Pharmacy News

UNIVERSITY HOSPITAL
Newark, New Jersey

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Special Points of Interest:

- P&T Update-Formulary Additions/ Deletions
- Policy and Procedures Update
- Dr. Helen Horng – Board Certified Critical Care Pharmacists (BCCCP®)
- 340B Drug Pricing Program Overview
- Lactational Pharmacology at University Hospital
- Formulary transactions approved by the P&T committee from January 2016 to December 2017

P&T Update

Formulary Additions

- **Ocrelizumab (Ocrevus®)- Formulary addition approved.**
  Ocrelizumab is a humanized anti CD20 monoclonal antibody indicated for the treatment of adults with primary progressive or relapsing multiple sclerosis (MS). The formulary addition was approved with the following criterion:

  The medication must be approved by the patient's insurance in advance (prior authorization) and supplied to the inpatient hospital pharmacy through the patient's outpatient/specialty pharmacy.

- **Naltrexone (Vivitrol®) 380mg IM monthly Formulary addition approved** – It is an opioid antagonist with highest mu receptor affinity. The formulary addition was approved with the following restriction criterion:

  Prescribing will be restricted to the Psychiatry division attending physicians and physicians credentialed in addiction medicine.

- **Edaravone (Radicava®)-Formulary addition approved**
  Edaravone is indicated for the treatment of amyotrophic lateral sclerosis (ALS). It is the second FDA approved agent for ALS. The formulary addition was approved with the following restriction criterion:

  The medication must be approved by the patient's insurance in advance (prior authorization) and a 6 month audit of use and safety analysis be performed and reported to the P&T committee.

Formulary Deletions

- Chloroquine - Formulary deletion approved
- Quinupristin/dalfopristin - Formulary deletion approved
- Neomycin/polymyxin 1mL ampules - Formulary deletion approved
- Amiodarone 150mg/100ml (Nexterone®) in dextrose premixed infusion bags - Formulary deletion approved
- Bethanechol - Formulary deletion approved
- Pencillamine - Formulary deletion approved
  Podophyllum Resin- Formulary deletion approved
- Lecithin- Formulary deletion approved
- Peginterferon Alfa-2a (Pegasys), Interferon Alfa-2b (Intron A®), Interferon Gamma 1b (Actimmune®), Peginterferon Alfa-2b (PegIntron®) – Formulary deletion approved
- Indigo Carmine - Formulary deletion approved
- Mivacurium - Formulary deletion approved
- Acebutolol 200mg tablet - Formulary deletion approved

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P&T Updates

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- Didanosine all strengths deletion approved
- Stavudine all strengths deletion approved
- Fosamprenavir all strengths deletion approved
- Nelfinavir all strengths deletion approved
- Saquinavir all strengths deletion approved

Line of Extension Approvals

- Etonogestrel (Nexplanon®) Implant - Line extension approved. Extended formulary approval for the outpatient/ambulatory clinic use. The medication was earlier approved for inpatient use restricted to ordering by OB attending physician. To be procured by the OB department from a grant funding for inpatient use
- Levonorgestrel Intrauterine Device (Liletta® IUD) - Line extension approved. Extended formulary approval for the outpatient/ambulatory clinic use. The medication was earlier approved for inpatient use restricted to ordering by OB attending physician. To be procured by the OB department from a grant funding for inpatient use
- Copper Intrauterine Device (Paragard T® IUD)- Line extension approved. Extended formulary approval for the outpatient/ambulatory clinic use. The medication was earlier approved for inpatient use restricted to ordering by OB attending physician. To be procured by the OB department from a grant funding for inpatient use
- Potassium Chloride Oral Powder - Line extension approved. The powder packet formulation will replace (except for pediatrics or doses outside of 20meq or 40meq) the commercially available oral liquid formulation to realize significant cost savings.
- Amiodarone 360mg/200ml (Nexterone®) in dextrose premixed infusion bags- Line extension approved
- Phytonadione tablet deletion & extemporaneous prepared oral liquid from the injectable formulation – Formulary line extension of oral liquid formulation and tablet deletion approved

Sample request addition

- ACC F level: Basaglar Kwikpen (Insulin Glargine 100units/ml) – approved

Policies & Procedure/Floor stocks Updated

- 707-500-115 Standard Concentrations for Intravenous (IV) Infusion Medications (Adults and Pediatrics) Update – approved
- 707-600-103 Automatic Stop Order Policy updated An update on the policy to change the default stop order time of calcitonin injection to 24 hours in epic was presented – approved
- 707-400-108 Resuscitation Equipment Checks & Exchanges ED trauma trays content has been revised Furosemide, albuterol, nicardipine, nitroglycerin SL, and flumazenil were removed. Additional supplies of epinephrine and sodium bicarbonate were added along with naloxone 2mg (in addition to 0.4mg) and magnesium sulfate.
- Acetaminophen IV (Ofirmev®) – Restriction criterion modification. The updated criterion includes unrestricting IV acetaminophen for 24hrs and any subsequent order requires anesthesia approval
- Care of malignant hyperthermia patients policy update- The existing policies from the PCS and Pharmacy division were combined.

Dr. Helen Horng
Board Certified Critical Care Pharmacists (BCCCP®)

Board of Pharmacy Specialty (BPS) currently recognizes eight clinical specialties: pharmacotherapy, oncology, nuclear, ambulatory, nutrition support, psychiatric, pediatric and critical care. Future specialties to be developed include cardiology, infectious disease, geriatric, and emergency medicine.

