CLINICAL PHARMACIST SPOTLIGHT

Clinical Assistant Professor and Ambulatory Care Pharmacist
Rebecca H. Stone, Pharm.D., BCPS, BCACP
By Stella Hur, Pharm.D. Candidate

What made you choose to be an ambulatory care pharmacist?
I really enjoy working with people, and I selected an ambulatory care setting so I can work closely with patients. I am able to see the same patient multiple times, and this gives me a chance to really get to know them. I get satisfaction from seeing the patients improve their chronic conditions, and I am able to participate in this process through medication management and patient education. Working in academia also allows me to work closely with students, and I appreciate the variety of experiences I encounter in this role.

What are your current academic and research interests?
My research primarily focuses on women’s health in the ambulatory care setting. I am most interested in women’s access to contraception, medication use during pregnancy, and access to women’s specialty medication during pregnancy. Right now, my research is evaluating Georgia pharmacists’ provision of patient counseling for emergency contraception. Hopefully, this project will allow us to identify any issues that patients may encounter when accessing emergency contraception from the retail pharmacy. Ultimately I would like to use this information to create a continuing education program (CE) for Georgia pharmacists and technicians.

Why is it important for a student pharmacist to understand women’s health?
Women make up half of the population. Community pharmacists are accessible and often engage with healthy women of reproductive age who may not be receiving regular care at a physicians office. Pharmacists are the front line and are well positioned for intervention and education regarding many types of Women’s Health issues.

Which professional organizations are you involved in, and how have they helped you grow as a pharmacist?
As a clinical pharmacist, I think American College of Clinical Pharmacy (ACCP) has been most the helpful organization for me. I am currently the Vice Chair for the Women’s Health Practice Research Network (PRN) in ACCP. It gives me a unique opportunity to network with other people who have similar practice and research interests. I have had multiple opportunities to author publications and participate in Women’s Health focused projects because of my connections through ACCP. The ACCP PRNs are a great way to get to know the leaders in the field.

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Rivaroxaban for prevention of bleeding in atrial fibrillation patients undergoing percutaneous coronary intervention (PCI)

By Ashni Patel, Pharm.D. Candidate

Atrial fibrillation (AF) is the most common form of arrhythmia in the United States, with an increased prevalence and incidence in elderly patients. Coronary artery disease (CAD) is one risk factor for AF, therefore, patients with AF often have coexisting CAD requiring percutaneous coronary intervention (PCI). Patients with AF undergoing PCI pose a clinical dilemma regarding appropriate anticoagulation therapy. These patients require dual antiplatelet therapy (DAPT); in addition to the fact that patients with AF require anticoagulation for prevention of stent thrombosis thromboembolism. Hence, AF patients undergoing PCI will require triple antithrombotic therapy, which significantly increases the risk for bleeding. New studies are being conducted to explore the use of newer oral anticoagulants in AF patients undergoing PCI to reduce the risk of bleeding.

The open-label PIONEER AF-PCI trial compared the standard therapy, warfarinΔ plus DAPT, with either low-dose rivaroxaban (15mg QD) plus P2Y12 inhibitor†† or very-low-dose rivaroxaban (2.5mg BID) plus DAPT. The primary safety outcome measured was clinically significant bleeding with secondary endpoints of all-cause mortality or recurrent hospitalizations. The trial found the groups using rivaroxaban had decreased bleeding compared to the warfarin plus DAPT group (P<0.001).

Additional post hoc analysis showed rivaroxaban groups had reduced hospitalizations related to bleeding and CV events and reduced all-cause mortality compared to the standard therapy. Limitations of the study should be kept in mind while interpreting the results. Dose reduced rivaroxaban has not been formally studied for efficacy in stroke prevention. The result that low dose anticoagulation causes lower bleeding should not come as a surprise. Although this trial has significant limitations, these findings pave the way for other trials to contribute to the currently limited evidence. Further research and testing in this area can lead to more streamlined regimens than compared to full dose triple antithrombotic therapy with warfarin leading to an assumed decrease in overall cost associated with reduced hospitalizations.

†P2Y12 inhibitor + low dose aspirin
††Clopidogrel, ticagrelor, or prasugrel
ΔWarfarin dosed to INR of 2 to 3


Probuphine: The first buprenorphine implant

By Baotran Van, Pharm.D. Candidate

The United States is in the middle of an unprecedented opioid crisis, affecting the communities, economy, and health systems of our country. Each year approximately 55 billion dollars in healthcare and social costs are associated with prescription opioid abuse, and 20 billion dollars in costs are attributed to emergency department and inpatient care for opioid poisonings. There was a record number of drug overdoses in 2014, with more than 60% of cases involving opioids, which resulted in 47,055 deaths. Though increased education and training of lifesaving treatments for opioid overdose, including naloxone use, cannot be understated, there is a continued need for improved treatment options to combat opioid use disorders. An estimated 2 million people were affected by these disorders in 2015. Opioid addiction is a complex chronic disease that affects brain circuitry and is characterized by reward seeking behavior, changes in perception and memory, and diminished judgment and behavioral control. Despite therapy including medication and psychosocial support, drug use dependence often involves multiple cycles of relapse and remission. Development of new strategies to address these high rates of relapse are necessary to reduce rates of opioid overdose and death.

