P&T Update

Formulary Addition/Deletion

Anti-Infective Subcommittee

P&T members discussed the formulary status of two tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccines: Adacel® and Boostrix®. Both vaccines are currently maintained on the hospital formulary. The subcommittee agreed to keep Adacel® as the formulary Tdap vaccine and remove Boostrix® from the hospital formulary based on comparable clinical efficacy and cost effectiveness. Delete Boostrix® from formulary – approved. Keep Adacel® as formulary item.

Rivaroxaban (Xarelto®) – formulary addition – approved

Rivaroxaban is an oral factor Xa inhibitor that selectively blocks the active site of factor Xa and does not require a cofactor (such as antithrombin III) for activity. It is FDA approved for prophylaxis of deep vein thrombosis (DVT) in patients undergoing knee or hip replacement surgery and to reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation patients.

Available formulary anticoagulants are subcutaneous enoxaparin (Lovenox®) and oral warfarin; subcutaneous fondaparinux (Arixtra®) is non-formulary. Studies comparing rivaroxaban to enoxaparin for DVT prophylaxis following knee or hip replacement surgery or warfarin for management of nonvalvular atrial fibrillation have demonstrated similar clinical outcomes.

Safety concerns with rivaroxaban were discussed, particularly the risk for major bleeding events. There is no reversal agent for rivaroxaban induced bleeding, and it is not dialyzable. Clinical trials have not identified significant differences in bleeding rates between rivaroxaban and enoxaparin or warfarin. It was recommended to restrict use of rivaroxaban to its FDA-approved indications.

Aflibercept (Eylea®) intravitreal injection – not approved

Aflibercept is a vascular endothelial growth factor (VEGF) inhibitor recently approved for the treatment of neovascular (wet) age-related macular degeneration (AMD). Formulary addition not deemed necessary at this time.

Bendamustine (Treanda®) – formulary addition – approved

Bendamustine (Treanda®) is a DNA-alkylating agent that has been in use in Europe for years to treat lymphoma. It was FDA approved in 2008 for treatment of chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin’s lymphoma (NHL) that has progressed during or within 6 months of treatment with a rituximab containing regimen.

Drug interaction precautions include use of CYP1A2 inhibitors (ex: ciprofloxacin) which may increase bendamustine concentration. CYP1A2 inducers (ex: carbamazepine) may decrease bendamustine concentration.

(Continued on page 2)
P&T Update (Continued from page 1)

Fosaprepitant dimeflumine (Emend®) 150mg injection – line extension – approved

A line extension request for fosaprepitant dimeflumine (Emend®) 150mg injection was presented. The formulary addition of this medication was approved by the Oncology Sub-Committee.

Oseltamivir (Tamiflu®) 6mg/mL oral liquid – line extension – approved. A line extension request for oseltamivir (Tamiflu®) 6mg/mL oral liquid was presented. The manufacturer recently changed the concentration of the oral liquid formulation from 12mg/mL to 6mg/mL.

Tolvaptan (Samsca®) – Formulary addition – Not deemed necessary at present. Tolvaptan, a selective vasopressin receptor antagonists, is indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium < 125mEq/L) or less marked hyponatremia that is symptomatic and has not corrected with other modalities such as water restriction in patients with heart failure, liver failure, SIADH.

Menthol-benzocaine (Cepacol®) 3.6-15 mg lozenges – line extension – approved

Ceftaroline (Teflaro®) – formulary addition – approved with restriction to ID service approval and ID hospitalists. Ceftaroline is a new parenteral cephalosporin antibiotic approved for the treatment of acute bacterial skin and skin structure infections and community acquired pneumonia. It is the first beta lactam antibiotic to have activity against MRSA and common community acquired respiratory pathogens. It has no activity against enterococcus and Pseudomonas.


Autosubstitution of benazepril, fosinopril and ramipril to lisinopril incorporated into Automatic Therapeutic Exchange policy – Approval obtained from the Cardiology, Nephrology and Endocrinology services.