Critical care pharmacists have been integral members of interprofessional critical care teams for decades, working to ensure safe and effective use of pharmacotherapy in critical care patients. Board certification validates pharmacist has advanced knowledge and experience to optimize patient outcomes in these settings. There are currently over 1,600 Board Certified Critical Care Pharmacists across the United States.

BCCCP ensures certified critical care pharmacists has the skill set to quickly assess clinical data and deliver direct patient care to critically ill and injured patients who may require specialized pharmacologic or technologic interventions. These life-saving interventions may be required to stabilize blood pressure, respiration, nutritional and other homeostatic functions while simultaneously treating the patient's primary condition. This involves frequent analysis, review and reassessment of clinical and technological data to help the healthcare team make efficient decisions for patients with life-threatening conditions and complex medication regimens who's pharmacokinetic and pharmacodynamics parameters vary substantially from non-critically ill patients.

Congratulations to Dr. Horng for receiving Board Certification in Critical Care Pharmacy Specialty.

References:

- *Board of Pharmacy Specialties* (BPS®) Critical Care Pharmacy (2017)

The use of Ketamine to reduce opioids demand for opioids- tolerant patients

Treating acute pain in patients who chronically use opioids can be challenging. The goal of therapy for these patients is to prevent withdrawal, to provide adequate analgesia, and, for patients with a history of a substance use disorder, to avoid triggering a relapse or worsening of the addiction disorder. In patients requiring high-dose opioids and in the presence of opioid hyperalgesia, ketamine has played a significant role in perioperative pain management. The role of subanaesthetic doses of ketamine in the prevention of opioid tolerance in perioperative patients can make an impact on total analgesic requirements, and studies have also shown a significant reduction in opioid consumption in the first 24 hours without an increase in adverse effects when used as an adjunct. Ketamine is used in combination with opioids to optimize pain control in opioids dependent patients. Using ketamine and opioids together have a synergistic analgesic effect, while lowering their side effects. Ketamine's predominant effect is NMDA receptor antagonism by binding noncompetitively to the phencyclidine binding site of NMDA receptors and modifying receptors via allosteric mechanisms.

Ketamine is a sedative hypnotic used to provide anesthesia that was developed in 1962. It acts on receptors in the cortex and limbic system by non-competitively blocking the N-methyl-D-aspartate (NMDA) receptors. The activity on NMDA receptors may be responsible for the analgesic and the psychiatric effects of ketamine. The NMDA-glutamate receptor is a calcium channel closely involved in the development of central sensitization of dorsal horn neurons, which transmit pain signals. At normal resting membrane potentials, the channel is inactive and blocked by magnesium. When the resting membrane potential is changed as a result of prolonged excitation, the channel unblocks and calcium moves into the cell. This results in neuronal hyperexcitability in the spinal cord and consequently a reduction in Opioid-responsiveness, hyperalgesia and allodynia. Therefore, it can evoke chronic pain at surgical

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The use of Ketamine to reduce opioids demand for opioids - tolerant patients

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incision sites, as well as at sites surrounding incisions. These effects are probably mediated by the intracellular formation of nitric oxide.

The blunting of central sensitization has played an important role in the prevention and treatment of both postoperative pain and chronic pain. Ketamine is rapid acting with minimal effects on bowel motility. The low sub-anesthetic doses produce analgesia, without causing respiratory depression. The proposed dose in clinical trial is 1-5 mcg/kg/min (median 5) while decreasing opioids by 25%. The result was a decline in morphine equivalency rate changed significantly from 0mg/hr before ketamine to -0.256 mg/hr in the 12 hours following ketamine. In critically ill patients, as an adjunct to an opioids analgesic for non-neuropathic pain the initial IV dose is 0.1 to 0.5 mg/kg bolus, followed by a continuous infusion of 0.83 to 6.7 mcg/kg/minute, (equivalent to 0.05 to 0.4 mg/kg/hour). A 2014 study by Pacheco et al. which used specific opioid receptor blocking agents suggests that interaction with μ - and δ - opioid receptors is responsible for the central anti-nociceptive effects of ketamine. Studies show that prevention of opioid tolerance may be another mechanism of pain prevention by ketamine. It has been reported that μ -receptor activation by opioids leads to a sustained increase in glutamate synaptic effectiveness at the level of NMDA receptors. Although the mechanisms that allow ketamine to be an analgesic and opiate-sparing agent after opiate exposure remain poorly understood. Rat studies in brain ischemia have found a role of postsynaptic density (PSD), proteins, specifically PSD- 95, in potentiating NMDA function and signaling to nitric oxide synthase resulting in chronic and neuropathic pain. Studies show that ketamine may decrease injury-triggered increases in interactions between the NMDA receptor, postsynaptic density protein 95 (PSD95), and protein kinases, thereby reducing nitric oxide-related neuronal injury

Ketamine has a sympathomimetic activity resulting in tachycardia, hypertension, increased myocardial and cerebral oxygen consumption, increased cerebral blood flow, and increased intracranial and intraocular pressure. Ketamine is a potent bronchodilator and can be used to treat refractory bronchospasm. Clinical side effects observed following ketamine administration include increased blood pressure, increased muscle tone, opening of eyes, accompanied by nystagmus, and increased myocardial oxygen consumption. Ketamine has no effects on pharyngeal or laryngeal reflexes, thus, the patient's airway remains intact. Side effects increase at doses higher than 10mcg/kg/min.

Ketamine can be used in subanesthetic low doses to decrease the demand for chronic opioid users who experience acute pain of trauma or surgery. Although the data is not robust, it has been successfully used for that indication. The side effects have limited its use; however, these side effects are very rare considering the low doses used for pain control. Randomized clinical trials are needed to confirm the results of the small trial, and case studies.