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On May 26th, 2016, Probuphine was the first buprenorphine subdermal implant to be approved by the FDA as maintenance treatment for opioid dependence.¹ Probuphine provides six months of continuous low-dose buprenorphine via four ethylene vinyl acetate rods subdermally implanted into the upper arm. Each implant contains 80mg of buprenorphine, which acts as a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor to reduce opioid withdrawal symptoms and to reduce desire for further opioid use. Withdrawal can occur from abrupt discontinuation or in patients who have a dependence on full opioid agonists. Thus, Probuphine is only indicated for patients who have demonstrated sustained clinical stability on low-to-moderate doses of transmucosal buprenorphine-containing products as part of a treatment program that includes counseling and psychosocial support.²

Probuphine insertion and removal must be performed by a healthcare professional who successfully completed a live training program and is Risk Evaluation and Mitigation Strategy (REMS) certified. Rare, but serious complications from improper insertion can occur, and include nerve damage, protrusion, expulsion, and migration. Patients may experience administration-related side effects, including implant-site pain, pruritus, and erythema. Other treatment-related adverse events include headache, depression, constipation, vomiting, back pain, toothache, and oropharyngeal pain. Concurrent use of CNS depressants and sedative-hypnotics results in significant respiratory depression and serotonin syndrome, respectively. Patients who are elderly, pregnant, or have hepatic impairment or hepatitis should be monitored closely while using this medication.²

Compared to placebo, Probuphine has been shown to reduce opioid use and has demonstrated non-inferiority in maintaining abstinence compared to sublingual buprenorphine and sublingual buprenorphine/naloxone tablets.⁷⁻⁹ This implantable formulation of Probuphine shows potential benefit in addressing certain problems experienced with sublingual buprenorphine.

Probuphine essentially eliminates non-adherence and drug concentration fluctuations that may occur from the use of sublingual formulations, which are dosed daily. Like other opioid drugs, potential for abuse and misuse of Probuphine remains a concern. However, the implant poses more resistance to diversion than its sublingual counterpart. Though more studies are needed to broaden its scope of use and clarify its place in therapy, Probuphine, as part of a complete treatment program, shows promise for the maintenance of opioid dependence.


"MORE THAN 60% OF CASES INVOLVING OPIOIDS, WHICH RESULTED IN 47,055 DEATHS"
NEW DRUG UPDATE

Bezlotoxumab (Zinplava™) Antitoxin Agent  
By Justin Moore, Pharm.D. Candidate

**Indication**: Adjunct to concurrent antibiotic therapy to prevent recurrent *Clostridium difficile* infections (CDI) in high risk adults

**New Drug Comparison Rating (NDCR)** = 5

**Comparable drug(s)**: n/a

**Disease State/Drug Class Summary**: Recurrent C. difficile infection is defined by subsequent return of disease after resolution of CDI symptoms with appropriate antibiotic therapy which occurs in up to 35% of patients and contributes to increased hospitalizations, diminished patient outcomes, and higher healthcare costs. Risk factors for recurrent CDI include age greater than 65 years, concomitant antibiotic treatment for CDI, lack of response to CDI toxins, and underlying comorbidities. These infections are associated with the presence of toxins A and B circulating in the body. As a monoclonal antibody, Bezlotoxumab neutralizes toxin B, which is believed to be beneficial in the prevention of recurrent CDI when used in addition to antibiotic therapy.

**Efficacy**: In two placebo-controlled studies, MODIFY I and MODIFY II, the rates of recurrent CDI were 17% versus 28% (P<0.001) and 16% versus 26% (P<0.001) in favor of single-dose bezlotoxumab over placebo, respectively. Along with concurrent standard-of-care antibiotic therapy, use of 10 mg per kilogram doses of bezlotoxumab was associated with a 38% lower rate of recurrent infection compared to rates with placebo. Of those patients who had one or more risk factors for CDI, bezlotoxumab therapy was consistently associated with lower rates of recurrence and sustained clinical responses, defined by a clinical cure of CDI and no CDI recurrence for 12 weeks following therapy.

