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Special Points of Interest:

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P&T Update

Formulary Addition/Deletion

1. Formulary reviews of the macrolide and fluoroquinolone antibiotic classes were presented. It was recommended to delete ciprofloxacin oral suspension and erythromycin stearate tablets from the formulary given their low usage. Formulary deletions – approved.
2. Formulary deletion of erythromycin 200mg/5mL oral suspension approved.
3. 6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride injection (Voluven™) is a synthetic colloid which is FDA approved for the treatment and prophylaxis of hypovolemia in adults and children. Formulary addition approved with restriction to OR/PACU only.
4. Anti-thymocyte Globulin (Rabbit) (Thymoglobulin®) is a polyclonal IgG derived from rabbits approved for use as an immunosuppressant in treatment and prophylaxis of kidney transplant rejection. It is requested by the liver transplant surgeons at UH due to discontinuation of OKT3 (Muromomab-CD3). – Approved with restriction to Liver Transplant Team only.

Policies and Procedures Update

1. Malignant hyperthermia cart policy and procedure (#707-400-111)
2. Malignant hyperthermia prevention and management guidelines for adults

The malignant hyperthermia carts are to be maintained in the OR (one cart in the Main OR on E Level and one cart in the Same Day OR). Dantrolene IV is also available in the Pyxis machines in the following areas: CT PROC, E-Green, GPED and LDOR. – Approved

Current Drug Options for Management of Chronic Hepatitis B Infections

Currently, there are 7 drugs that have an approved Chronic Hepatitis B (CHB) infection indication by the Food and Drug Administration (FDA). These 7 drugs are interferon alfa-2b, peginterferon alfa-2a, lamivudine, adefovir, entecavir, telbivudine, and tenofovir. The choice of antiviral therapy requires the consideration of many factors including safety profile, comorbidities, efficacy of viral suppression, and patient preference. Advantages and disadvantages of each of these agents will be discussed in this article.

Interferon alfa-2b was the standard interferon based therapy until replaced by peginterferon alfa-2a. This allowed patients more convenient administration schedules, while providing similar or improved efficacy. Although the use of

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Current Drug Options for Management of Chronic Hepatitis B Infections

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interferon-based antiviral regimens is declining, they have the highest reported sustained response off-treatment. After 48 weeks of interferon therapy, HBeAg seroconversion was reported as high as 27%, with undetectable HBV DNA among 25% of patients. At 6 months follow up, 4-6% of patients experienced HBsAg loss after development of anti-HBs. Despite these advantages, interferon treatment regimens have significant side effect profiles (fatigue, arthralgia, depression, and insomnia) relative to newer oral agents.



Lamivudine, is a nucleoside analog with activity against HIV and HBV. With 100 mg once daily dosing for HBV infection, lamivudine is convenient for patients and well tolerated due to its good safety profile. It also has profound viral suppression, demonstrating HBV DNA serum levels undetectable in 90% of patients on lamivudine. The biggest disadvantage with lamivudine therapy is that resistance is inevitable, with resistance rates as high as 70% reported after 5 years of therapy.

Adefovir is a nucleotide analog that acts by inhibiting HBV DNA polymerase. Daily 10 mg dosing for 48 weeks has shown to be effective in improving

histologic findings, reducing serum HBV and ALT levels, and increasing HBeAg seroconversion. It is also well tolerated by patients and has good durability of response, with 90% of patients sustaining seroconversion. Although adefovir is still available, use is declining due to development of resistance and availability of better treatment options.

Entecavir is an oral nucleoside analog of guanosine (dosed 0.5 mg daily for treatment-naive patients) that inhibits HBV polymerase. It is more potent than both lamivudine and adefovir in suppressing serum HBV DNA levels and is effective in lamivudine resistant patients. Also, entecavir has a low rate of the resistance developing compared to other agents; however, in lamivudine resistant patients, it has decreased efficacy and increased resistance.