References:

- Buchheit JL, Yeh DD, Eikermann M, Lin H. Impact of Low-Dose Ketamine on the Usage of Continuous Opioid Infusion for the Treatment of Pain in Adult Mechanically Ventilated Patients in Surgical Intensive Care Units. *Journal of Intensive Care Medicine*. March 2017:088506661770690. doi:10.1177/0885066617706907. Accessed on December 13, 2017.
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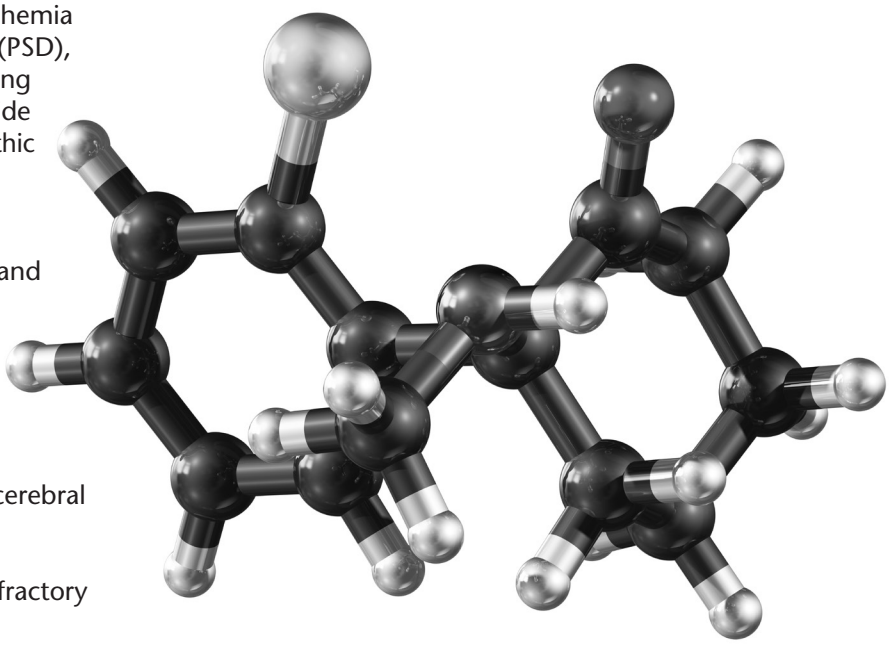

The use of Ketamine to reduce opioids demand for opioids - tolerant patients

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- De Bartolomeis, C. Sarappa, E. F. Buonaguro et al., "Different effects of the NMDA receptor antagonists ketamine, MK-801, and memantine on postsynaptic density transcripts and their topography: role of Homer signaling, and implications for novel antipsychotic and pro-cognitive targets in psychosis," Progress in Neuro-Psychopharmacology and Biological Psychiatry, vol. 46, pp. 1–12, 2013. Accessed on December 13, 2017

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Danielle Tropea - Board Certified Lactation Consultant

I recently joined University Hospital as our first dedicated board certified lactation consultant in many years. While most of my patients are in F-Green, lactating patients can be found throughout our campus. Any number of postpartum complications such as preeclampsia and severe postpartum depression, can send women back to University, in addition to elective as well as emergent procedures and surgeries, such as sterilization or gall bladder surgery.

Given the American Academy of Pediatrics' strong recommendation that infants be breastfed (or be breastmilk-fed) exclusively for their first six months, it is prudent to take lactation into consideration when developing pharmaceutical treatment plans. A breastfed child's lifelong health is at risk when premature or even temporary weaning takes place.,.

Pregnant women are warned to avoid most medications due to placental perfusion but the mechanism for excretion into the milk-making compartments operates differently. Most medications do enter milk through one of two methods (passive diffusion or carrier-mediated transport), but it is rare that they reach clinical levels. Multiple pharmacokinetic factors determine the extent of these levels: molecular size, lipid solubility, protein-binding, ionization, oral bioavailability, and half-life. But even if a drug has been measured in mother's milk, the most crucial measurements of infant risk are the milk/plasma ratio and the theoretical infant dose. Even then, in some cases, the risk may be null if the drug is one that is routinely directly administered to children. (Understanding this, in 2003, the AAP reversed their long-held position and declared that most maternal medications are, in fact, safe for breastfed babies.)

So, how can a clinician put this knowledge to good use? The good news is that the most comprehensive resources to reference are at your fingertips! LactMed, https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm, is a peer-reviewed and fully referenced database provided by the National Institute of Health, and is updated monthly. Thomas Hale PhD's *Medications and Mother's Milk*, aggregates studies as well but also provides risk categories: L1 (safest), L2 (safer), L3 (moderately safe), L4 (possibly hazardous), L5 (contraindicated). This information can be accessed by calling the InfantRisk Center Hotline – (806) 352-2519, Monday – Friday, 9am – 6pm, as well as through the InfantRisk app ($10). I also have access to MedsMilk.com, the InfantRisk website, and can provide you with summaries at your request.

What should be done if the drug that is prescribed to your patient is incompatible with lactation? If no alternative can be given, mothers can minimize the peak of levels in her blood (Tmax), by taking the drug immediately after nursing her baby. With advance notice, a mother should be able to pump and store her milk to be fed to the baby once she starts taking the medication, then pump and discard until several half-lives half passed. When in doubt, the mother should be brought a breast pump as soon as possible and advised to pump and –store- her milk until more information can be gathered.

It is my goal and pleasure to serve as a resource to the entire institution. My office is located in F-Green F-427, my extension is 2-6868, my cell phone is 973-609-2697, and my email is tropeadb@uhnj.org.