**Most important risks/adverse events**: Heart failure (weigh risk vs. benefit in patients with preexisting congestive heart failure; cardiovascular function should be monitored during therapy); infusion-related reactions, mostly mild to moderate and included nausea, vomiting, headache, fatigue, fever, and hypertension (monitor and treat as necessary)

**Most common adverse events**: Nausea (6.6%), diarrhea (6%), pyrexia (4.6%), headache (4.5%), abdominal pain (4.3%), urinary tract infection (4.1%), vomiting (3.9%),

**Advantages**: May be beneficial to prevent recurrent CDI in patients who may have risk factors and are currently taking antibiotic therapy for CDI. Drug-drug interactions are not expected to occur as bezlotoxumab is eliminated via catabolism. May be used in patients with severe hepatic or renal impairment. No dose adjustments are necessary in elderly patients greater than 65 years old.

**Disadvantages**: Heart failure and cardiovascular-associated death have been infrequently reported in clinical studies and benefit must outweigh risk prior to use in patients with preexisting congestive heart failure. Patients under the age of 18, as well as pregnant and nursing women, should not use bezlotoxumab as its safety and efficacy in these populations has not been established. This drug is not indicated for the treatment of CDI and should only be used in combination with antibacterial therapy.

**Usual dosage**: Recommended single dose of 10mg/kg administered as an intravenous (IV) infusion via central or peripheral line over 60 minutes. Do not administer as IV bolus. Repeated administration of bezlotoxumab in patients with CDI has not been studied.

**Available Products**: Injection - 1,000 mg/40 mL (25 mg/mL) solution as single-dose via

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Having too much fun: Importance of missed drug interactions

By Sendy Tran, Pharm.D. Candidate

A pharmacist dispenses Viagra (sildenafil) to a new patient. One month later, the patient is hospitalized due to a hip fracture from a fall. He took sublingual nitroglycerin tablets upon experiencing chest pain, became dizzy, and fell, breaking his hip. He also took Viagra the previous night. Both sildenafil and nitroglycerin are vasodilators, decreasing blood pressure. The synergistic hypotension increases the risk of falls and injury from the fall. Since the patient was vacationing when he filled sildenafil at the pharmacy, the pharmacy did not have the patient’s complete medication profile. The pharmacy staff was too busy to request a complete patient profile to identify that the patient was also on the nitroglycerin. The pharmacist missed the interaction between the sildenafil and nitroglycerin.

The majority of drug interactions is one drug inhibiting or inducing the metabolism of another drug, thus increasing or decreasing, respectively, the effected drug’s concentration. Too much drug increases the risk of toxicity or too much of the pharmacologic effect. Too little drug means the patient is not receiving adequate pharmacologic benefit.

The Chicago Tribune Media Group revealed that pharmacists missed drug interactions half the time. Reporters brought two prescriptions of drugs to chain and independent pharmacies in the Chicago area. Some pharmacists overlooked the interactions between these medications: clarithromycin-ergotamine, simvastatin-clarithromycin, colchicine-verapamil, tizanidine-ciprofloxacin, and norgestimate/ethinyl estradiol-griseofulvin. Due to an increased concentration of the effected drug, the first three lead to potentially fatal effects of gangrene or stroke, muscle tissue breakdown and kidney failure, and multiple organ failure, respectively. The fourth interaction causes synergistic hypotension, similar to the sildenafil-nitroglycerin interaction. The fifth may lead to unplanned pregnancy due to the decreased effectiveness of the oral contraceptive.

All the patient wanted was to have fun with his wife and took nitroglycerin as prescribed when he had chest pain, but then he was hospitalized with a hip fracture. At least, the pharmacist really dispensed sildenafil and not some other drug. With that being said, humans make mistakes. Part of being a pharmacist is making sure those mistakes are addressed appropriately to prevent future problems, including potential lawsuits. Pharmacists may not be aware a problem exists; therefore, proper systems should be implemented to catch any potential problems.
2. Prepare for the interview:
Prior to the interview, reach out to current residents to obtain an impression of the program if you may know them or chat with them at residency showcases or meetings. A large portion of your residency training will include interactions with your preceptor as well as physicians, so learn about the relationship the residents foster with these individuals. How often do doctors utilize the pharmacist’s recommendations? What does a typical day look like? You are interviewing the program just as much as the selection committee is interviewing you, and displaying your genuine interest in their program will leave a positive impression. Have questions for the interviewer when the day of your interview arrives, and be prepared for “throw off” questions such as “what is the most important drug on earth, if you were a drug, what would you be and why?” These are designed to see a candidate’s thought process and how adaptable one may be in a difficult situation. If you are at all anxious about your abilities, sign up for a mock interview with the career center or SCCP to further sharpen your expertise.

