THE UNIVERSITY HOSPITAL
Pharmacy News
UMDNJ The University Hospital
University of Medicine & Dentistry of New Jersey

Forth Quarter 2010
Vol. VII, Issue 4

Special Points of Interest:

- P&T Update
- Policy and Procedures Update
- New FDA Approvals
- 4th Quarter 2010 Employee of the Quarter

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P&T Update

Formulary Addition/Deletion

- Formulary class reviews – Anti-psychotics Trifluoperazine (Stelazine®, Loxapine (Loxitane®), Molidone (Moban®) due to no use, are recommended for UH Formulary Deletion – Approved
- Anti-depressants class review: no change to current Formulary – Approved
- Aminoglycoside Formulary class review: no change to current Formulary – Approved
- Tetracycline Formulary class review: no change to current Formulary – Approved

Formulary Transactions Requests

- Rifaximin (Xifaxan550®) – Rifaximin is a semi-synthetic, non-systemic antibiotic structural analog of rifampin. It acts on beta-subunit of DNA dependent RNA polymerase enzyme of bacteria to inhibit RNA synthesis. Rifaximin 550mg approved with restriction to hepatology service. Rifaximin 200mg – Not Approved
- Benzylpenicilloyl polylysine (Pre-Pen®) – is a diagnostic skin test antigen. It is to test specifical reacts with benzylpenicilloyl IgE antibodies. Patients with IgE antibody to PCN will result in the production of chemical mediator and produce positive skin test of immediate wheal and flare reactions at the skin test site.
- Pre-Pen approved with restriction to Allergy & Immunology approval.
- Moxifloxacin ophthalmic soln 0.5% (Vigamox®) – is a 4th generate Fluorquinolone with activity against gram-positive & gram negative bacteria. The antibacterial activity is through inhibition of DNA gyrase and DNA topoisomerase IV which are involved in DNA replication, transcription and repair of bacterial DNA. moxifloxacin (Vigamox®) – Approved
- Remifentanil 5mg injection line extension – Anesthesiology section requests for Formulary line extension on remifentanil to include 5mg vial to use in long neurosurgical cases. Remifentanil 5mg line extension – Approved
- Amylase/Lipase/Protease (Pancrease®), Measles Vaccine Live (Attenuvax®), and Rubella vaccine (Meruvax®) formulary deletion – Approved

Polly Jen, Pharm.D. Becomes Board Certified Pharmacotherapy Specialist (BCPS)

Polly Jen, the Infectious Diseases Clinical Pharmacy Specialist, received board certification in the specialty of Pharmacotherapy.

The Board of Pharmacy Specialties (BPS) is an independent non-governmental certification body that provides recognition of persons involved in the advanced practice of pharmacy specialties. The organization establishes standards for certification, develops effective certification programs for specialty practices in pharmacy, and grants qualified pharmacists certification. The primary purpose of specialization is to improve the quality of care of patients and promote positive treatment outcomes. Pharmacotherapy is the area of pharmacy practice that is responsible for ensuring the safe, appropriate, and economical use of drugs in patient care. As a clinical pharmacy specialist, Polly participates in direct patient care and serves as a primary source of drug information for other healthcare professionals. As a Board Certified Pharmacotherapy Specialist, she will continue collaborate with other healthcare professionals to optimize patient care and treatment outcomes at The University Hospital.

Congratulations Polly!

Future of Pharmacy: Medication Therapy Management

The role of a pharmacist has been expanding with changes in the healthcare environment. From a solely dispensing standpoint with medication-oriented knowledge to a patient-oriented clinical approach, the responsibilities of a pharmacist have broadened with the advancements in technology and changes in legislature. Big steps in the past include the introduction of the Pharm.D. degree, development of clinical clerkships, involvement in investigational drug studies, and board certification for subspecialties among others. The most recent advancement in the profession is the increasing role in medication therapy management (MTM). MTM is a collaboration between healthcare providers to ensure optimal therapeutic outcomes for the patient via the safe and effective use of medication. As the most accessible healthcare professional, it makes sense for the pharmacist to be the center of care in medication therapy management.

In the hospital, it has clearly been the pharmacists' role to manage patients' medications as they profile new orders. They need to identify patients at risk for adverse events and monitor patient safety and medication efficacy. Once a patient is discharged, the community pharmacist is in the perfect position to reinforce medication adherence and continuity of care. According to a 2009 report from the New England Healthcare Institute, the overall cost of poor medication adherence is as much as $290 billion a year, or 13% of total healthcare expenditures. MTM in the community is essential to future of healthcare as it will improve outcomes, reduce costs, and manage risk.