For more in-depth explanation of pharmacokinetics as it relates to lactation, please refer to www.medsmilk.com/pages/introduction or email me for my paper, *Lactational Pharmacology*. I can also provide a list of medications that Hale and LactMed have deemed unsafe for breastfeeding. (These mostly include anti-retrovirals and chemotherapy drugs.)

Danielle Tropea - Board Certified Lactation Consultant *(Continued from page 5)*

Medications Frequently Prescribed to Postpartum Women	
Class	**Drug and category**
Acid-Reducing Agents	Famotidine – L1
	Ranitidine – L2
Analgesics	Ibuprofen – L1
	Hydromorphone – L3
	Morphine – L3
	Naproxen – L3
	Oxycodone – L3
Antibiotics/antivirals	Acyclovir – L2
	Azithromycin – L2
	Cephalexin – L1
	Fluconazole – L2
	Gentamicin – L2
	Metronidazole – L2
	Nitrofurantoin – L2
	Penicillin - L1
	Sulfamethoxazole and Trimethoprim - L3
	Oseltamivir - L2
Anticonvulsants	Lamotrigine – L2
Antidepressants	Citalopram – L2
	Escitalopram – L2
	Paroxetine – L2
	Sertraline – L2
	AntihistaminesLoratadine – L1
	Diphenhydramine – L2
Antihypertensives	Amlodipine besylate - L3
	Hydralazine - L2
	Methyldopa - L2
Benzodiazepines	Clonazepam – L3
	Diazepam – L3
Cardiovascular	Furosemide – L3
	Nifedipine – L2
	Propranolol – L2
Contrast dyes and radiopaque agents	Barium Sulfate – L1
	Diatrizoate – L2
	Metrizamide – L2
	Metrizoate – L2
Imaging techniques	MRI, PET, MIBI, EIT, CT, CAT, thermography
Social drugs	Alcohol – L4 BUT mothers who ingest alcohol in moderate amounts can
	generally return to breastfeeding as soon as they feel neurologically
	normal (approximately 2 hours for each drink consumed)
	Caffeine – L2
	Nicotine – L3
Sources: www.medsmilk.com/ and toxnet.nlm.nih.gov/newtoxnet/lactmed.htm	

1 Sachs, M.D., Hari Cheryl. "The Transfer of Drugs and Therapeutics Into Human Breast Milk: An Update on Selected Topics." AAP Pediatrics. Volume 132, Issue 3 (2013): 796-809. <http://pediatrics.aappublications.org/content/132/3/e796>

2 It has recently been recommended for use in breastfeeding mothers by the Center for Disease Control. http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

3 Furosemide is frequently used in neonates in pediatric units, so pediatric use is common.

4 http://prdupl02.ynet.co.il/ForumFiles/5764419.pdf

5 http://breastfeedingtoday-llli.org/cancer-and-breastfeeding/

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Leech Therapy for Anticoagulation

Biomedical leech therapy is an innovative, yet very ancient practice in medicine. For countless centuries, prior to the advent of modern medicine, civilizations such as the Ancient Egyptians, Ancient Greeks, Medieval Europe, Chinese and many other cultures have utilized these techniques. This practice began to fall off in the 19th century, however recent discoveries have displayed many relevant clinical applications. The use of blood sucking leeches may seem like quackery, however its efficacy is difficult to dispute. Not only is leech therapy incredibly effective, it also comes with little risk of adverse effects. Uses range from applications in cardiovascular disease therapy to arthritis relief.

Of the many clinical applications for leech therapy, its uses for cardiovascular disease and microsurgery are among the most promising. It has established itself as a viable and beneficial alternative to vascular disorder treatment due to marked improvements in blood flow and relief of connective tissue hyperalgesia. Leech saliva contains a chemical known as hirudin, which was shown to possess a potent inhibitory effect on both free and clot-bound thrombin. A study done by Corral-Rodriguez M, et al. revealed that hirudin is actually more effective than heparin in deep venous thrombosis (DVT) and ischemic event prophylaxis in patients with unstable angina. Unlike heparin and low molecular weight heparins (LMWH), hirudin directly inhibits thrombin without the use of antithrombin III. This advantage gives hirudin clinical applications in disseminated intravascular coagulation, heparin-induced thrombocytopenia and in patients with platelet disorders. Other active compounds derived from leeches include factor Xa inhibitors, glycoprotein IIb-IIIa inhibitors, antiplatelet, fibrinolytic, and fibrinogenolytic agents which may prove to have countless clinical applications in the coming years. In Russia an anticoagulant with the trade name Pyavit, produced from extracted leech saliva, is currently on the market. In addition to this, leech therapy has been shown to provide tremendous benefit to patients undergoing microsurgical procedures as a prophylactic agent. Venous occlusion is a significant threat to newly transplanted tissues that may cause thrombus formation, stasis, and ultimately tissue necrosis. The use of leech therapy works to mitigate these effects by preventing venous congestion. It does so by actively draining blood during a procedure and passive wound oozing after leech detachment due to the long-acting anticoagulants found in leech saliva.

Leech therapy has shown very promising results in the field of medicine and truly does have a place in our modern practice. Its high risk to benefit ratio makes it a viable alternative that must be studied more vehemently and utilized more frequently. However, it is important to remember that much of the current data is extracted from case series and case reports rather than randomized clinical trials, particularly regarding its use for microsurgical procedures. No standardized protocols for duration or administration are established, therefore new and improved research must be studied and analyzed. Despite this fact, there is still a place for leech therapy as a viable alternative for cardiovascular disease and thrombosis prophylaxis. In addition to these uses leech therapy has also shown benefit in cancer and metastasis, complications from diabetes, infectious disease and countless other afflictions. Further studies of this possible breakthrough in medicine can benefit many patients and advance medical practice for years to come.

