)** - hold dose

b. **Basal insulin (Levemir, Lantus, Toujeo, Tresiba, Basaglar)** - administer 1/2 of usual dose

c. AM doses of **Mixed insulin (70/30, 75/25)** - administer 1/2 of usual dose

WEIGHT:
HEIGHT:

DATE/TIME ORDERED

PRE-OPERATIVE ANESTHESIA ORDERS FOR ADULT PATIENTS

d. AM doses of **NPH** - administer 1/2 of usual dose

e. AM doses of **U-500** - hold dose (unless administering via insulin pump)

f. **Sliding scale/correction insulin** - administer as usual, hold if BG < 150

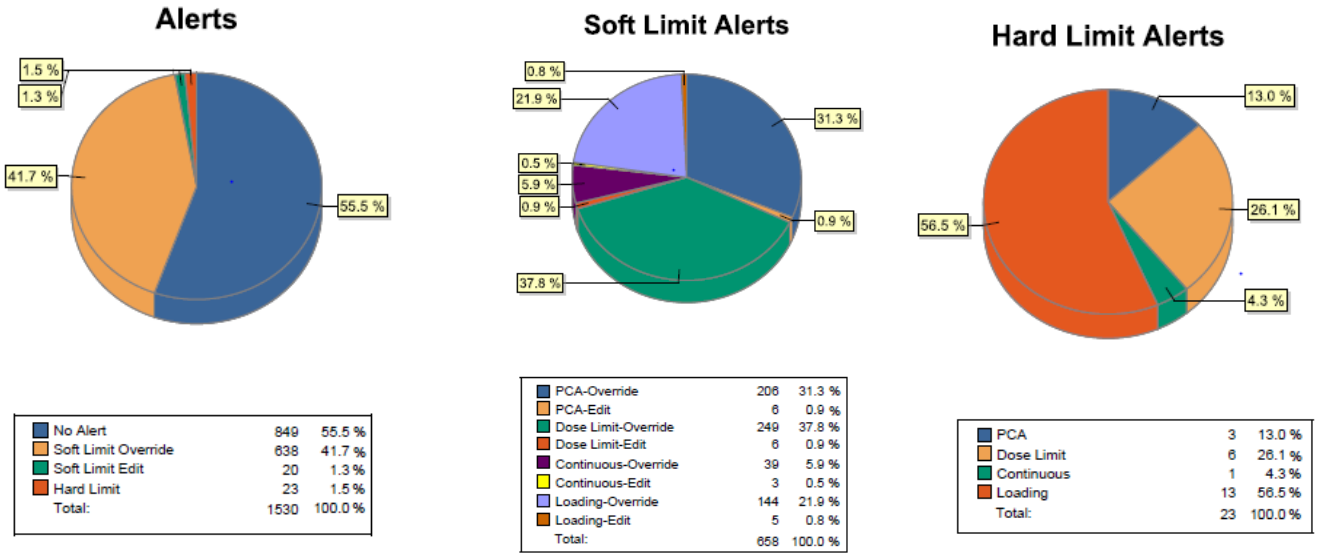
PATIENTS ON INSULIN PUMPS
Insulin pumps should be turned on unless other orders from anesthesiologist.

AFTERNOON CASES
Patient to check blood glucose prior to hospital arrival; if < 70 patient should drink 4 oz of sugar-containing clear liquid (apple juice, sprite). Patient should notify hospital staff upon arrival of hypoglycemia episode/treatment. Blood glucose to be checked upon arrival to pre-op. If BG < 70 treat as above and re-check in 15 minutes and re-treat if needed.

Patient Controlled Analgesia (PCA)
Smart Pump – Standard Settings

Background:
A recent patient safety event due to a programming error (incorrect hydromorphone continuous rate) prompted a review of the existing soft and hard limits for morphine and hydromorphone PCAs.

PCA Alert Review (Oct 2016 – Jan 2016):
A review of the PCA alerts revealed a significant number of alerts that would prompt the nurse to review the programmed settings prior to proceeding with final programming. The high number of alerts is likely contributing to alert fatigue and rendering these alerts not as useful as they could be in preventing significant programming errors. In total, 45% of all attempted programmed settings triggered a soft or hard limit alert with 95% of the total alerts related to hydromorphone.