Telbivudine is a HBV-specific nucleoside analog that acts as a competitive inhibitor of viral reverse transcriptase and DNA polymerase. It has a high potency in lowering HBV DNA and is well tolerated by patients. Additionally it is pregnancy category B, making it the most favorable option relative other treatments for pregnant patients. Disadvantages include the intermediate resistance rate and the risk of myopathy and peripheral neuropathy.

Tenofovir is a nucleotide analog that has an approved indication for HBV. With similar activity to adefovir, doses of 300 mg can be given once daily. When compared with adefovir, tenofovir was shown to have more HBeAg-positive patients with undetectable HBV DNA, ALT normalization, and loss of HBsAg. Rates of histological response and seroconversion were similar. Despite these advantages, there is still limited data on resistance with tenofovir use.

References:

Deming P. Chapter 47. Viral Hepatitis. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 8th ed. New York: McGraw-Hill; 2011. <http://www.accesspharmacy.com/content.aspx?alD=7979809>. Accessed April 17, 2013.

Sorrell MF, Belongia EA, Costa J, Gareen IF, Grem JL, Inadomi JM, Kern ER, McHugh JA, Petersen GM, Rein MF, Strader DB, Trotter HT. National Institutes of Health Consensus Development Conference Statement: management of hepatitis B. *Ann Intern Med* 2009 Jan 20;150(2):104-10.

Wong R, and Ayoub W. Current treatment strategies for the management of chronic hepatitis B. *JCOM* 2013; 20; 36-47.

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Proper Inhaler Technique is a Crucial Component of Asthma Therapy

Inhaled medications are the cornerstone of therapy for patients with asthma. Regardless of asthma severity, all patients need to have a short-acting beta-agonist (SABA) rescue inhaler on hand for rapid relief during acute exacerbations. Patients with moderate-to-severe asthma typically require additional inhaled medications for long-term management, such as a long-acting beta-agonists (LABA) or an inhaled corticosteroid (ICS). It is not uncommon for a patient to be using two or three different inhalers concurrently. The metered dose inhaler (MDI) is the most common delivery device for inhaled medications. It is also the most difficult type of inhaler to use properly. Most MDIs are not breath actuated, meaning it is not the act of the patient inspiring that results in the release of drug from the canister, but rather the user must actuate the inhaler with the hand and coordinate that to a deep but slow inspiration. Many patients are unaware that proper technique requires them to begin taking in a deep slow breath prior to actuating the inhaler, continue breathing in after actuation, and then hold their breath for 10 seconds after inhaling the dose. A recent Respiratory Medicine review article focused on inhaler competence in patients with asthma notes data that suggests at least 50% of patients have sub-optimal technique when using an MDI. The authors surmise that this is likely linked to poor understanding of proper inhaler technique among healthcare professionals. One study of medical interns revealed that only 5% could properly demonstrate use of an MDI.

Inhaler technique has a profound effect on the amount of drug that is actually delivered into the lungs with each dose, and therefore the efficacy of the drug. In a review conducted by the Aerosol Drug Management Improvement Team (ADMIT), the authors found that out of 1173 patients who were observed using an MDI, 51% had serious difficulty coordinating actuation with inspiration, 24% did not continue to inspire long enough after actuation, and 12% were breathing in through the nose and not the mouth as the dose was actuated. MDIs remain popular because they are inexpensive compared to other alternatives, not because they are easy to use. The fact is that most patients who use an MDI struggle to coordinate

actuation with inspiration and are therefore not getting the maximum benefit from their medication.

It is our responsibility as health care providers to give patients adequate instruction and training when prescribing or dispensing inhalers to ensure each patient understands how to properly use the device. In the outpatient setting, this can be extremely challenging since we rarely have the opportunity to actually observe



the patient using the inhaler. With the inpatient population, however, we are afforded the rare opportunity to observe and instruct each and every time a patient uses an inhaler during their hospital stay. Given that the annual healthcare expenditure for a patient with uncontrolled asthma is more than double that of a controlled patient, we should be doing all we can to help our patients get the maximum benefit from their inhaled medications. Doing so can potentially reduce emergency room visits, hospitalizations, and the economic burden of poorly controlled asthma.