Challenges to providing MTM including training students and current pharmacists, finding the right balance between counseling and dispensing, educating patients to the services available to them, and developing models for providing and receiving reimbursement for these services. With the healthcare reform on the horizon, pharmacy organizations are working to increase patient-centered care and urging for more recognition of the pharmacist's role in MTM. As the population ages and medications become more complex with genetic advances, pharmacist will surely be in the forefront to provide MTM and patient care.

Contributed by:
Linda Wang, PharmD. Candidate 2011

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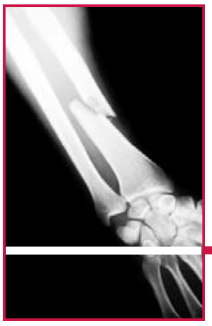
Blank, Christine. "Medication adherence: NACDS urges acknowledgement of pharmacists' role." Drug Topics. Published Online Nov 1 2010. http://drugtopics.modernmedicine.com/drugtopics/Associations/Medication-adherence-NACDS-urges-acknowledgment-of/ArticleStandard/Article/detail/693414?contextCategoryId=47443

Increased Risk of Bone Fracture with Bisphosphonates

The FDA is warning patients and health care providers of an increased risk of a typical femur fracture, a rare but serious thigh bone fracture, in patients taking bisphosphonates. The warning will be reflected in labeling changes and medication guides for those only for osteoprosis. Bisphosphonates reflecting this change are Fosamax, Fosamax plus D, Actonel, Actonel with Calcium, Bonvia, Atelvia, their generic counterparts and injectables such as Reclast and Bonvia. However, changes to labeling and medication guides will be made for bisphosphonates indicated for Paget's disease or cancer/hypercalcemia such as Didronel, Zometa, Skelid and their generics.

Bisphosphonates are a class of drugs that inhibit bone mass loss in patients with osteoporosis. They have been shown to reduce the rate of osteopathic fractures which can result in pain, hospitalization and surgery. It is not clear whether bisphosphonates are the primary cause of femoral fracture but they have been predominately reported among patients prescribed them. One reason for this may be the uncertainty in treatment induration. Currently there is no optimal duration of bisphosponate use for osteoporosis and fractures may be related to use of more than five years.

The warning follows a March 10, 2010 Drug Safety Communication announcing the FDA's ongoing safety review of bisphosphonate use and the occurrence of atypical femur fractures.The FDA has since reviewed all available data on the bisphosphonate use, including data summarized in the American Society for Bone Mineral Research Task Force report. The report recommended additional product labeling, better identification and tracking of patients experiencing these fractures and more research to determine whether and how these drugs cause atypical femur fractures. The FDA recommends that physicians consider periodic re-evaluation of the need for continued bisphosphonate therapy for patients who have been prescribed for more than five years. Patients and health care providers should report any cases of atypical fracture to the FDA's MedWatch Adverse Event Reporting program.



Contributed by:
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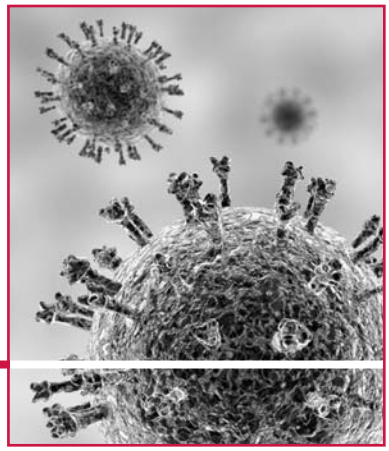
Influenza in Solid Organ Transplant Patients: Staying One Step Ahead

There has always been prevailing concern about the risk of influenza infection in patients with immunosuppression, such as Solid-Organ Transplant (SOT) patients. It is estimated that up to 17% of SOT patients suffer from respiratory infections caused by the flu. Unfortunately, no concrete data concerning the management of infection in this population existed until recently. An August 2010 trial has compiled data about common symptoms and therapies in SOT patients with influenza.