Amiodarone IV premixed bags (Nexterone® 150mg/100ml D5W – for code cart use only – approved

IV sotalol for code use only – line extension – approved

Formulary deletion of manufacturer discontinued medications – approved

1. Drotrecogin alpha (Xigris®) – Eli Lilly and Co. withdrew it from market due to PROWESS-SHOCK study failing to show improved survival.

2. Paregoric, camphorated opium tincture 2mg/5mL oral liquid. UH formulary option is tincture of opium 10mg/mL oral solution

3. Neomycin 125mg/5 mL oral liquid

4. Oseltamivir (Tamiflu®) 12mg/mL oral liquid

5. Thiopental sodium – all strengths

6. Menthol (Cepacol®) 3mg lozenges

Automatic rounding of Hepagam® (hepatitis B immune globulin) dose. Rounding of the Hepagam® (Hepatitis B immuneglobulin) doses to utilize the lower vial size of the 5ml vial as outlined in the Automatic Therapeutic Exchange policy was proposed to eliminate wastage of this expensive medication – Approval. Obtained from the liver transplant service. Member provided recommendation to express doses both in units and ml.

Alaris Smart Pump Changes PICU – IVF Guardrail changes, IVF bolus addition. Addition of IV fluid bolus to the PICU library and Guardrail changes of IVF rate to hard max of 700ml/hr, soft min/max rates of 0.1ml/hr and 101ml/hr, respectively Tham® (tromethamine) – Continuous infusion in adult ICU Addition of Tham® (tromethamine) to the adult ICU library.

831-200-057 Patient care incident reporting – revision – approved

The patient care incident reporting policy was revised to categorize medication errors and adverse drug reactions using the AHRQ Harm Scoring System.

The Agency for Healthcare Research and Quality (AHRQ) harm scale is intended: 1) to measure an event’s impact on a patient’s functional ability, including quality of life; and 2) to be applied after any attempt to prevent, reduce, or halt the progression of harm to following the event. The AHRQ harm scale simplifies a complex situation by collapsing into a few scale points multiple dimensions, including 1) the

(Continued on page 3)
Deferiprone Approved by FDA for Iron Overload

Iron overload is responsible for the majority of the morbidity and mortality associated with thalassemia.1 When iron from transfused red blood cells can no longer be stored in reticuloendothelial macrophages, it is released into the plasma.2 There, transferrin binds the free iron. After transferrin is saturated, hepatocytes store additional iron. If there is still excess iron after storage by hepatocytes, free iron starts to exist in the plasma. Eventually, it enters and forms deposits in cardiomyocytes, hepatocytes, anterior pituitary cells and pancreatic beta cells. Free iron is also responsible for the accelerated production of damaging free radical species.1

Chelating therapy can double the life-expectancy of a patient with thalassemia.1 The mechanism of action involves forming a complex with iron to allow for excretion. The most commonly used agent is deferoxamine. However, disadvantages of deferoxamine use include its route of administration (parenteral only) and adverse effects (increased risk of infection, infusion reactions, growth retardation).2 Deferasirox is another chelating agent that has the advantage of an oral route of administration.

The US Food and Drug Administration recently approved Ferriprox® (deferiprone) for the treatment of iron overload from transfusions in patients with thalassemia and when current chelation therapy is insufficient.3,4,5 The advantages to using this agent are its oral route of administration, its ability to remove intracellular iron, and an increased ability to remove myocardial iron.3 Its limitations are its adverse effects, which include hepatotoxicity, agranulocytosis, and zinc deficiency.6

(Continued on page 4)
Recent studies have shown that the oral diabetic drug metformin (a biguanide), prescribed for the treatment of Type 2 diabetes, is showing promising signs of cancer treatment potential. This was first observed in epidemiological studies of diabetics who had cancer. In one of the largest studies of its kind, a team of researchers analyzed cancer risk among 8,000 diabetics treated with metformin. Over a ten year period, a 54% lower incidence of all cancers compared to the general population was observed. Not only did it exert a major protective effect against cancer development, but a higher survival rate with those who developed cancer of the lung, colon, and breast. Of equal significance was the finding that the earlier the metformin regimen was initiated, the greater the preventive benefit.