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Proper Inhaler Technique (Continued from page 3)

MDIs currently available from the University Hospital Pharmacy

Formulary MDIs	Drug (generic name)	Drug class	Indication
Ventolin	Albuterol	SABA	Rescue
Flovent	Fluticasone	ICS	Longterm control
Symbicort	Budesonide/formoterol	ICS/LABA	Longterm control
Atrovent*	Ipratropium	Anticholinergic	COPD
Non-formulary MDI			
Xopenex	Levalbuterol	SABA	Rescue
*Note that Atrovent is not indicated for asthma – it is indicated for bronchospasm in patients with COPD			

How to take a dose from an MDI:

1. Remove mouthpiece cap
 2. Shake the inhaler well
 3. Breath out fully through mouth, expelling as much air as possible from lungs
 4. Place mouthpiece into mouth & close lips around it
 5. Begin to breathe in DEEPLY & SLOWLY
 6. WHILE slowly breathing in, push down on top of canister (with middle finger) to release dose through the mouthpiece
 7. Remove finger from top of canister as soon as dose released (keep breathing in!)
 8. Continue breathing in deeply but slowly. AFTER breathing in ALL THE WAY, remove inhaler from mouth & begin holding breath
 9. Hold your breath for 10 seconds, or as long as you can
 10. Breath out normally
- If another dose is indicated wait 1 minute, shake the inhaler again, and repeat the dose.

References:

1. Price D, Bosnic-Anticevich S, Briggs A, et al. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Resp Med* 2013; 107: 37-46.
 2. Broeders MEAC, Sanchis J, Levy ML, et al. The ADMIT series – issues in inhalation therapy. 2) Improving technique and critical effectiveness. *Prim Care Resp J* 2009; 18(2): 76-82.
 3. Fink JB, Rubin BK. Problems with inhaler use: a call for improved clinician and patient education. *Respir Care* 2005; 50(10): 1360-1374.
 4. National Institutes of Health, National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Full Report of the Expert Panel: Guidelines for the Diagnosis and Management of Asthma (EPR-3); July 2007.
 5. Kelly HW, Sorkness CA. Chapter 33. Asthma. In: Talbert RL, DiPiro JT, Matzke GR, Posey LM, Wells BG, Yee GC, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 8th ed. New York: McGraw-Hill; 2011.
- By: Lindsey Sperzel, PharmD candidate 2013, Rutgers University

Overuse of Proton Pump Inhibitors

Proton pump inhibitors are effective for the prevention of stress ulcers, but they are often over prescribed in the hospital setting. A retrospective study done at a single institution in Brooklyn, New York showed that from a sample size of 1472 patients who had received proton pump inhibitors, nearly 70% of them did not have an indication for use.¹ Another problem with PPI overuse in the hospital is that many times it does not get discontinued when patients no longer have indications for use and at times patients are discharged unnecessarily on the medication.² This puts patients at risk because they are taking medications with no indication and face potential harm.

Unnecessary use of proton pump inhibitors can cause patients to experience adverse side effects. These side effects can include: rebound acid secretion, increased risk of infections, bone fractures, osteoporosis, and nutritional deficiencies due to the change in gastric acidity.³ A more recent risk associated with proton pump inhibitors is the development of *C. difficile* infection. A meta-analysis done on 23 studies encompassing 300,000 patients in the American Journal of Gastroenterology showed a 65% increased risk of *C. difficile* infection development in patients who take proton pump inhibitors.⁴ The FDA also released a drug

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Overuse of Proton Pump Inhibitors

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safety communication in 2012 describing the association of *C. difficile* with the use of proton pump inhibitors.⁵ Proton pump inhibitors should be prescribed conservatively and based on guidelines to prevent the development of these adverse effects.

The American Society of Health System Pharmacists (ASHP) and the Eastern Association for the Surgery of Trauma (EAST) recommend stress ulcer prophylaxis be given for certain risk factors. The primary risk factors include: mechanical ventilation > 48 hours, coagulopathy, or history of GI bleed or ulceration.^{6,7} Prophylaxis should be discontinued when patients no longer have these risk factors and efforts should be made to not discharge patients on these medications if they do not have any other indications for use.