Review of Existing Alert Settings (non-hospice PCA settings):
The review of the various alert triggers revealed that the bulk of all the programming alerts were related to hydromorphone PCAs. Most notably it was discovered that the current upper soft limits for PCA dose (n=187), loading dose (n=140), dose limit (n=250), and continuous rate (n=31). The triggering of the upper hard limits were much more rare for both medications (morphine=1, hydromorphone=7) although keeping these limits at logical values is imperative in order to prevent significant programming errors (0.2 vs 2 mg, etc.).

Proposed Modifications: (previous settings highlighted yellow in parentheses)

Hydromorphone	USL (mg)	UHL (mg)	Morphine	USL (mg)	UHL (mg)
PCA dose	0.5 (0.2)	1	PCA dose	2 (1.2)	5
Continuous	0.5 (0.4)	1.9 (3)	Continuous	4 (2)	20
Dose Limit	2.5 (1.2)	3.7 (7)	Dose Limit	10	20
Loading dose	1 (0.4)	2	Loading dose	4 (2)	10

Commonly utilized physician standing orders (PCA Standard Infuser, orthopedic order sets, etc.) were reviewed in order to help devise the above proposed revisions. The upper soft limits (USLs) were designed so that these more commonly utilized settings would not routinely trigger soft limit alerts and decrease the potential for "alert fatigue". This should allow the upper soft limits to be better utilized to alert nursing of potential programming errors. In addition, the upper hard limits (UHLs) were lowered in order to better align with reasonable dosing ranges for opioid tolerant patients. Dosing exceeding these limits should be reevaluated or programmed using the "hospice" PCA dictionary when applicable.

PPI (pantoprazole) Medication Use Evaluation
CHI Memorial & CHI Memorial Hixson

The purpose of this evaluation was to reexamine usage of pantoprazole hospital-wide after the changes made in spring 2016. Using the same criteria as the medication use evaluation that led to the removal of acid suppression therapy from admission order sets, this review assessed drug usage rates since the changes were implemented.

Background:

Stress ulcer prophylaxis (SUP) has become a routine medical practice among healthcare practitioners. Up until the last 10 years, it was thought that utilization of Proton Pump Inhibitors (PPIs) were relatively benign. Studies have shown that up to 73% of patients in the hospital under general medicine care are on acid suppression therapy without an appropriate indication. In 2009 Heidelbaugh, et al published a systematic review[1] detailing the major complications associated with PPI usage. PPIs have been shown to contribute to pneumonia, *Clostridium difficile* associated diarrhea, and osteoporosis. Another literature review[2] in 2013 also details the risks associated with PPI overuse. As a result of these findings, a medication use evaluation was conducted to determine pantoprazole usage trends at Memorial Hospital.

With an increase in gastric acid pH, more aerobic bacteria are able to grow. Many patients in the hospital are considered high risk for aspiration. Aspiration and even microaspiration events can lead to pulmonary colonization with potential to cause pneumonia. Three meta-analyses show an increased risk of pneumonia, both CAP and HAP, with long- and short-term (<30 days) use of PPIs. A case-control study also showed increased risk of CAP in patients currently on PPI therapy and those on short-term (1-15 days) therapy.

Along similar lines, an increase in gastric pH can lead to less inhibition of enteric bacteria, such as *Clostridium difficile*, allowing for clinically significant *C. diff* - associated diarrhea. A meta-analysis of 30 trials showed PPIs were associated with increased risk of *C. diff* infection regardless of antibiotic use ($p < 0.00001$). The risk was also higher even if the patient was on an H_2RA, daily PPI, or a dose larger than daily.

Acid suppression can lead to decreased calcium absorption, due to the needed acidic environment for ionization and absorption of calcium. Decreased calcium can lead to increased parathyroid hormone, which causes increased production of osteoclasts for bone resorption. With prolonged use and higher dosage of PPIs, increased risk of bone fracture can occur. While this may not be considered an acute problem, many patients started on PPI therapy as inpatient are continued indefinitely as outpatients. A randomized, double-blind, placebo-controlled crossover trial with omeprazole demonstrated a significantly decreased rate of calcium absorption from 9.1% to 3.5% after 7 days of therapy. After 6-12 months or longer on PPI therapy, a retrospective study found an association of osteoporosis medication prescribing and PPI usage. The FDA has issued a warning about risk of developing fractures on PPIs.