In a recent study lead by Dr. Ryan J. Dowling of the Ontario Cancer Institute at University Health Network, Canada, the epidemiological, preclinical, and clinical evidence all give a green light signal for metformin’s use as an anticancer drug. Other supportive studies involving 12,000 patients have shown metformin users died of cancer 30% less than those taking sulfonylureas (glyburide, glipizide). Of even greater significance, insulin users had a 90% greater death rate than metformin users in that study. Clinical analysis has confirmed that diabetics have as much as a 40% increase risk of all cancer types compared to healthy subjects. Elevated blood-sugar levels increase the risk of cancer including those of the kidney, pancreas, and skin.

At the cellular level, metformin activates AMP-activated Protein Kinase (AMPK), an energy sensor involved in regulation of cellular metabolism. Its dysregulation plays a role in diabetes and cancer initiation. Its anticancer effects are associated with both direct (insulin independent) and indirect insulin-dependent actions of the drug. Its indirect effects are mediated by AMPK inhibiting transcription of gluconeogenesis genes in the liver to stimulate glucose uptake in muscle, reducing fasting blood glucose levels. These insulin lowering effects play a major role in its anticancer activity since insulin has mitogenic and prosurvival effects. Tumor cells often express high levels of the insulin receptor, an indication of sensitivity to its growth promoting effects.

The direct insulin independent effects originate by activation of AMPK, leading to inhibition of (mTOR) signaling in protein synthesis, a key integrator of growth factor and critical mediator of the phosphatidylinositol-3 kinase/protein kinase (PI3K/PKB/AKT) signaling pathway, which is the most frequently deregulated molecular network in human cancer.

Further clinical research is necessary to identify key patient and tumor factors that govern metformin sensitivity, which is critical for the design of clinical trials and identification of patients best suited for metformin treatment. For example, patients exhibiting hyperinsulinemia and tumors expressing the insulin receptor LKB1 and TSC2 would benefit most from
Proton-pump inhibitors (Protonix®, Nexium®, Prevacid®, etc.) have several uses in both inpatient and outpatient populations. For hospitalized patients, they can be used for stress-ulcer prophylaxis, concomitant use with corticosteroids, and H. pylori eradication. A study at Massachusetts General Hospital1 showed that stress-ulcer prophylaxis is the most common reason for proton-pump inhibitors in hospitalized patients. However, several studies, including one by Gupta et al, showed that proton-pump inhibitors were inappropriately prescribed in 73% of patients.4 Stress-ulcer prophylaxis is indicated for all patients that are mechanically ventilated, have a traumatic brain injury, coagulopathy, or major burn injury. It is also indicated for intensive care patients with multiple traumas, sepsis, acute renal failure, or high-dose corticosteroids. Stress-ulcer prophylaxis is not recommended for general medical and surgical patients in non-ICU settings with fewer than two of the previously mentioned risk factors.5 When seeing the limited indicated uses for proton-pump inhibitors, it is easy to see how they can be overused in the hospital setting. Gupta et al also noted that of the 73% of patients inappropriately prescribed proton-pump inhibitors, 69% were discharged on the medication; 80% were taking the medication three months after discharge and 50% after six months.4

On February 8, 2012, the FDA released a Safety Watch to notify the public that the use of proton-pump inhibitors (PPIs) may be associated with an increased risk of Clostridium difficile-associated diarrhea (CDAD).3 PPIs work by increasing the pH of the gastric acid in the stomach, thus decreasing its irritating effects to the lining of the gastrointestinal tract. Clostridium difficile is unable to survive at normal gastric pH levels, but with the increased pH from PPIs, it is able to survive. This bacterium can survive on a moist or dry surface for up to 6 hours, leading to its transmission throughout a hospital.2