Common symptoms include cough, fever, muscle pain, runny nose, sore throat and headache. Influenza is especially dangerous for transplant patients because it can lead to other serious complications. The American Society of Transplantation recommends vaccines for patients after transplant annually. Over half of the patients had received a vaccination before they caught influenza, so even though getting the vaccine is important, it did not always guarantee that patients would be safe from disease. A strong immune system is necessary to gain the defense that vaccines are designed to provide. However patients that have immune dysfunction may not elicit the same response from a vaccine as a healthy patient, despite the fact that they are at greater risk at getting the flu. Patients and family members should ask their health-care providers if getting vaccinated is for them. The most important finding of this study showed that starting antiviral treatment within 48 hours within symptom onset was associated with a decrease in hospital/ICU admission, mechanical ventilation and death. Healthcare professionals may start medication empirically before blood tests confirm flu or treat post exposure if there was a family member with flu in the house.



It is important for SOT patients to keep open dialogue with their health care providers. Patients should be educated on how to identify flu symptoms, what should be done if they suspect flu, and what to expect if diagnosed with influenza. Health care providers should discuss the risks and benefits with patients on the use of aggressive antiviral treatment and the flu vaccine each year. These steps will increase awareness and facilitate more successful control of influenza in the SOT population.

Contributed by:
Vishal Amin Pharm D. Candidate 2011

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Adherence to Oral Contraception in Women on Category X Medications

A recent study by Medco Health Solutions evaluated the oral contraceptive adherence of women taking teratogenic medications. The study used prescription claims of 6 million women of childbearing age between January 1, 2008 and June 30, 2009 and calculated the medication possession ratio (MPR) of each patient. The MPR is the number of days that the patient had a supply of her contraceptive divided by the total number of days. The MPR of women prescribed Category X drugs was compared to women not taking these kinds of medications. Category X drugs have been shown to cause fetal harm in animal or human studies and are contraindicated in pregnancy. Some commonly prescribed Category X medications include statins, warfarin, retinoids, and methotrexate.

This study aimed to evaluate if women are adherent with oral contraceptives while taking these teratogenic medications. Adherence levels were defined based on MPR as low (0-79%), moderate (80-94%), or adherent (95-100%). Ninety-five percent was chosen as the cutoff for adherent because missing more than 2 pills in a month greatly increases the risk of pregnancy. In the study population, 6.2% (146,758 women) were taking Category X medications. Of these women, 17.8% were also taking oral contraceptives. Adherence levels were high in 59.8%, moderate in 21.7%, and low in 18.5% of women on Category X medications. These adherence levels are very similar to women not taking Category X medications.

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Adherence to Oral Contraception in Women

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About 6% of US pregnancies occur in women who are known to be taking teratogenic medications. The results of this study show that many patients on these medications may be unaware of the risks associated with these drugs. Therefore, counseling on these medications should always include a conversation about the risk of fetal harm and pregnancy prevention. Pharmacists can play a major role in this situation by increasing awareness of the potential harms that these medications can cause. Pharmacists should ensure that patients understand these risks before taking these medications and also understand that improper use of oral contraceptives will increase the risk of pregnancy. Even though oral contraceptives are the most common form of birth control used by women on teratogenic medications, other options exist and should be utilized if appropriate. If patients are having difficulty remembering to take oral contraceptives and are concerned about the risk of pregnancy, pharmacists can provide assistance by suggesting alternative birth control methods that patients can discuss with their physicians.

Contributed by:
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GLP-1 Receptor Agonists and DPP-4 Inhibitors for Type II Diabetes

Current GLP-1 Receptor Agonists and DPP-4 Inhibitors Options:

- **(Byetta™)** is an injectable GLP-1 receptor agonist used for Type 2 diabetes mellitus (T2DM). It is administered BID SC in doses of 5 or 10 ug within 1 hour before the two major meals of the day. Exenatide has drug interactions with warfarin (increased INR is possible so monitor INR). If severe renal impairment or ESRD is present then discontinue exenatide.
- **Sitagliptin (Januvia™)** is the first oral DPP-4 inhibitor approved for adjunctive therapy for T2DM. The recommended dosage is 100 mg once daily with or without food. Sitagliptin has drug interactions with digoxin (monitor digoxin level, but no dosage adjustment is necessary). Renal insufficiency or ESRD require dose adjustment. A combination of metformin and sitagliptin **(Janumet™)** is available. Contraindications to Janumet™ include: renal dysfunction, metabolic acidosis, and radiologic studies involving IV administration of iodinated contrast materials. Janumet™ has interactions with cationic drugs eliminated by renal tubular secretion (use with caution). Do not use Janumet™ in hepatic disease.
- **Saxagliptin (Onglyza™)** is an oral DPP-4 inhibitor for T2DM, has not been studied with insulin. Recommended dose is 2.5 mg or 5 mg once daily taken regardless of meals (2.5 mg once daily is recommended for patients with moderate or worse renal impairments or when patient is also on medications that are strong CYP3A4/5 inhibitors).
- Exenatide, sitagliptin, and Janumet™ must be discontinued if pancreatitis is present. All medications have an increased risk of hypoglycemia.