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1. Abdualkader AM, Ghawi AM, Alaama M, Awang M, et al. Leech Therapeutic Applications. *Indian Journal of Pharmaceutical Sciences*, 2013;75(2): 127–137.
2. Michalsen A, Roth M, Dobos G, et al. Medicinal Leech Therapy. Germany: Apple Wemding; 2007.
3. Corral-Rodríguez MA, Macedo-Ribeiro S, Pereira PJ, et al. Leech-derived thrombin inhibitors: From structures to mechanisms to clinical applications. *J Med Chem*. 2010;53:3847–61.
4. Markwardt F. Historical perspective of the development of thrombin inhibitors. *Pathophysiol Haemost Thromb*. 2002;32(Suppl 3):15–22.
5. Knobloch K. Leeches in microsurgery – An evidence-based approach. In: Kini RM, Clemetson KJ, Markland FS, McLane MA, Morita T, editors. Toxins and Hemostasis. *Netherlands: Springer Science*; 2011; 735–45.

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University Hospital Formulary Additions and Deletions for January 2016 – December 2017

Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Meningococcal conjugate vaccine	Menveo	Jan 2016	X			Menveo® costs less per dose compared to Menactra®
Meningococcal conjugate vaccine	Menactra	Jan 2016			X	Menactra® costs more per dose compared to Menveo®
Diphenhydramine-zinc 1% cream		Jan 2016			X	Product no longer available commercially
HPV 9-valent vaccine	Gardasil-9	Feb 2016	X			Protects against more strains of HPV compared to the 4-valent vaccine on formulary
HPV 4-valent vaccine	Gardasil	Feb 2016			X	Replaced by HPV 9-valent vaccine
Ticarcillin/clavulanate	Timentin	Feb 2016			X	Discontinued by the manufacturer
Sodium Chloride 7% nebulization solution		Feb 2016 Feb 2016	X X			Restricted to pulmonary division for patients who do not respond to sputum induction or treatment of bronchiectasis to hypertonic saline 3% nebs
Morphine Sulfate preservative free 200mg/ 20mL and 500mg/20mL	Infumorph	Feb 2016	X			Requested by anesthesia dept. for intrathecal/epidural use
CAPS D5W neonatal starter TPN 250mL bag		Feb 2016	X			CAPS eliminated currently used neonatal starter TPN formulation (D5W with trophamine 2g/dL and calcium gluconate 0.46mEq/mL)
CAPS D10W neonatal starter TPN 250mL bag		Feb 2016	X			CAPS eliminated currently used neonatal starter TPN formulation (D10W with trophamine 2g/dL and calcium gluconate 0.46mEq/mL)
Pancuronium bromide solution for injection		Mar 2016		X	X	Low usage; rocuronium and vecuronium preferred formulary neuromuscular blocking agents
Codeine injectable solution		Apr 2016			X	Discontinued by manufacturer
Hemorrhoidal suppository	Anusol	Apr 2016		X	X	Never purchased nor kept in UH pharmacy stock
Hydroxypropyl methylcellulose	Tearsol	Apr 2016			X	Never purchased nor kept in UH pharmacy stock
Pantoprazole 40mg oral packet		Apr 2016			X	Never purchased nor kept in UH pharmacy stock
Cledivipine 2.5mg/50mL	Cleviprex	May 2016		X	X	Lack of usage and availability of formulary alternatives
Argatroban 100mg/100mL		May 2016			X	Commercially available products not coming as 100mg size

University Hospital Formulary Additions and Deletions

Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Benzocaine otic drops	Auralgan	Jun 2016			X	Discontinued by manufacturer
Tromethamine (THAM) solution for injection		Jun 2016		X	X	Discontinued by manufacturer
Desflurane inhalation vapor	Suprane	Jul 2016	X			Approved for anesthesia use only; restricted to the following indications: bradycardia, severely or morbidly obese patients, patients with operations of very short duration, low flow anesthesia
Idarucizumab	Praxbind	Jul 2016	X			Novel drug for treatment of patients who require emergent reversal of dabigatran-induced anticoagulation
Sugammadex	Bridion	Jul 2016	X			Clinical trials showed faster and more complete reversal of neuromuscular blockade compared with cholinergic agents
Filgrastim-sndz	Zarxio	Jul 2016	X			Significantly cheaper than Neupogen and approved for almost similar indications
Filgrastim	Neupogen	Jul 2016		X		Not automatically interchangeable with Zarxio
Regadenoson	Lexiscan	Jul 2016	X			Expanded restriction criteria
Gamma hexachlorocyclohexane 1% lotion	Lindane	Jul 2016			X	Discontinued by manufacturer
Isovue multipack 370		Jul 2016			X	Not used nor stocked by radiology dept.
Pentamidine powder for nebulization	Nebupent	Jul 2016		X	X	Not used and nebulizer needed to administer the product not carried
Prothrombin Complex Concentrate	Kcentra Kcentra	Sept 2016 Sept 2016	X X			Restricted to trauma, intensivist, hematology/oncology, ED, and neurosurgery approval
Immune globulin	Privigen Gammunnex-C	Sept 2016	X			Brand change
Amoxicillin/clavulanate 600mg-42.9mg/5mL oral suspension	Augmentin	Sept 2016	X			Line extension
Amoxicillin/clavulanate 125mg-31.5mg/5mL, 200mg-28.5mg/5mL, 250mg-62.5mg/5mL oral suspension	Augmentin	Sept 2016			X	Other acceptable concentration exists on the formulary
Sacubitril/valsartan	Entresto	Oct 2016	X			Combination drug shown to reduce the rate of hospitalization and mortality from cardiovascular causes in patients with heart failure compared to enalapril alone