There is clinical data available to back-up the overuse of proton-pump inhibitors in hospital and outpatient settings.2,4,6-7 This increase in use of proton-pump inhibitors has coincided with the increased incidence of Clostridium difficile, leading to its association with each other. It is also worth noting that antibiotic prescribing and hospital hygiene have improved during this time, making this association even more likely.2

In conclusion, over-prescribing of proton-pump inhibitors leads to patients being on unnecessary medication and increases the risk of Clostridium difficile-associated diarrhea (CDAD). CDAD should be considered for all patients taking PPIs who develop diarrhea that does not improve. While this warning is not in package inserts, the FDA is working with manufacturers to make this a part of the drug labels.

Author: Tyler McCamish, PharmD

(Continued on page 6)
Proton-Pump Inhibitors: (Continued from page 5)


Updates for the Use of Hepatitis B and HPV Vaccinations

Hepatitis B Vaccine1-2

The Center for Disease Control and Prevention (CDC) has released new recommendations for the use hepatitis B vaccines (HBV) in adults with diabetes mellitus. The Advisory Committee on Immunization Practices (ACIP) came to this recommendation after a review showed that 25 of 29 outbreaks of HBV infection in long-term-care facilities involved adults with diabetes. The recommendation is for all previously unvaccinated adults aged 19-59 with diabetes (type 1 and 2) to be vaccinated against hepatitis B as soon as possible after a diagnosis of diabetes is made. There is less data to support vaccinating adults over the age of 60, so these patients are to be vaccinated at the discretion of their physicians based upon their likelihood of contracting the virus. Adults with diabetes are more prone to liver disease and are twice as likely to develop a chronic infection than people without diabetes.

HPV (Gardasil®)2

There has also been a recommendation for the human papillomavirus (HPV) vaccine in boys. The recommendation from the CDC suggests boys aged 11-12 and those up to 21 that have not yet been vaccinated, receive the HPV vaccine for a reduction in the risk of genital warts and precancerous lesions and the ability to pass HPV on to their partners. Gardasil® is recommended for boys, as Cervarix® is only approved for females.

Author: Tyler McCamish, PharmD


metformin therapy. Patients with normal circulating insulin levels and tumors lacking those insulin receptors would likely be unresponsive to the drug. The challenge is predicting how non-diabetic patients will respond to metformin and differentiating between its direct and indirect effects. Currently, a number of clinical trials are underway including studies in prostate, breast, endometrial and pancreatic cancer patients. The National Cancer Institute of Canada Clinical Trials Group is examining the effect of metformin vs. placebo in 3,500 patients with early stage breast cancer.6

Significant renal disease (serum creatinine > 0.16 mmoles/L), hepatic disease, alcoholism, and conditions associated with hypoxia (e.g. cardiac and pulmonary disease, surgery) are contraindications to metformin use. Significant mortality can result with drug-induced lactic acidosis. This is characterized by low pH in body tissues and blood considered a distinct form of metabolic acidosis. This potentially fatal adverse effect can lead to life-threatening complications such as shock.

In conclusion, the clinical safety, well-characterized pharmacodynamic profile, and low cost make metformin an ideal candidate as an anti-cancer agent.

References:

Contributed by: Joseph Licata, RPH

American Society of Health-System Pharmacists (ASHP) House of Delegates 2012 - Mr. Andre Emont

Congratulations to Mr. Andre Emont, RPh , MS, Director of Pharmacy for his 2-year term election by the New Jersey Society of Health-System Pharmacists (NJSHP) to the American Society of Health-System Pharmacists (ASHP) House of Delegates.