GLP-1RA and DDP-4I in Treatment Algorithms:

- In the 2007 **AACE medical guidelines,** exenatide was recommended for combo therapy with metformin, a sulfonylurea, and/or a TZD. Sitagliptin was recommended for use as monotherapy or in combo with metformin with TZD. (http://www.aace.com/pub/pdf/guidelines/DMGuidelines2007.pdf)
- In the 2009 **American Diabetes Association (ADA) and the European Association for the Study of Diabetes** algorithm for T2DM patients, GLP-1 receptor agonists were considered appropriate in certain clinical scenarios such as when hypoglycemia or weight loss was a major concern during treatment. (http://care.diabetesjournals.org/content/29/8/1963.full)
- In clinical "road maps" developed by **AACE and the American College of Endocrinology,** for T2DM patients who were naïve to therapy, DPP-4 inhibitors were recommended as first options when initial HbA1c is 6.0-7.0% and as a combo component when HbA1C is 7.0-9.0%. For patients on monotherapy for 2 to 3 months and who have HbA1c between 6.5-8.5%, DPP-4 inhibitor with metformin or TZD, or a GLP-1 receptor agonist with TZD, metformin, and/or a sulfonylurea is recommended.

Contributed by:
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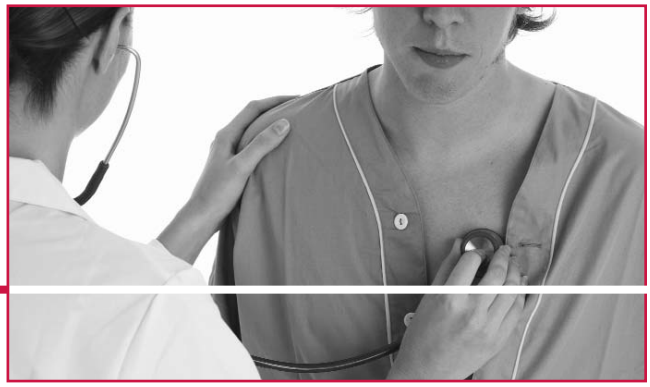
Are We Ready to Say "Good Bye" to Warfarin? Dabigatran versus Warfarin in Patients with Atrial Fibrillation (Re-LY Trial)

Dabigatran etexilate (Pradaxa®, Boehringer Ingelheim) is a newly FDA approved antithrombic agent that may replace warfarin as the primary antithrombic therapy to prevent strokes in patients with atrial fibrillation.



Despite its effectiveness, Warfarin increases the risk of intracranial hemorrhage and also is cumbersome to use due to its frequent lab monitoring, variable individual dosing, and food/drug interactions.[1] A recent study shows that 22% of the patients were non-adherent to the warfarin therapy.[2] On the other hand, dabigatran, a direct thrombin inhibitor, does not need to be monitored as frequently and has a fixed dosing of 150 mg BID for most atrial fibrillation patients.

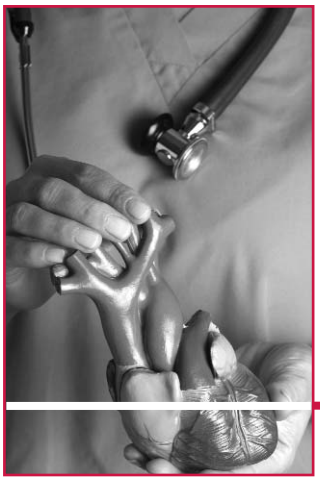
Dabigatran etexilate is a prodrug with a rapid absorption that becomes hepatically metabolized into dabigatran, the active form. Dabigatran requires low pH to be absorbed, and consequently contains a tartaric acid core. Its half life is 12-17 hours, with a time to peak of 1 hour and 2 hours with food. There is currently no reversal agent, therefore the dose should be withheld 1-2 days (CrCL>50) or 3-5 days (<50)before surgeries, Due to its predominant renal excretion (80%), dose should be adjusted to 75 mg BID in patients with CrCl of 15 - 30mL/min. [1]

In 2009, Re-LY trial compared the two blinded doses of dabigatran 110 mg BID or 150mg BID to the unblinded doses of warfarin determined by the patients' INR levels.[1] The study participants had an average age of 71 years old and almost two-thirds of them were male. The study showed that dabigatran 110mg was noninferior in the number of incidence of stroke when compared to warfarin, while 150mg showed a decrease (1.56%/yr vs 1.01%/yr).