References:

1. Perwaiz MK, Posner G, Hammoudeh F, et al. Inappropriate use of intravenous PPI for stress ulcer prophylaxis in an inner city community hospital. *J Clin Med Res.* 2010;2:215-19
2. Heidelbaugh JJ, Inadomi JM. Magnitude and economic impact of inappropriate use of stress ulcer prophylaxis in non-ICU hospitalized patients. *Am J Gastroenterol.* 2006;101:2200-05
3. Lexi-Comp Online™, Lexi-Drugs Online™, Hudson, Ohio: Lexi-Comp, Inc.; April 20, 2013.
4. Janarthanan S, Ditah I, Adler DG, et al. Clostridium difficile-associated diarrhea and proton pump inhibitor therapy: a meta-analysis. *Am J Gastroenterol.* 2012;107:1001-10
5. FDA Drug Safety Communications. Food and Drug Administration Web site. <http://www.fda.gov/drugs/drugsafety/ucm290510.htm>. Accessed April 20, 2013.
6. Guillamondegui OD, Gunter OL, Bonadies JA, et al. Stress Ulcer Prophylaxis. The Eastern Association for the Surgery of Trauma web site. <http://www.east.org/resources/treatment-guidelines/stress-ulcer-prophylaxis>. Accessed April 20, 2013.
7. Martindale R. Contemporary strategies for the prevention of stress-related mucosal bleeding. *Am J Health-Syst Pharm* 2005;62: S11-S17.

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Compounded Products: What Prescribers Should Keep in Mind

A previous Pharmacy News issue described a meningitis outbreak that resulted from New England Compounding Center, Framingham, Mass. On April 10, 2013, the Food and Drug Administration (FDA) announced that 30 more specialty pharmacies in the US, including some in the state of New Jersey, were cited for unsanitary conditions¹. The FDA Commissioner Margaret Hamburg asked Congress to pass a regulation requiring large compounding pharmacy to register with the FDA¹. Recent events show that it is important for prescribers to understand the regulations regarding compounding and the differences between compounded medications vs. commercially available drugs.

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Differences between commercially available drugs vs. compounded drugs².

	Commercially Available Drugs	Compounded Drugs
Oversight and jurisdiction	FDA as assurance of safety and efficacy	State Boards of Pharmacy
Drugs	Have package insert Tested in large scale clinical trials (brand products) Tested to be bioequivalent and therapeutically equivalent (generics) Generalizable onto specific patient populations Package insert lists warning, precautions, and side effects Can be shipped across state borders	No package insert Clinical evidence not robust (efficacy and safety) Drug interactions and adverse effects information may not be readily available Must be prepared pursuant to a prescription or in anticipation of prescriptions Must be prepared from pure ingredients Cannot be a replica of commercially available drugs Stability data may not be available
Preparation of drug	Manufacturer adheres to Good Manufacturing Practices enforceable by the FDA	Compounding pharmacy must fulfill requirements of State Board of Pharmacy and/or United State Pharmacopeia (USP) <797> and <795>
Liability	Manufacturer assures quality of a drug product	Compounding pharmacy for product quality, prescriber for use



Compounded Products: What Prescribers Should Keep in Mind

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Unless commercially available medication is cost prohibitive or if prescribers exhausted other options, it is safer not to prescribe extemporaneously prepared products. Dr. Sellers, PharmD, suggests that doctors should protect themselves from liability by verifying the credentials of the compounding pharmacy (recalls, citations, etc), the source of the active ingredient, and whether it is pharmaceutical grade for humans if they decide to use compounded medications for outpatients². Information on recalls may be found at the FDA website and New Jersey Board of Pharmacy website³⁻⁵. University Hospital Pharmacy Department uses primarily commercially available products. Only select medications are outsourced to compounding pharmacies (ex, TPN).