Other small studies and case reports have also shown an association with hypomagnesemia, Vitamin B12 deficiency, and rare incidence of rhabdomyolysis with long-term PPI use.

A recent medication use evaluation done at CHI-Memorial Glenwood and CHI-Memorial Hixson during October 2015 demonstrated that a large percentage of acid suppression therapy in both floor and ICU patients was inappropriate (80% Floor, 44% ICU). As a result, acid suppression therapy was removed from the hospitalist admission order sets. This review will evaluate appropriateness of use for acid suppression therapy across the months of July, August and September 2016 to determine if appropriate usage has improved since the changes were implemented.

Data Analysis/Methods:

A random sample of patients given pantoprazole and/or famotidine at CHI-Memorial Glenwood and CHI-Memorial Hixson during July-September 2016 were collected. Patients were excluded if they were on home acid suppression therapy, if they had a GI bleed at or during admission, or if they were diagnosed with and treated for GERD. Patients were then separated based on ICU or floor status when the H2RA or PPI was initiated.

The ASHP Guidelines for Stress Ulcer Prophylaxis from 1999 were used to determine if ICU stress ulcer prophylaxis was initiated appropriately. Patients with one of the following risk factors were considered appropriately treated: mechanical ventilation > 48 hours, history of GI ulceration or bleeding within the past year, coagulopathy (Plt < 50, INR > 1.5 , PTT > 2x control), traumatic brain, spinal cord or burn injury (burns > 35 % BSA), sepsis.

Table 1: Floor Patient Risk Factors	
Age > 60	2
Male	2
Acute Renal Failure	2
Liver disease	2
Sepsis	2
Prophylactic anticoagulation	2
Coagulopathy	3
Medicine Service	3

Table 2. Percent Bleeding and NNT per Risk Group		
Risk Group	Percent with Bleeding	NNT
Low risk (≤ 7 points)	0.10	> 1000*
Without prophylaxis	0.04	
With prophylaxis	0.16	
Low-Medium risk (8-9 points)	0.54	556
Without prophylaxis	0.67	
With prophylaxis	0.49	
High-medium risk (10-11 points)	0.68	159
Without prophylaxis	1.16	
With prophylaxis	0.53	
High risk (≥ 12 points)	1.47	48
Without prophylaxis	3.24	
With prophylaxis	1.14	

*Estimated NNT based on the results of the Low Risk group and confounding by indication.

Floor patient charts were assessed for gastrointestinal bleeding risk based on the SURGIB risk criteria recently published in Hong et al. and Herzig et al. Hong et al. was a cohort study that evaluated patients with nosocomial gastrointestinal bleeding. These patients were reviewed in order to establish a set of criteria to determine need/appropriateness of stress ulcer prophylaxis. The investigators evaluated and compiled characteristics that made patients more susceptible to gastrointestinal bleeding and established scoring criteria and risk categories (Table 1). They then determined the percentage of patients likely to bleed within each risk category and the number needed to treat (NNT) (Table 2). We utilized this scoring system in our evaluation of pantoprazole usage at CHI-Memorial. Scores < 10 were considered inappropriate and further analyzed. Other data points collected included ordering physician and length of stay.

Results:

Table 3. Usage of PPI in the ICU and on the floor		
ICU		**Percentage of Evaluated Patients**
Total Patients	85	
Appropriate*	38	78%
Inappropriate	11	22%
Excluded	36	
Floor		
Total Patients	691	
Appropriate**	30	27%
Inappropriate	80	73%
Excluded	581	

*Appropriateness in the ICU is based on the 1999 ASHP SUP Guidelines. If the patient meets any one of the following, PPI is considered appropriate: Mechanical ventilation > 48hrs, history of GI ulceration in past year, coagulopathy, trauma, sepsis, ICU LOS > 1 week, or occult GI bleed ≥ 6 days.
** Scores > 10 were considered to be at an increased risk for gastrointestinal bleed and PPI use was determined to be appropriate.
***Exclusion Criteria: patients with a PPI home medication, GI bleed or GERD