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University Hospital Formulary Additions and Deletions

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Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Ferrous Fumarate 50mg ER tablet		Oct 2016			X	Minimal usage; availability of ferrous sulfate 300mg/5mL
Ferrous sulfate 220mg/ 5mL oral liquid		Oct 2016			X	
Phenoxybenzamine	Dibenzyline	Oct 2016		X	X	Increase in price 10 fold and minimal usage
Radiopharmaceuticals		Nov 2016	X			Addition required by regulatory agencies of radiopharmaceuticals being used by nuclear medicine
Carmustine in Polifeprosan wafer 7.7mg	Gliadel Wafer	Nov 2016			X	No usage in previous 4 years
Humalog U-200 KwikPen Sample	Humalog	Nov 2016	X			Requested by Care Clinic
Codeine containing products for pediatric inpatients		Nov 2016			X	Restriction of codeine to patients ≥ 18 years old
Ivabradine	Corlanor	Dec 2016	X			Restricted to cardiology for approved indication
Nivolumab	Opdivo	Feb 2017	X			No current formulary alternatives; significantly lower ADRs with nivolumab than other 2nd line therapy options
Meningococcal polysaccharide vaccine	Menomune	Mar 2017			X	Discontinued by manufacturer
Polyethylene glycol	Miralax	Mar 2017	X			Line extension
Nicardipine 20mg and 40mg capsules	Cardene	Mar 2017		X		Line extension for addition denied
Reslizumab	Clinqair	Apr 2017	X			Restricted to authorizing providers in allergy/immunology prescribers only
Isradipine 2.5mg and 5mg capsules	Dynacirc	Apr 2017			X	No usage
Thiothixene 5mg and 10mg capsules	Navane	Apr 2017			X	No use and better side effect profile options available on UH formulary
Thioridazine 25mg, 50mg, 100mg tablets	Mellaril	Apr 2017			X	No use and better side effect profile options available on UH formulary
Ceftazidime/Avibactam	Avycaz	May 2017	X			Increased activity against multidrug resistant organisms, specifically those resistant to carbapenems. Approved as restricted anti-infective authorized by ID service
Dabigatran 110mg capsule	Pradaxa	May 2017	X			Line extension
Nusinersen	Spinraza	Jun 2017	X			Restriction criteria includes approval from patient's insurance in advance and limited prescribers allowed to order

University Hospital Formulary Additions and Deletions

Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Loratidine D 12/24 hour	Claritin	Jun 2017			X	Low usage and constant replenishment of expired stock
MVI oral liquid		Jun 2017			X	Discontinued by manufacturer; oral MVI tablets still available on formulary
Levonorgestrel intrauterine device	Liletta	Jul 2017	X			Restricted to ordering by OB attending physician and must be procured by the OB department from a grant funding for inpatient use and brought to the pharmacy for stocking in Pyxis
Copper intrauterine device	Paragard T380A	Jul 2017	X			Restricted to ordering by OB attending physician and must be procured by the OB department from a grant funding for inpatient use and brought to the pharmacy for stocking in Pyxis
Etonorgestrel implant	Nexplanon	Jul 2017	X			Restricted to ordering by OB attending physician and must be procured by the OB department from a grant funding for inpatient use and brought to the pharmacy for stocking in Pyxis
Tolnaftate 1% cream/solution		Jul 2017			X	Non-usage and availability of alternative topical antifungals
Glatiramer	Copaxone	Jul 2017			X	Minimally used expensive medication
Pioglitazone 30mg, 45mg tablets	Actos	Jul 2017			X	Minimal usage; 15mg will remain on formulary
Triamterene 50mg capsule	Dyrenium	Sept 2017			X	
Sotalol IV		Sept 2017			X	
Buprenorphine/Naloxone	Suboxone	Sept 2017			X	
Hydrocortisone Valerate cream and ointment		Sept 2017			X	
Colloidal Bath Granules		Sept 2017			X	
Calcipotroene 0.005% cream	Dovonex	Sept 2017			X	
Mafenide cream and solution	Sulfamylon	Sept 2017			X	
Benzyl Peroxide 5%		Sept 2017			X	
Dibucaine 1%	Nupercainal	Sept 2017			X	
Imipramine 50mg tablet	Tofranil	Sept 2017			X	
Triple Dye		Sept 2017			X	
Tiagabine 2mg, 4mg tablets	Gabitril	Sept 2017			X	
Hyaluronate	Amvisc	Sept 2017			X	