Mr. Emont is one of four distinguished hospital-based delegates to represent New Jersey in such a capacity. The House of Delegates is the ultimate authority over ASHP professional policies, which express the Society’s stance on important issues related to health-system pharmacy practice and medication use. ASHP’s professional policies contain varying levels of detail. Policy positions are short pronouncements on one aspect of practice. Statements express basic philosophy, and guidelines (including what were formerly called “technical assistance bulletins”) offer programmatic advice. Therapeutic position statements are concise responses to specific therapeutic issues, and therapeutic guidelines are thorough, evidence-based recommendations on drug use. The House of Delegates meets annually at the ASHP Summer Meeting, (this year in Baltimore) where it reviews policy proposals that have been approved by the Board of Directors. Most professional policies are initially drafted by ASHP Councils or the Executive Committee of Sections and Forums.

Mr. Emont’s dedication to the profession of Pharmacy on all levels demonstrates the strength and quality of Pharmacy leadership in New Jersey as well as nationally.

Respectfully submitted by Michael Chu, Pharm.D.
As a call to duty, we diligently made our way to attend the Rutgers Pharmacy Career Day. This annual event hosted by the Ernest Mario School of Pharmacy takes place at the Busch Campus Student Center in Piscataway, New Jersey. Historically, this event is heavily attended by major corporations, hospital organizations and professional societies and this year was no exception. This event provides NJSHP with the opportunity to speak with pharmacy students of all grade levels about their career options and opportunities available as members of NJSHP. This year’s Career Day has also addressed obstacles to students because of the economic uncertainties of today’s job market.

The current market environment strengthens our opportunity as a professional pharmacy organization to show students that NJSHP has the unique ability and responsibility to be an ally to students and help them navigate through these unusually difficult times. NJSHP is uniquely positioned to accomplish this via the cumulative knowledge and expertise of its members. It is crucial to educate students and new graduates to see NJSHP not only as a source for CE credits but as an organization that can provide opportunities for professional growth through internships, mentoring and networking. The Rutgers Career Day offers NJSHP a unique opportunity for this open dialogue.

NJSHP’s participation in this event is crucial as we forge new relationships with those who will ultimately be at the helm of our profession.

Contributed by: Victor Pardo, Pharmaceutical Services Operations Manager.

Welcome Two New Pharmacists

Gwan Y. Jang, Pharm. D. obtained his doctor of pharmacy degree from St. John’s University College of Pharmacy in May 2011 and was previously working in a community pharmacy. Outside work, he is a pianist for his church and a keyboardist in a worship band. He spends most of his time in church.

Neerav Vaidya, Pharm.D. is excited to start his career at UMDNJ as a staff pharmacist. He earned his Doctor of Pharmacy degree in May 2011 from the University of the Sciences in Philadelphia. Outside of work, he enjoys going to the gym and spending time on outdoor activities.
Aztreonam (Cayston®): the Second FDA Approved Inhaled Antibiotic for Cystic Fibrosis

Cystic fibrosis is an autosomal recessive disease that primarily affects newborns of Northern European descent. Each year, about 1 out of 3,200 newborns are diagnosed with this disease in the United States. In cystic fibrosis, there is a constant buildup of sputum in the lungs, which puts them at risk of infection and ultimately the devastating complications of the disease. Over the past 30 years, the overall survival age has increased into the mid 30’s due to the advancement in research and improved medical treatments.1,2,3

The role of antibiotic therapy in the management of cystic fibrosis is to treat acute exacerbations of the infection caused by mainly the pathogen, Pseudomonas aeruginosa. The unique aspect of the antibiotic therapy for cystic fibrosis is the utilization of the inhalation route of administration. The rationale behind this formulation is to better target the site of infection and decrease risk of systemic toxicity.

According to the treatment guidelines established by the Cystic Fibrosis Foundation, they are not for or against the use of concomitant inhaled and IV antibiotics due to the lack of sufficient evidence. Because these patients are on chronic antibiotic therapy, the issues of cost, toxicity, and resistance come into consideration.4 Tobramycin (TOBI®) was the first nebulized antibiotic (aminoglycoside) that was FDA approved in 1997. It has been the only one of its kind in the market until recently with the FDA approval of the second inhaled antibiotic, aztreonam lysine (Cayston®) in 2010. The pivotal clinical trial was a randomized, doubleblind, placebo controlled, multicenter trial that evaluated the use of inhaled aztreonam in cystic fibrosis patients for 28 days.