Table 4. Percentage of PPI ordered by physician specialty	
ICU	
Hospitalist	45%
Intensivists/Pulmonologists	35%
Surgery (Cardiovascular & General)	10%
Other	10%
Floor	
Hospitalist	74%
Surgery (Cardiovascular, Ortho & General)	9%
GI/GE	7%
Nephrology/Urology	4%
All other disciplines	<2%

Summary & Conclusion:

ICU

ICU PPI use was improved significantly since previous analysis, with 77.6% of patients evaluated determined to be appropriate. It would be prudent to note that over half of inappropriate PPI usage was ordered by a general medicine physician (55%) prior to transfer to the ICU. As ICU PPI use has improved with limited intervention thus far, it is reasonable that any future interventions should likely focus more on floor patients.

Floor

As shown above, only 27% of all floor patients evaluated were initiated on SUP appropriately. This represents no significant change since the last MUE, which demonstrated 30% appropriate use. The majority of patients were initiated on PPI upon admission

via handwritten orders added to admission order sets; SUP prophylaxis options were removed from admission order sets as a result of the last MUE. Using the scoring system, the most common risk factors leading to initiation of PPI were age > 60, prophylactic anticoagulation, and the general medicine service. The median score for risk of stress ulcer bleeding was 7. According to Table 2, patients with a score ≤ 7 were associated with a negligent risk for bleeding. The hospital as a whole would need to treat over 1000 patients in this risk category in order to prevent 1 patient from developing a GI bleed. When considering this number needed to treat and overall cost per dose of acid-suppression drugs, if SUP is utilized appropriately, the hospital could see significant cost savings with little resultant risk of harm.

In light of data regarding SUP usage -- which did not change after removal of acid suppression therapy from admission order sets -- it is difficult to determine an appropriate intervention. While pharmacy is capable of evaluating the appropriateness for patients already on PPI and discontinuing per approved protocols, more proactive measures should be taken to avoid PPI use altogether to prevent short- and long-term complications as described earlier. Education of SUP indications and risks of PPI use should be initiated to prevent further overuse. With proper education, PPI use should decrease and lead to an added cost savings per month.

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Ricky Shane Church, Pharm.D.
Residency Research Project
Pharmacy & Therapeutics Meeting – Meeting Summary
April 13, 2017

Total Population

Type of Inpatient Management	Percentage of Patients	# of Patients
BBI	16.04%	34
BPI	25.00%	53
None	4.72%	10
PO + Insulin	18.87%	40
SSI	34.43%	73
SSI + 70/30	0.94%	2
Total	**100.00%**	**212**

- Overall, 212 patients and their inpatient glycemic management strategies were evaluated
  - Most patients (34.43%) were managed with sliding scale insulin (SSI)
  - Other popular management strategies were basal-bolus insulin (BBI) and basal-plus insulin (BPI)

Inpatient Management Strategy	Average of A1c (%)	Average Blood Glucose (mg/dL)
BBI	10.0	191.4
BPI	8.3	176.2
None	6.3	119.3
PO	N/A	134.9
PO + Insulin	8.0	160.9
SSI	6.6	147.3
SSI + 70/30	9.1	196.3
Total	**8.0**	**164.7**

- Patients managed by SSI, along with patients not requiring treatment, boasted the lowest A1C values (6.6 and 6.3, respectfully)
- Patients not receiving therapy, those managed with PO medications, and patients controlled with SSI also demonstrated the lowest average blood glucose levels (119.3, 134.9, and 147.3 respectfully)
- The average blood glucose for all patients could be skewed by those managed with PO and SSI regimens
- A1c values were obtained from 138 out of 213 patients (64.8%)

Inpatient Management Strategy	Average BG Checks > 140 (%)	Average BG Checks > 180 (%)	Average BG Checks > 250 (%)	Average BG Checks < 40 (%)	Average BG Checks < 70 (%)
BBI	72.9%	51.4%	24.5%	0.7%	4.8%
BPI	69.4%	43.1%	17.6%	0.2%	5.5%
None	66.7%	-	-	-	-
PO	31.6%	15.8%	-	-	-
PO + Insulin	63.3%	32.8%	21.2%	0.3%	3.7%
SSI	49.6%	28.4%	13.9%	0.0%	2.3%
SSI + 70/30	91.6%	66.4%	12.9%	0.0%	0.0%
Total	**61.9%**	**38.4%**	**19.3%**	**0.3%**	**4.0%**