3. Evaluate your goals: Think about your career path and how a residency will assist you in accomplishing your goals. Many programs may be located out of state, which can be a fresh experience for some while an obstacle for others. Keep in mind that pharmacy residencies also require significant time commitments as well as lesser financial compensation compared to those who begin to work immediately upon graduation. Think about your motivation for pursuing a residency. If you are in pursuit of a subject you are passionate about, the path to a residency becomes more clear, and you will have an easier time making the process work for you.


As to how to save lives, Dr. David Holdford prefers the systems thinking approach. Systems thinking implies each problem has complex causes, and the solutions have intended and unintended consequences. If pharmacist miss drug interactions because they are too busy, then will pharmacists catch drug interactions with more time? Probably not. Redefine the problem statement to focus the problem and to reach an appropriate solution. Reassess the progress periodically to ensure quality improvement and to ensure no drug interaction goes out the pharmacy’s door unaddressed.


Penicillin allergy testing cuts antibiotic use

By Tim Jones, Pharm.D. Candidate

Approximately 10% of all U.S. patients report having an allergic reaction to a penicillin antibiotic. However, when evaluated, less than 1% of the population has a true penicillin allergy. A true penicillin allergy would consist of an IgE-mediated hypersensitivity reaction. The problem occurs when many patients report various non-allergic reactions to penicillin products, which may or may not even be related to penicillin itself. In addition to the low amount of true allergies, only about 20% of patients will retain a penicillin allergy after 10 years owing to desensitization.¹

Patients with a listed penicillin allergy on their profile are more likely to receive broader-spectrum antibiotics and have a higher risk of readmission.² By implementing penicillin allergy testing within a health-system, health care providers can avoid the use of broad-spectrum antibiotics and remain able to prescribe penicillins when they are the most appropriate choice. Overuse of the broader spectrum antibiotics results in larger healthcare costs, increased antibiotic resistance, and suboptimal antibiotic therapy. Wider spectrum antibiotics, such as fluoroquinolones and vancomycin, are associated with multiple–antibiotic resistant bacteria, such as vancomycin-resistant enterococci. Fluoroquinolones have also recently been shown to be the antibiotics most associated with severe Clostridium difficile infections.³ Patients with penicillin allergies are disproportionately treated with the two aforementioned drugs,⁴ suggesting that allergy testing could ease the use and side effect development of both drugs.

At the Parkland Health and Hospital System in Dallas, a team approach to penicillin allergy screening was initiated. An allergy pharmacist reviewed patient charts flagged by an algorithm to identify patients who need screening for penicillin allergy. The hospital system tested 252 patients with skin tests followed by oral amoxicillin 500 mg. Of the 252 patients, 223 (88.5%) showed no allergy, allowing the penicillin allergy label to be removed from the medical record. In 34% of patients, their therapy was switched from alternative broader spectrum therapies to a penicillin or cephalosporin resulting in reductions in use of vancomycin by 34%, clindamycin by 61%, aztreonam by 68%, carbapenems by 50%, and fluoroquinolones by 36%.⁵

Other studies have also demonstrated low rates of true penicillin allergies among patients with the label in their medical history. Research published in The Journal of Allergy and Clinical Immunology: In Practice showed consistency in the low rate of penicillin allergy. Macy and Ngor tested 505 patients with a history of penicillin allergy and 8 patients (1.6%) were found allergic. Del Real et al tested 596 patients and 49 patients (8.2%) were found to be allergic.⁶ Del Real et al also noted a decrease in the use of vancomycin and fluoroquinolones from 37% to 16 and 36% to 13% respectively.⁷ In another study, Picard et al addressed the economical impact of penicillin allergy. The use of alternatives to the standard of care antibiotic treatment resulted in additional cost of $326.50 per patient.⁸ The low rate of true penicillin allergies indicates the necessity of screening programs in health systems to prevent the unwarranted use of non-standard of care broader spectrum antibiotics, leading to better patient outcomes and reduced costs. Pharmacists are positioned to be leaders on this frontier as they are the drug information specialists and can relay the importance of optimal antibiotic prescribing to physicians. Parkland Health and Hospital system has already demonstrated the impact a pharmacist can have on antibiotic prescribing, and more pharmacists should bring this issue to their respective hospitals and other areas of practice to reduce overall healthcare costs and curtail the advancing problem of antibiotic resistance.

2. Van Dijk, Savannah M. et al The High Impact of Penicillin Allergy Registration in Hospitalized Patients. The Journal of Allergy and Clinical Immunology: In Practice , Volume 4 , Issue 5 , 926 - 931
3. Solensky R. The time for penicillin skin testing is here. Journal of Allergy and Clinical Immunology: In Practice 2013:1:264-5