The study analyzed clinical improvement through FEV1 values and quality of life via questionnaire pertaining to respiratory symptoms. Clinical improvement in FEV1 values in the treatment group was statistically significant; however the difference was more profound among the pediatric patients than the adult patients.5 From an adverse event perspective, inhaled antibiotics are not absorbed systemically, so the toxicity issues are less of a concern; however, there are currently no studies comparing aztreonam to tobramycin, so further studies are warranted in assessing the efficacy data of aztreonam to tobramycin. Hopefully, the use of inhaled antibiotics can improve survival and quality of life for cystic fibrosis patients.

References:
4. Flume PA, Mogayzel PJ Jr, Robinson KA, Rosenblatt RL, Quittell L, Marshall BC; Clinical Practice Guidelines for Pulmonary Therapies Committee; Cystic Fibrosis Foundation Pulmonary Therapies Committee. Cystic fibrosis pulmonary guidelines: pulmonary complications: hemoptysis and pneumothorax. Am J Respir Crit Care Med. 2010 Aug 1;182(3):298-306.
Contributed by: Regina Yoon, PharmD. Candidate of 2012, Rutgers University
Employee of the 1st Quarter

Polly Jen, Pharm.D., BCPS, ID Clinical Pharmacy Specialist

The Pharmacy Department is pleased to introduce another employee with the Employee of the Quarter Award for the first quarter of 2012. The Essential Piece Award this time around goes to Polly Jen, Pharm. D. BCPS, whom from day one has demonstrated to be a remarkable employee who continues to reveal her abilities. Polly joined UMDNJ in August 2009, and from that point on, the department has been very fortunate to have her on the Clinical Pharmacy staff as an Infectious Diseases Specialist. Polly has worked diligently to advance not only the Pharmacy Department, but also the education of medical students, residents, and fellows, especially within the Infectious Diseases Division. She has improved patient care and developed strong inter- and intra-departmental relationships. One of the ID attending physicians stated “Polly has become a central member of the daily ID consult service rounds. Her input regarding choice and dosing of antibiotics has become an integral component of decision making. In areas where the data are controversial, Polly frequently looks up relevant literature on the topic and contributes immensely to patient care. Most of all, her affable, easy-going personality make her extremely well-liked by everyone in the division.” Polly is a consummate professional. She is hard-working, dedicated, and tenacious in her ability to effect positive change at The University Hospital for the patients she serves. Her calm demeanor and soft voice hide the true warrior of healthcare within. She is a pleasure to work with and a great asset to our department. Congratulations Polly! Your enthusiasm and passion continue to motivate all of us.

Contributed by
Michael Chu, Pharm. D.
Clinical Pharmacy Manager

Welcome Two New Pharmacy Technicians

Jennifer Procell, CPhT, is thrilled to join UMDNJ as the Pharmacy’s newest pharmacy technician. She is a graduate of The Cittone Institute and is currently attending Middlesex County College, pursuing a degree in Chemistry. Jennifer was previously employed with Walgreens Pharmacy and overall, brings over six years of experience. Outside of work, she enjoys physical fitness activities, reading and spending time with her family.

David Narouz, CPhT, started as a staff pharmacy technician at UMDNJ in December of 2011. He is very passionate about the profession, and has strong hopes of continuing his journey to becoming a Pharmacist. David was one year shy of graduating from the College of Pharmacy in Egypt, and is taking this great opportunity to increase his knowledge and practice of the pharmacy profession, while working at The University Hospital, a teaching facility. Outside of work, David enjoys reading and traveling to different countries in order to enjoy new cultures.