References:

1. Hamburg M. Proactive Inspections Further Highlight Need for New Authorities for Pharmacy Compounding. FDA Voice. <https://blogs.fda.gov/fdavoices/>. Published April 11, 2013. Accessed April 14, 2013.
2. Sellers S, Utian W. Pharmacy compounding primer for physicians: prescriber beware. Medscape Website. <http://www.medscape.com/viewarticle/776329>. Published December 19, 2012. Accessed April 14, 2013.
3. Pharmacy compounding. FDA website. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm#news>. Updated April 14, 2013. Accessed April 14, 2013.
4. Drug Recalls. FDA website. <http://www.fda.gov/drugs/drugsafety/DrugRecalls/default.htm>. Updated April 12, 2013. Accessed April 14, 2013.
4. State Board of Pharmacy, Med Prep enter voluntary agreement, extending halt to pharmacy's operations following recall. New Jersey Board of Pharmacy website. <http://www.njconsumeraffairs.gov/press/03222013.htm>. Updated April 8, 2013. Accessed April 14, 2013.

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Welcome to Two New Pharmacists



Greg Eilinger, Pharm D. graduated from Rutgers Ernest Mario School of Pharmacy in May 2012 and is happy to start his career as a staff pharmacist at University Hospital. Outside work, he enjoys movies, music, sports, travel and spending time with family and friends.



Shiao Wang, Pharm. D. is glad to be a part of University Hospital. He graduated from Rutgers in 2009 and practiced in community pharmacy in Washington D.C. for 4 years before joining University Hospital in May 2013. He enjoys music and theatre in his spare time.



IRB PHARMACIST SHU LIN RETIRES ON JUNE 30, 2013



After thirty-four years of dedicated service, the Pharmacy Department is both pleased and saddened to announce the retirement of our Investigational Drug Pharmacist, Shu Lin. Shu first joined the Pharmacy Department as an intern after earning her

Bachelor of Science in Pharmacy degree from Rutgers University. After obtaining her pharmacist license, Shu became a Staff Pharmacist at University Hospital, and then transitioned to her current position of Investigational Drug Pharmacist. For more than 10 years, Shu has been responsible for implementing and managing the medication protocols of clinical trials conducted at University Hospital and its associated outpatient clinics.

Shu has been an integral member of the Pharmacy Department and the UMDNJ Newark Campus Institutional Review Board (IRB). It has been noted that "Ms. Lin's contribution to the Newark Campus IRB and the manner in which she has discharged her duties have been exemplary...The many hours Ms. Lin devotes to review of research studies, performing the other duties of an IRB member, and in continuing education about regulatory changes, are above and beyond the norm." Members of the New Jersey Medical School faculty regard Shu as an essential element to the success of their clinical research programs. Within the Pharmacy Department, Shu is considered as a key member of our staff; she has strived to provide optimal patient care and to improve the pharmacy processes that guide our daily workflow. She is approachable, knowledgeable and tireless in her efforts to make the Pharmacy Department and the institution the best they can be.

To Shu,

We are truly honored to have worked with you over the years. Your loyalty and dedication to both University Hospital and the Pharmacy Department are greatly appreciated. We will remember your diligence and determination, always doing what is best for the patients and helping your fellow colleagues. Your great work

ethic has allowed you to make significant contributions to the Pharmacy Department and this institution throughout your career. You truly not only emulate the philosophy held within the department, but of the pharmacy profession as well. For these reasons, we are proud to celebrate and honor the many years of hard work and remarkable service you have given to University Hospital.

Your departure leaves behind mixed emotions for many. We are excited to see someone as deserving as you retire; however, you will be sorely missed. Deep within our hearts will forever remain the amazing memories we've shared and the remarkable relationships we have developed over the years. We are extremely grateful for your honest commitment to improving the lives of so many that were a part of your career. You are a true inspiration to all of us. Thank you for gracing us with your wonderful friendship over the years; you are one of a kind and can never be replaced.

Congratulations on your retirement! We wish you all the best as you begin the next chapter in your life.