- 38.4% of all blood glucose values recorded are above the recommended target of 180 mg/dL
- Hypoglycemia rates are approximately 4% for all patients screened

Insulin Dependent (ID) Patients

Inpatient Glycemic Management Strategy	Number of ID Patients	Percentage of ID Patients	Average A1c (%)	Average Blood Glucose (mg/dL)
BBI	30	29%	10.0	**192.2**
BPI	45	44%	7.9	**174.8**
PO + Insulin	15	15%	9.4	172.8
SSI	11	11%	7.8	166.3
SSI + 70/30	2	2%	9.1	196.3
Total	**103**	**100%**	**8.8**	**179.1**

- ID patients that were admitted during the study period appear to be improperly controlled by their respective outpatient regimens
    - This is evidenced by an average A1c of 8.8% for all 103 ID patients
- Most ID patients were managed via BBI or BPI regimens, with those two groups demonstrating the highest average blood glucoses with the exception of 2 patients using 70/30 insulin

Home Regimen Continued	Average 1st BG Reading (mg/dL)	Average Initial Basal Insulin Dose (unit/kg)	Number of Patients	Average Blood Glucose (mg/dL)
No	234	0.27	27	201.9
Yes	210	0.40	71	171.7
Total	**216.67**	**0.36**	**98**	**180.0**

- Patients experiencing modifications in therapy upon admission presented with higher initial average BG values compared to those who were continued on their home regimens
    - These patients also experienced higher average BG values as compared to their counterparts

Home Regimen Continued	Average Outpatient Basal Insulin Dose (units/day)	Average of Initial Basal Insulin Dose (units/day)
No	50.4	23.1
Yes	42.8	42.2
Total	**44.6**	**36.9**

- Of all ID patients, approximately 26% of patients experienced a change in their outpatient insulin regimens once hospitalized
    - These patients experienced average BG values > 200 mg/dL
    - Initial basal insulin doses for those experiencing a modification in therapy were decreased by approximately 50% upon admission
- Approximately 69% were continued on their home regimens upon admission
- Specific outpatient data was not available for the remaining 5 patients.

WEIGHT:
HEIGHT:

DATE/TIME ORDERED

IV IRON REPLACEMENT - INPATIENT PROTOCOL

Medication (CHECK ONE):

☐ Iron Dextran (InFed) - pharmacy to calculate dose using formula below (single dose replacement).

1. Total dose in ml = [0.0442 x (desired Hb - observed Hb) x LBW] + (0.26 x LBW)
   - Maximum total dose of 1500 mg
   - InFed concentration = 50mg/ml
   - Use actual body weight if < lean body weight (LBW)
   - Desired Hb = 14.8 unless otherwise specified by physician
2. Give test dose = 25 mg (0.5 ml)
   - Monitor patient for 1 hour for s/s of infusion/anaphylactic reaction
   - If an allergic reaction occurs, initiate the Allergic Reactions/ Anaphylaxis Orders (PSO#2039)
3. Once test dose completed, give remaining amount as infusion over 4-6 hours

☐ Sodium Ferric Gluconate (Nulecit) - pharmacy to calculate dose using formula below (multiple dose replacement)

1. Total dose in mg = total body weight (kg) x(15 - current Hb) x 2.4 + 500
   - Maximum total dose of 1500 mg
   - Use adjusted body weight (kg) for patients with BMI > 25
   - Round total dose to the closest 250 mg
   - Divide rounded total dose by 250 mg to calculate number of doses needed
   - Order will read: Give 250 mg in 100 ml NS over 2 hours every 12 hours x _____ doses until total dose completed or patient discharged

Physician Signature:_____ Date:_____ Time:_____

TOBACCO CESSATION
REVIEW OF CURRENT PROTOCOL & LITERATURE REVIEW

Summary of Evidence

Evidence-based, randomized controlled trials exploring strategies for tobacco cessation are lacking in current medical literature. The most recent resource for tobacco cessation management is provided through the United States Public Health Service (USPHS) Guideline for Treating Tobacco Use and Dependence in 2008. This report details a few points that are not currently being addressed with our hospital's Nicotine Replacement Therapy Protocol, and in light of recently published CMS Core Measures pertaining to this issue, a review of current practices was warranted. Note: the CMS core measure for nicotine replacement was recently suspended although it is unclear if th