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Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Vitamin C oral liquid		Sept 2017			X	
Hepatitis B vaccine	Engerix B	Sept 2017	X			Line extension
Sodium Hyaluronate 0.85mL	Provisc	Sept 2017	X			Line extension
Meningococcal Group B vaccine	Bexsero	Sept 2017	X			Requires only 2 injections; included in new guidelines for asplenic patients
Naltrexone 380mg IM monthly	Vivitrol	Oct 2017	X			Treatment option for patients who failed oral therapy
Phytonadione tablet and oral liquid	Mephyton	Oct 2017			X	Significant cost increase
Acebutolol 200mg tablet	Sectral	Oct 2017			X	Not recommended by hypertension treatment guidelines; no use in last 2 years
Didanosine all strengths	Videx	Oct 2017			X	Current treatment guideline does not include agent as 1st nor 2nd line treatment; no use in last 2 years
Stavudine all strengths	Zerit	Oct 2017			X	Current treatment guideline does not include agent as 1st nor 2nd line treatment; no use in last 2 years
Fosamprenavir all strengths	Lexiva	Oct 2017			X	Current treatment guideline does not include agent as 1st nor 2nd line treatment; no use in last 2 years
Nelfinavir all strengths	Viracept	Oct 2017			X	Current treatment guideline does not include agent as 1st nor 2nd line treatment; no use in last 2 years
Saquinavir all strengths	Invirase	Oct 2017			X	Current treatment guidelines does not include agent as 1st nor 2nd line treatment; no use in last 2 years
Ocrelizumab	Ocrevus	Nov 2017	X			The medication must be approved by the patient's insurance in advance (prior authorization) and supplied to the inpatient hospital pharmacy through the patient's outpatient/ specialty pharmacy
Amiodarone 360mg/200ml	Nexterone	Nov 2017	X			
Amiodarone 150mg/100ml	Nexterone	Nov 2017			X	
Podophyllum Resin		Nov 2017			X	
Pencillamine		Nov 2017			X	
Bethanechol		Nov 2017			X	
Lecithin		Nov 2017			X	
Peginterferon Alfa-2a Interferon Alfa-2b Interferon Gamma 1b Peginterferon Alfa-2b	Pegasys® Intron A® Actimmune®) PegIntron®	Nov 2017			X X X	
Indigo Carmine		Nov 2017			X	

Generic Name	Brand Name	P&T Date	Approved	Denied	Deleted	Reason/Comments/Criteria
Mivacurium		Nov 2017			X	
Edaravone	Radicava®	Dec 2017	X			
Nexplanon Implant		Dec 2017	X			
Liletta IUD		Dec 2017	X			
Paragard T IUD		Dec 2017	X			
Potassium Chloride Oral Powder		Dec 2017	X			
Chloroquine		Dec 2017			X	
Quinupristin /dalfopristin		Dec 2017			X	
Neomycin/ polymyxin 1mL ampules		Dec 2017	X			

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Technology in Healthcare

The use of technology is increasing progressively. As a society, we depend on technology to accomplish our daily tasks. Technology is developing at a rapid rate and innovation is revolutionizing healthcare. The healthcare transformation over recent years has improved the experience for patients and healthcare professionals. For example, the widespread implementation of electronic health records has enhanced standards in patient care and improved operational efficiency. Many other innovations are transforming the healthcare field. Can you imagine verifying IV preparations remotely or tracking medication in real time? These technologies currently exist and will be some of the future trends modern technology has to offer.

The process of compounding sterile products must be precise. A slight error can increase the risk of contamination or can lead to a fatal outcome. Sterile compounding is one of the highest risk areas of pharmacy practice; however little technology is involved to assist in safe compounding. When a technician prepares a sterile product, a pharmacist verifies the final product without visualization of the compounding steps, leaving chance for error. One solution to this problem is PharmacyKeeper. PharmacyKeeper provides web and mobile based applications to improve operational processes. One feature of this product is that it uses photo-based documentation to allow pharmacists to remotely review and approve the IV preparation process. In addition, audit logs and photos are recorded. PharmacyKeeper is designed to exist in the current workflow and involves a simple camera placed in the IV hood. This mobile based solution is customizable and can easily set up with iPads, scanners, and printers. The reporting feature of the PharmacyKeeper system allows users to track each item made and the technician or pharmacist responsible for completing each step. PharmacyKeeper has the potential to improve efficiency and operate as a safeguard for compounding regulations.

Many health care facilities are increasing the use of medication tracking. PharmTrac.PD is one example of medication dose tracking technology. This mobile tool has barcode medication tracking and collects data through a web-based portal. EPIC, the electronic health record system, has an in-basket message queue for communication among nurses, pharmacists, pharmacy technicians, and other health care professionals. In-basket messaging allows nursing staff to send messages to pharmacy staff and is often used for communicating medication requests. Many of these requests are due to missing

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Technology in Healthcare

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medications. Missing medications result in re-dispenses, increase in staff workload, and medication waste. Medication dose-tracking technology has the potential to improve efficiency and reduce costs associated with re-dispensing medication. Implementation of scanning a medication at pick-up from the pharmacy and at drop-off on to the patient care unit allows for real time medication tracking. Dose tracking helps visualize the location and status of medication from the pharmacy to the patient care unit as well as records the responsible party for each step. With tracking medication, there will be decreases in lost and missed doses as well as improved communication between nursing and pharmacy.

Technology advancements have been valuable in healthcare. There are many tools that can help areas of the healthcare system to safely and efficiently improve workflow while reducing errors. We can anticipate more extensive innovation and development in the years to come.

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2. Verification. Verification | MedKeeper. http://www.medkeeper.com/products/verification/. Accessed December 1, 2017

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340B Drug Pricing Program Overview

The 340B drug pricing program (340B program) allows hospitals and other "covered entities" to receive discounted prices on outpatient medications from manufacturers. The original program with discounted prices was the 1990 Medicaid rebate program. This program required manufacturers to provide rebates for "covered outpatient drugs" which was based on the "best price" for the drug. Similarly, when the 340B program was enacted in 1992, it extended these discounts to the covered entities serving vulnerable patient populations. According to the congressional report language, the purpose of the 340B program is "to stretch scarce federal resources as far as possible, reaching more eligible patients and providing more comprehensive services."