Intracranial bleeding, was lower in 110 mg and 150mg of dabigatran when compared with warfarin (0.23%/yr, 0.30%/yr, 0.74%/yr respectively). Major bleeding in dabigatran 110mg was also lower than warfarin (2.71%, 3.36%). It is important to notice that the rate of major bleeding for warfarin was much higher in this study than the previously reported by the same author (1.78% to 2.92%).[3] This is most likely due to high aspirin use in both dabigatran and warfarin group (about 40%). However, aspirin is not indicated concomitantly with warfarin in stroke prevention with atrial fibrillation patients unless the patient has mechanical heart valves. A study without such high aspirin use may be warranted to obtain a more realistic comparison.[3]

Dabigatran had a higher myocardial infarction rate when compared with warfarin (0.71%/yr vs 0.53% yr). Although difference of 0.2% may seem small, there are approximately 2.3 million adults with atrial fibrillation, and a substantial amount of patients may be affected.[3] Interestingly, the discontinuation percentage at 2 yrs were higher in dabigatran groups compared to the warfarin group. The most frequent adverse event that occurred for dabigatran was dyspepsia.

Dabigatran 150mg BID, with its lower incidence of strokes and intracranial bleeding, combined with its fixed dosing schedule, holds a strong promise in becoming an effective alternative, perhaps a primary treatment option in the prevention of strokes in atrial fibrillation patients. However, the significant increase in myocardial infarction and the lack of antidotes for dabigatran toxicity may warrant a second consideration.



Contributed by:
Tae H Kim, PharmD Candidate of 2011

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Employee of the 4th Quarter

Asma Zohny, Pharm. D.

It is our pleasure to bring to you the pharmacy's year ending employee of the quarter. Regardless of the challenge our recipient has remained committed to doing her best year around. Asma Zohny is presented with the Essential Piece award and we agree that it is well overdue.

We all agree that Asma is very dedicated, cooperative, diligent and sweet spoken. She is dependable, shows leadership when need be and has a great attitude that we could all learn from. Please join us in congratulating Asma for a job well done.

Keep up the good work.

Contributed by
Tara R Shaw
Lead Pharmacy Technician

IRB & Me

I am proud to be a member of the UMDNJ Institutional Review Board (IRB). The members of this federally mandated board are each charged with the responsibility of ensuring that patients' rights are protected when they participate in clinical research at The University Hospital.

As a student pharmacist/technician and co-inventor on 4 pharmaceutical patents, I bring a unique perspective to the IRB. Shu Lin RPh, Bruce Ruck PharmD, and I provide a well rounded voice of the pharmacy department during board meetings with other healthcare providers, scientists, and patient advocates. At these meetings we review the potential risks and benefits outlined in the study protocols as well as the informed consent documents which all patients sign prior to participating in research studies.

My experience with the IRB has shown me the important role that the pharmacy department plays in both clinical care as well as clinical research. I have witnessed first-hand how pharmacists can use their medication expertise to identify drug-drug interactions, drug-disease state interactions, and other potential risks to patients receiving experimental therapy. We also play an important role in identifying the potential benefits of participating in research at UMDNJ. These benefits are often far-reaching. They may improve the health and well being of the individual patients participating, and also provide information which may help future patients, extending these benefits to society at large.

Before joining The University Hospital as a pharmacy technician per diem, I resigned from a medicinal chemistry research position with Merck in order to pursue a PharmD at Rutgers University. At Merck I was the first chemist to "test-pilot" the e-lab notebook which was later transitioned into use by all basic research departments.

I look forward to sharing this experience as the IRB transitions to the new e-IRB. This new electronic system is designed to allow board members to more efficiently protect the rights and welfare of our community. The e-IRB will increase our access to information as we continue to review the cutting edge research conducted by New Jersey's experts in medicine.

Contributed by:
Marc D. Chioda
PharmD class of 2013