USPHS guidelines recommend the use of combination nicotine replacement therapy (NRT) as a means of providing symptomatic and baseline control for patients accustomed to smoking. If NRT is selected for treatment, a combination therapy of nicotine patches and short-acting NRT is usually preferred over monotherapy with a short-acting NRT product. Short-acting NRT is best used for the acute management of nicotine withdrawal symptoms and cravings in combination with longer-acting medications such as patches, bupropion, or varenicline. This technique is similar to strategies employed with insulin therapy in diabetics, with a need for both basal and bolus insulin. These guidelines also recommend a dosing strategy for NRT based on the amount of tobacco used by the patient over a set period of time, as summarized in the table below.

Tobacco Product	Recommended Therapy
<20 cigarettes/day <1 can/pouch smokeless tobacco/week	14 mg patch Lozenge/gum, 1 piece q1h prn
20-30 cigarettes/day 1 can/pouch smokeless tobacco/week	21 mg patch Lozenge/gum, 1 piece q1h prn
30-40 cigarettes/day 2 cans/pouches smokeless tobacco/week	35 mg patch (14 mg + 21 mg) Lozenge/gum, 1 piece q1h prn
>40 cigarettes/day ≥3 cans/pouches smokeless tobacco/week	42 mg patch (21 mg + 21 mg) Lozenge/gum, 1 piece q1h prn

While higher dose, multiple-patch strategies may be efficacious for highly dependent tobacco users, USPHS guidelines do not routinely recommend that strategy for most patients, unless they are very highly reliant on tobacco. Furthermore, the guideline evaluated the potential for increased cardiovascular risk among patients with high-dose NRT, and found that no additional risk was associated with the high-dose strategy above what a smoker/smokeless tobacco user had already incurred. Treatment should be evaluated and assessed on a patient-specific level, based on their response to NRT and their withdrawal symptoms.

Discussion

The current NRT replacement protocol allows the prescriber to select either a 21 mg patch, a 14 mg patch, or a piece of Nicorette® gum q1h prn withdrawal symptoms. It is clear that our NRT protocol does not meet or follow the USPHS guidelines from 2008, and could serve to be updated in conjunction with new CMS Core Measures targeting this issue. While a multi-patch strategy could offer benefit to highly dependent users, it also offers a host of challenges, including the patient having multiple patches and the risk of not removing them/replacing them both correctly.
An alternative option may be to update the verbiage and selection options for our current protocol. A proposed update is found in the figure below – notable changes include the number of cigarettes/day cutoff and the addition of smokeless tobacco, as well as an automatic order for gum to be used for cravings.

Recommended Nicotine Replacement:

- <20 cigarettes/day or <1 can/pouch per week
  - 14 mg patch
- >20 cigarettes/day or ≥1 can/pouch per week
  - 21 mg patch

Withdrawal Symptoms and Cravings:

- Nicotine (Nicorette) gum
  - 4 mg (1 piece) every 1 hour prn withdrawal symptoms or cravings
    - Chew until tingling sensation, then place between cheek and gum
    - Repeat every 5 minutes until tingle does not return
    - Maximum = 24 pieces/24 hours

A potential barrier to continued tobacco abstinence is the cost of NRT for patients. Most commercial insurances will not pay for NRT, leaving the cost of these products to be paid by the patient exclusively.

NRT Product	Approximate Cost
Brand transdermal patch (14 count)	$40-45/box $80-90/month
Generic transdermal patch (14 count)	$25-30/box $50-60/month
Brand gum/lozenges (20 pieces)	$7-12/box Cost/month dependent upon use
Generic gum/lozenges (20 pieces)	$10-18/box Cost/month dependent upon use

As a point of reference, the average cost of a pack of cigarettes in Tennessee is $5.30, while a can/pouch range between $3-5 each according to Fair Trade Reports. While the cost of the NRT products is relatively expensive, a person who smokes 20 cigarettes (1 pack per day) will pay approximately $160/month in cigarettes.

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