There are 6 types of hospitals and 10 types of clinics that are eligible to participate in the 340B program; University Hospital is classified as a disproportionate share hospital (DSH). There are many types of covered outpatient drugs including prescription drugs as well as biologics excluding vaccines. Note that this program excludes inpatient drugs and drugs that are bundled with other services. The 340B program also prevents the resale or transfer of discounted medications to anyone other than a patient of the covered entity. The covered entity must have a valid relationship with the patient and this is demonstrated by maintaining the individual's health records.

The 340B program works by having the covered entity register during a specific time period to obtain the discounted pricing; the wholesaler then displays the discounted prices once enrolled. The usual 340B ceiling price is the average manufacturer price (AMP) reduced by the unit rebate amount (URA). A greater discount must be offered if the best price for a drug is lower than AMP minus URA and/or if the price has increased faster than the rate of inflation. As a result, the discounted drug prices are significantly lower

340B Drug Pricing Program Overview

than retail and wholesale prices. In 2015, the Government Accountability Office reported an estimated savings of 20-50% off drug costs.

In addition to all the benefits of this program, there is also regulatory oversight and processes that must be followed. The Office of Pharmacy Affairs (OPA), which is part of the Health Resources and Services Administration (HRSA) which is part of the Department of Health and Human Services (HHS), is responsible for interpreting and implementing the 340B law. HRSA is authorized to audit covered entities to ensure they are compliant with the program. Likewise, manufacturers are also authorized to audit but must do so under HRSA guidelines.

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Does Targeting Lower SBP in HFpEF Patients Lead to Increased Morbidity/Mortality?

Heart failure (HF) is known as a clinical syndrome affecting the ability of the heart to pump or fill with blood.[1] Much is known about treatment of heart failure with reduced ejection fraction (HFrEF), defined as left ventricular ejection fraction (LVEF) of less than or equal to 40%, to lower blood pressure. This is due to the significant improvement of morbidity and mortality with up-titrating guideline directed medical therapy (GDMT) to tolerability, implying that targeting a systolic blood pressure < 130 mmHg is reasonable.[2] Hypertension treatment for heart failure with preserved ejection fraction (HFpEF), however, is less clear and is based on extrapolated data from non-HF patients.[2] Although it is suggested in the updated 2017 HF guidelines that HFpEF patients should similarly be targeted to attain SBP < 130 mmHg, up-titrating GDMT for HFrEF in HFpEF patients have not shown improvements in morbidity and mortality in large randomized clinical trials.[2] Furthermore, patients who develop HF and have lower SBP levels may, counter- intuitively, have an increased risk of cardiovascular morbidity and mortality.[3]

Tsimploulis and colleagues sought to determine the association of lower SBP levels of < 120 mmHg in HFpEF patients.[3] They used a propensity score-matched observational study of the OPTIMIZE-HF registry to collect data for 3,915 patients who had stable **SBP levels with < 20 mmHg in variation** from admission to discharge, matching for over 50 baseline characteristics. Of those 3,915 patients, 1,076 patients had **SBP levels less than 120 mmHg**, of whom 901 were matched by propensity scores with 901 patients with SBP levels > 120 mmHg or greater. Overall, the 1,802 patients had a mean age of 79, 1,147 (63.7%) were women, and 134 (7.4%) were African American. The results showed that for hospitalized patients with HFpEF, 30-day mortality occurred in 91 (10%) and 45 (5%) of matched patients with discharge SBP of less than 120 mmHg vs. 120 mmHg or greater, respectively (hazard ratio [HR], 2.07; 95% CI, 1.45-2.95; P < 0.001). Furthermore, SBP < 120 mmHg was also associated with higher mortality at 1 year (39% vs. 31%; HR, 1.36; 95% CI, 1.05-1.30; P=.005) and higher HF readmission at 30 days (HR, 1.47; 95% CI, 1.08-2.01; P=0.02) but with no difference in readmission at 1 or 6 years. In a further analysis, it was interesting to note that **SBP < 130 mmHg** was also significantly associated with a higher risk of the combined end point of HF readmission or all-cause mortality at 30-day, 1 year, and 6 years.[3]

Based on this, Tsimploulis and colleagues concluded that these findings provide evidence of a "consistent

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Does Targeting Lower SBP in HFpEF Patients Lead to Increased Morbidity/Mortality?

association between a lower SBP level and poor outcomes in HFpEF patients" that may "reflect differences in cause, pathophysiology, and stage of disease."[3] It should be made known that patients who had an SBP < 120 mmHg prior to propensity score matching had lower rates of hypertension, diabetes, and atrial fibrillation, suggesting that the etiology of HFpEF are not likely due to those causes.[3] This is important because it is well known that hypertension can lead to HFpEF so the extrapolation of the data may not be generalizable to those patients who developed HFpEF due to hypertension. As the authors state, it is possible that the lower SBP level in HFpEF may reflect an advanced disease state associated with lower cardiac output whereby lowering BP leads to worse outcomes.[3] Furthermore, it is important to note that the study analyzed hospitalized patients with SBP at discharge measured in a supine position. No follow-up outpatient ambulatory data was collected through the 30-day, 1 year, and 6 year follow-ups. Mortality and re-admission rates were thus based only on what the initial SBP was at discharge, making it difficult to extrapolate the data to ambulatory patients.

This study further emphasizes the importance of individualized treatment given that optimal BP targets in HFpEF patients is unclear. Although lower SBP levels was found to be a marker for poor outcomes, the authors suggest that future prospective randomized clinical trials are needed to examine the effect of additional targets on outcomes in patients in HFpEF.3 Additionally, monitoring of blood pressure in ambulatory patients may make the results more generalizable. Determining effective therapies to reduce morbidity and mortality in HFpEF patients undoubtedly continues to be the greatest challenge.

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